Rise and fall of Civilizations

Is Europe doomed?

(Aufstieg und Untergang von Zivilisationen)

(Untergang des Abendlandes?)

Systems-ecological Perspectives

(Systemökologische Perspektiven)

2019

Armin H.W. Seydack

(PhD Forestry/Nature Conservation)

Dedicated to

Europe

From the Ural Mountains to the Atlantic, from the Mediterranean Sea to and including the Sub-Arctic

Medical Disclaimer

All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

Declaration

Systems-ecological understanding of causal factors for the **rise and fall of civilizations** were investigated and presented in this book. It represents a synthesis of multidisciplinary and multidimensional **system-ecological insights** in the context of the evolutionary survival of geneto-ethnic entities (focusing on European ethnicities facing the challenges of globalization);

taking ***Biodiversity Conservation*** to a higher level.

This Book is not a political manifesto of any kind. Making any value judgements (positive or negative) in respect of race, religion or gender on the basis of the scientific insights or interpretations presented in this book is considered flawed, inappropriate and unprofessional, and is categorically rejected by the author.

Acknowledgments

The author is indebted to numerous scientists from diverse disciplines; notably those with holistic understanding, paradigm-expanding scientific competence and with multi-dimensional, intuitive-cosmic insights

Armin H. W. Seydack was born in Germany on 27 December 1951. (Father: Formerly eastern Prussian state forester Hellmuth H. O. Seydack; Mother: Mrs Adelheid Seydack, born Hossbach). Together with parents and brother emigration to Africa (Angola, Southwest-Africa/Namibia, South Africa) in 1960. Matriculation in Otjiwarongo, Southwest-Africa/Namibia (1970). Enrolled at the Forestry College Saasveld (George, South Africa) and therewith commencement of service with the South African forestry service (1971). Academic studies in forestry at the University of Stellenbosch (BSc, MSc, PhD). Therewith a career of over four decades began in the service of protection of natural species diversity (*Biodiversity Conservation*). Holistic, multiple use management of natural forests and mountain catchment areas (nature conservation, development of timber yield regulation systems ensuring sustainability and alignment with the requirements of nature conservation, sustainable timber utilization practices, fire management according to ecological principles in fynbos and savanna biomes). Marriage to Stefanie Seydack/Wutsdorff (one daughter). Career-linked visits to Canada, Germany, Malaysia, Sarawak, Kingdom of Bhutan, New Zealand and Australia. Founder and co-ordinator of the IUFRO (International Union of Forest Research Organizations) working group *Forest Dynamics and Yield Regulation Systems for Tropical/Subtropical Moist Forests* (1999-2009). In this context the development of timber yield regulation systems as basis for sustainable and biodiversity-friendly timber extraction from tropical-subtropical forests received priority attention. Furthermore, research was undertaken in respect of forest ecology (mainly in the Knysna forests, South Africa) and savanna ecology (Kruger National Park, South Africa).

Anti-plagiarism Protocol

Sources were referenced in all cases. Included in the book text are also selective summarizing texts of referenced authors which were presented in the format shown below (**Coleman & Rowthorn (2011)**: Reference text in single line spacing. All the contents of such summaries (including any wording, in part) are considered attributable and credited in full to the authors so referenced. Referenced authors of such summary texts appear in the reference list, except those indicated as op. cit. and thus not directly accessed by the author of this book. Inserted comments by the author of this book in summary texts were indicated by AS: bold lettering and in parentheses. Highlighting by AS: in bold/italics. References not followed by op. cit. were also directly accessed by the author (AS) and appear in the reference list of the Book.

Coleman & Rowthorn (2011): The last generations to completely replace themselves in Western Europe were those born in the 1950s (Sobotka 2008). Declining populations are notably represented by Germany and Eastern European countries. Regarding some Eastern European countries, declining of populations was linked to emigration (Haug 2005, op. cit. Coleman & Rowthorn 2011), very low fertility and high levels of mortality (Cawla et al. 2007, op. cit. Coleman & Rowthorn 2011; Vladov 2007, op. cit. Coleman & Rowthorn 2011). (**AS**: **low levels of well-being; anomy. LHS-mode Pm > pM → Pm↑:3**). Subreplacement fertility results in populations becoming older for about two generations, after which a new structure is established at an older, but stable age-distribution; with population sizes tending towards extinction over time. ***Small reductions in fertility have an increasingly large effect on population size*** (highlighting by AS). Perceived negative consequences of lowered population sizes of countries: population ageing, negative effects in respect of economic growth/prosperity, relatively lowered military security, decreasing strategic impact of smaller populations on the international level.

Table of Contents

3 EUROPE UNDER DEMOGRAPHIC INVASION IN THE ERA OF GLOBALIZATION

List of Tables

1. FUNDAMENTALS OF WORLD-HISTORICAL POWER DYNAMICS

1.1 Rise and fall of civilizations

(Ägyptische, Antike (Hellenic-Roman), chinesische und **Abendländische Kultur**)

For Spengler (1923) the demise of the Occident (Abendland) was a predicted outcome (destiny); the author poses it as a question to be investigated as to its system ecological causality.

For Europeans, "Untergang des Abendlandes" as revealed by Spengler (1923), is a topic which raises fundamental questions as to the purpose of life (Sinn des Lebens) in the context evolutionary logic (Sinnhaftigkeit) and pertinently in respect of evolution-competent leadership responsibility. Since the rise and fall of civilizations does not only involve cyclity in cultural expression, but can and often does result in extinction of the genetic-ethnic entites involved, an evolutionary *cul-de-sac* appears to be manifesting.

Spengler: Aufstieg und Verfall von Kulturen und damit auch des Abendlandes, als erkennbare sich replizierende geschichtliche Muster. Kulturen blühen auf die Menschen ihrer Landschaft zu Völkern heranzüchtet, die nicht Schöpfer, sondern Schöpfungen dieser Kulturen sind. According to Spengler (1923), cultures emerge in people of particular landscapes to form entities (Völker) of common destiny; implying that these entities (as biological entities: Völker) are not creators, but creations of associated cultures. This seems congruent with similar interpretations by Toynbee (1946, 1957). Der britische Historiker und Geschichtsphilosoph Arnold Toynbee untersuchte 26 Zivilisationen und folgerte das der Aufstieg solcher einherging mit der erfolgreichen Reaktion von elitären Führungsminderheiten auf grösstenteils umweltbedingte Herausforderungen (Toynbee 1946, 1957). However, from the perspective of natural science, civilizations (cultures) emerge from and are carried by genetically similar ethnicities. The issue to be explored thus is in which way and to what extent is the destiny of the relevant ethnic entities shaped or determined within the evolutionary context (within the reality subject to cosmic law, i.e. kharmic and natural laws).

Der Niedergang in diesen durch Spengler (1923) erkannten geschichtlichen Mustern kann aber ursächlich nur erklärt werden mit Bezug auf eine biologische Grundlage, einschliessend genetischer (Darlington 1959) und epigenetischer Mechanismen (Geist 1978; Kegel 2015; Jablonka & Lamb 2007; Jablonka & Lamb 2014). More re evolution

Three archetypes of wordly power manifestation, as derived from *inter alia* Spengler (1923), are identified: aristocracy, clerictocracy and plutocracy (Table 1.1a). Civilizations rise under the unfoldment of aristocratic rule, are disrupted by interludes clerictocratic imperialism, and fall, with the rise and disintegration of plutocracy subject to progressive disintegration in its advancing later stages (Table 1.1b).

Table 1.1a Fundamental forms of secular power expression (Formenkreise weltlicher Machtausübung)

	Aristokratie	**Kleriktokratie**	**Plutokratie**
Zentralimperativ	**Volksschutz-Elitenschutz**	**Religiöser Imperialismus**	**Geld-Macht Imperialismus**
Wertesystem	**Schutzfunktion genetischer Volks-/Entitäten (Ehre)**	**Absolutistischer, religiöser Imperialismus**	**Multinationaler Imperialismus (Kapitalismus)**
Werterealität	**Volksbezogene bzw. Familienbezogene Schutzpflicht (Pflicht)**	**Missionarismus Religionsdogma Hingabe**	**Profitopportionismus Individualbezogener Liberalismus (Rechte)**
Wertebezug	**Schutzpflicht**	**Frömmigkeit**	**Individualrechte**
Grundideologie	**Territorialintegrität Nationalismus**	**Kosmopolitisch**	**Kosmopolitischer Kapitalismus**
Machterhaltung	**Wehrkraft (militärisch)**	**Massenkontrolle durch Furcht**	**Finanzkontrolle Medienkontrolle**

AS: Systemökologische Kausalitätsanalyse

Table 1.1b Political Epochs of Western Civilization (Europe: Abendländische Kultur) cited from Spengler (1923)

(Egyptian, Hellenic-Roman, Chinese and **Abendländische Kultur** (Western civilization)	
	Western civilization
500-900	PRECULTURAL PERIOD

	Tribes and chieftains. As yet no true states. Frankish period. Charlemagne.
900-1500 1500-1800	CULTURE National groups (Völkergruppen) of distinct style and uniform; world feeling. Nations subject to an imminent state-idea. **I. Early period** Organic articulation of political thinking. Pimary classes: nobility and priesthood. Feudal economics: on purely agrarian values. ***Gothic period*** (900-1500) 1) System of feudal tenure (Lehnswesen). Spirit of the land predominating (rural). 'Towns' primarily market or castle. Changing rulers of vassal territorial holdings. Knightly-religeous ideals. Battles among vasalls and against the sovereign. Roman-German imperial period (Deutsche Kaiserzeit), crusading nobility. Empire (Kaisertum) and Papacy. **(Celibacy: 1079; Selling of indulgences: 1119: Inquisition: 1204)**. 2) Crisis and disintegration of patriarchal forms: from feudalism to aristocratic states. Territorial aristocratic rulers. Renaissance states, Lancaster and York. 1254 Interregnum. II. **Late period** Realization of the matured state-idea. Town (Stadt) versus countryside (Land). Rise of the third class (Bourgeoisie). Victory of money over landed property (goods). ***Baroque period*** (1500-1800). **(Wende des 15. Jahrhunderts mit dem Hervortreten der Ideen der Renaissance, Reformation und Revolution; Aufstieg 1500-1900, dann Absturz)**. 3) Establishment of states of strict form. Fronde. Dynastic family power and Fronde (Richelieu, Wallenstein, Cromwell), about 1630. 4) Highest fulfilment of the state-form (Absolutism). Unity of town (Stadt) and rural country (Land), and state and society. The three classes: nobility, priesthood and bourgeoisie. Ancien Regime, Rococo, Court nobility of Versailles. Cabinet politics. Habsburg and Bourbon. Ludwig XIV, Frederick the Great (Political testament of 1768). 5) Break-up of the state-form: Revolution and Napoleonism. Victory of the city over the country-side (of the 'people' over the privileged, of intelligence over tradition, money over politics). End of XVIIIth century. Revolutions in America and in France (Washington, Fox, Mirabeau, Robespierre). Napoleon.
1800-2000 2000-2200 2200 +	CIVILIZATION The body of the people (Volkskörper), now essentially of urban constitution, dissolves into formless masses. Megalopolis and Province. The fourth class: 'masses' (inorganic and cosmopolitan). 1. Rule of money (of "Democracy"). Economic powers permeating political forms and authority. XIXth century: From Napoleon to World War I. System of Great Powers, standing armies, constitutions. XXth century: Transition of constitutional to formless individual authority, wars of destruction, imperialism. 2. Formation of Caesarism. Victory of force politics over money. Increasingly primitive character of political forms. Inward disintegration of nations into formless populations. Uniting such populations into imperiums of gradually increasing primitive-despotic character (2000-2200). 3. Maturing of the final form: Private and family politics of individual leaders. The world as spoil. (Egyptianism, Mandarinism, Byzantinism). Paralysis and impotence also of the imperial machinery facing younger peoples (Völker) eager for spoil, or foreign conquerers. Progressive emergence of primitive conditions in a highly-civilized mode of living (after 2200).

Spengler (1923) considered the phases of upward development (500-1800 AD) under 'Culture', whereas the phases of decline were reviewed as phases of 'Civilization' (Table 1.1b). (Lohbeck 1966): Die technisch Zivilisation als Dekadenzerscheinung der Kultur).

In the context of the rise and fall of civilizations, and largely in congruence with Spengler (1923: Table 1.1b), the following developmental phases are outlined for the Western civilization (Occident/Abendland): Antiquity (< 500 A.D.), Frankish period (500-900), Gothic Period (900-1500: middle and late Middle Ages), Baroque Period (1500-1800), Civilization 1 (1800-2000): from Aristocracy to Plutocracy, Civilization 2 (2000-2200): dominance and fall of Plutocratic imperialism, and finally, Civilization 3 (2200+): Disintegration.

Antiquity (< 500 A.D.).

Referring to Germanic tribes (*sensu lato*: European tribes; Germanians), before their christianization during the Middle Ages, Geist (1978) describes the situation as follows. The Germanians lived and utilized a predominantly forested landscape with a plant- and animal-based agriculture. Hunting, fishing and the gathering of food items took place in the naural ecosystems. Homesteads were widely dispersed, largely requiring an independent selfsufficiency. Such required independance of families elevated women to socially high role positions (including religious positions; priestesses). The security of each family and their property depended on the standing/esteem of the male members of the family in respect of their fighting ability, but also their social competence (honourable, considerate behaviour) and their ability to form alliances with other families. Males accordingly had to protect their honour. This required competence in the use of a variety of weapons, notably in the use of the sword. To be socially successful, courage, abilities in the use of diverse weapons, in fights and sport were obligatory. Such skills were partly obtained by hunting. To sme extent hunting also served as training for war (planning, strategy, tactics). The importance of hunting was reflected by diverse hunting rituals and its prominent appearance in religion. Physical prowess and social competency were required. Such diverse physical-mental competencies were reflected in the phenotype of the Late Stoneage. Resource abundance was required in order to sustain the ontogenetic development of children with physical, intellectual and social competencies. Such a scenario was underpinned by the Peri-Artic metabolic performance syndrome (Section

2.5.1.1; Table **2.5.1.1a**); as forthcoming under K-selection in the peri-arctic realm. Also of crucial importance were close family ties and a supportive milieu for women (monogamy, allegiance to the family, faithfulness). Gender relationships were characterized by equality and role differentiation (congruent with gender role differentiation and complementarity underpinning of reproductive fitness: Table 2.3.2b). The combination of gender equality and role complementarity was gradually eroded over time with progressive christianization; reaching its dismantling under late plutocratic liberalism. MS germanenzeit

The nobility of this period and the Middle Ages consolidated their claim to lead on the basis of security they provided to their subjects. Protection requirements compelled that increasing numbers of people formed groups and created protective alliances. The aristocracy developed as leadership class in order to guarantee this protective function (core of value system: in honour bound to the protection imperative). As the entities of protection increased in size and complexity, a hierarchical differentiation developed within the aristocracy (proto-aristocratic clan leadership elites, earls, dukes, princes, kings and emperors).

In antiquity and pre-historic times the duties of aristocrats and priests were integrated and in harmony. Only later would this change as aristocracy and clerictocracy represented opposing forces.

Frankish period (500-900).

Tribes and their chiefs. Initially, as yet no true states (Table 1.1b).

Baumard et al. (2015): The term 'Axial Age' was coined by the German philosopher Karl Jaspers to describe the concomitant emergence of a range of doctrines that would eventually lead to the emergence of world religions (Jaspers 1949: 'Vom Ursprung und Ziel der Geschichte'; 1953: The Origin and Goal of History). In hunter-gatherer societies, early chiefdoms and archaic states, religions focused on performing rituals, offering sacrifices and respecting taboos in order to ward off misfortune and ensure prosperity (Bellah 2011, op. cit. Baumard et al. 2015; Boyer 2001, op. cit. Baumard et al. 2015). Between 500 and 300 BC (Axial Age) new doctrines appeared in three places in Eurasia (Axial Age religions/spiritual movements in parenthesis): Ganges valley (Ajivika, Samkhya, Buddhism, Jainism, Hinduism), Yellow/Yangzi Rivers (Taoism, Confucianism) and the eastern part of the Mediterranean (Pythagoreanism, Orphism, Platonism, Stoicism, Epicureanism, Second-Temple Judaism). These doctrines all emphasized the value of personalized transcendence (Morris 2013, op. cit. Baumard et al. 2015), that is, the notion that human existence has a purpose, distinct from material success, that lies in a moral existence and in the control of ones own material desires, through moderation (in food, sex, ambition, etc.), asceticism (fasting, abstinence,

detachment) and compassion (helping, suffering with others). This higher purpose was deemed to reflect in the condition of the universe itself (e.g. through *karma* or *logos*). In the Mediteranean, self-discipline and ascetic doctrines, combined with a moral outlook, appeared in Greek city-states in the late fifth century BC (Johnstone 1994, op. cit. Baumard et al. 2015; Herman 2006, op. cit. Baumard et al. 2015). This spiritual trend grew stronger and spread outside of continental Greece in the fourth century, developing into the Hellenistic movements known as Stoicism, Epicureanism, Skepticism and Cynicism. Although these ideas were still marginal in the fifth century BC, literary works such as Virgil's *Aeneid* and *On Superstitions* by Plutarch had become mainstream among elite Romans by 100 BC (Bernstein 1996, op. cit. Baumard et al. 2015; Segal 2004, op. cit. Baumard et al. 2015).

Baumard et al. (2015) raised the question why these Axial Age movements, giving rise to the major world religions (such as Christianity), emerged simultaneously; and suggested that absolute affluence (a sharp increase in energy capture) coming to bear at the time triggered life history strategy effects involving a shift from fast to slow life history mode expression; increasingly underpinning self-control techiques and cooperative interactions.

Expansion of Christianity in Europe and an ongoing rivalry between aristocracy and the Church for dominance of wordly power.

Frankish period. Charlemagne. MS Merovingian dynasty MS Carolingian empire; DL frankish empire; MS History of Europe;

Toynbee (1946) **The Franks under the Carolingian Dynasty estabished an empire during the later 8th-early 9th century.**

Toynbee (1946) The Papacy had turned its eyes towards this Transalpine Power (the Lombards), and whetted Pepins ambition in 749 by crowning him king and thereby legitimizing his de facto authority, because Austrasia had distinguished herself – Pepins generation by services as a march on two fronts: against the pagan Saxons beyond the Rhine and against the Muslim Arab conquerors of the Iberian Peninsula. In 754 the Austrasians were invited to divert their energies to the destruction of the Lombards who stood in the way of the political ambitions of the Papacy. The War lord Pepin responded to Pope Stephen's call to arms against their brethren the Lombards.

Toynbee (1946) Charlemagne's empire proved a fiasco because it was both grandiose and premature; and the arch instance of its unsoundness was the *tour de force* of Charlemagne's conquest of Saxony. Whenn Charlemagne set out in A.D. 772 to bring Saxony within the fold of Roman Christendom by military conquest, he was making a disastrous breach with the policy of peaceful penetration, conducted by missionaries.

Emergence of win-lose Christian clerictocratic imperialism; reaching its zenith during the Gothic period in the middle and late Middle Ages.

Gothic Period (900-1500).

High and Late Middle Ages

During the <u>High Middle Ages</u>, which began after 1000, the population of Europe increased greatly as technological and agricultural innovations allowed trade to flourish and the Medieval Warm period allowed crop yields to increase. The late Middle Ages was marked by difficulties and calamities including famine, plague and war, which significantly diminished the population of Europe, Black death: 1347-1350 killed about a third of the population of Europe. Controversies within the Catholic Church paralled interstate conflicts, civil strife and peasant revolts that occurred in the kingdoms. Sustained national and factual rivalries throughout

Catholic Christianity by intense partisanship: strong commitment, but no compromise with opponents; characteristic of the Middle Ages: fanatical hatred: 1300-1400+).

<u>Late Middle Ages.</u> The first years of the 14th century were marked by famines, culminating in the Great Famine of 1315-1317.the causes included the slow transition from the Medieval Warm Period to the Little Ice Age. The climate change, which resulted in a declining average annual temperature for Europe during the 14th century, was accompanied by an economic downturn. Black Death 1347. Europe lost about one third of its population. Return of the plague throughout the 14th century +.

Recent estimates of the lethality of the Black Death suggest a toll of of 50 million, or about 60 % of Europe's population (Benedictow 2004). Ex cummins

Aristocratic value system: in honour bound to protection of family (women and children) and tribe, chivalry (Ritterlichkeit; knightly system with its religious, moral and social code: gallantry, courtesy, gracefullnes, courage, discipline, loyality) and professional ethics (e. g. Prussian ethics: sense of duty and justice, diligence, integrity, incorruptibility, reliability).

The primary classes aristocracy and priesthood were the product of high breeding or education and also the expression of a notably personal culture. An idea underlies both of these primary classes, bestowing a strong realization to them of a God-given ranking, demanding self-reverence and self-confidence, but also strictest self-discipline; which under circumstances even requires fulfilment of duty until death. For the nobility, Sitte *in the sense of adherence to aristocratic values and customs, was paramount; for priests* morals (avoidance of sin in a theological sense) *were*

overriding. The basic concept of this ethics (*sensu* Sitte) *is honour. Everything else, faithfulness, humbleness, bravery, chivalry, self-control and resolve are contained therein. Loss of honour is the worst for aristocrats; for priests being without sin is supreme* (cited/translated ex Spengler 1923). *The nobility with its deep connection to the land primarily represents land ownership ('gesteigertes Bauertum'). Out of this type of cosmic connection an associated idea of property* ('*Idee des Eigentums'*) *arose. Property in its original sense is always land property. Families/clans ferociously defended their land ownership* (cited/translated ex Spengler 1923). *The true priest however negates private life, family lineage and home as idea* per se. *The recurrent form of priesthood involves celibacy, the monastry, suppression of sexuality and contempt for motherhood* (cited/translated ex Spengler 1923).

The nobility tended to integrate family politics to the benefit of their lineages with public office duty; that is, they served the purpose of protecting their populations (protection function: Table) within the framework of their family politics. When members of the nobility and priesthood were still *in form* (high vitality status: in win-win mode) they tended to exercise power in an integrated and synergistic manner. Such was still the case in antiquity up into the early Gothic period. *The existence of priests still* in form *resembled that of any farmer, knight or prince. The popes and cardinals in the Gothic period were feudal rulers, military leaders, hunting friends, lovers and pursued family politics* (cited/translated ex Spengler 1923). Given the fundamental differences between aristocratic and clerictocratic life modes, this harmony between aristocracy and priesthood in terms of exercising worldly power was bound to change as the Church pursued dominant wordly power (Clerictocracy), attempting to eclipse the dominance of the Aristocracy.

MS FEUDALISM

In the early Gothic period aristocratic power dominance became more fragmented as battling among feudal vasalls and against their sovereigns (kings) created a power vaccum in terms of an overarching consolidating force (Toynbee 1946). The clerics were no longer in *form* (vide Spengler 1923) and the integrated exercise of religious and wordly leadership was fading out. During the early clerictocratic phase the aristocracy was still spiritually-religiously naïve, allowing the psychological subjugation by the Church where the priesthood had become intensely and aggressively fundamentalist (in Win-lose mode). Kings were subservient to papal power. This

subservience however declined progressively during the 14th century and thereafter. 'The Teutons held their own against the challenge of the Hellenic Civilization but were subsequently worsted by the challenge of Catholicism' (Toynbee 1946). The existing overarching consolidating power vaccum was filled by the assertion of clerictocratic secular leadership dominance in the context of the establishment of a clerictocratic empire. Replacement of the feudal system of relations between classes to a system of relations between sovereign states and their individual citizens (Toynbee 1946). Rise of clerictocracy in the period between feudalism and sovereign aristocratic states (late Gothic period).

(The feudal system first appears in definite form in the Frankish lands in the 9th and 10th century. The powerful surrounded themselves with men who rendered them service, particularly military service in exchange for protection. More and more, this service-and-protection contract came to involve granting of a *beneficium*, the use of land which tended to become hereditary. Local royal officers and great landowners increased their power and forced the king to grant them rights of private justice and immunity from royal interference. By these processes feudalism became fixed in Frankish lands by the end of the 10th century. Feudalism spread from France to Spain, Italy and later Germany and Eastern Europe. In England the Frankish form was imposed by William I (William the Conqueror) after 1066, although most of the elements of feudalism were already present).

Rise and fall of clerictocratic imperialism.

The ascendancy and fall of clerictocracy (dominance of secular power: Table 1.1a) is here now explained and interpreted according to the life history strategy explanatory framework for demographic transitions (2.3.3e; Table 2.3.3n). During the initial phase of increasing resource availability levels and food security, especially applicable to the clergy and court-bound aristiocracy (Table 2.3.3n), the life history strategy mode for optimal resource utilization is the LHS-mode Pm > pM: maximized use of uninterrupted resource affluence (feast), manifesting in extremized LHS-mode Pm > pM expression by **Pm-types**; but progressively at the expense of pM (maintenance) capacity for autophagous self-healing patho-information-engram clearing processes, which require transient conditions of resource deficits, i.e. transient famine (2.1.3; 2.2.1; 2.5.1.4). Pm-type expression is characterized by high performance realization in terms of assertiveness and competitive vigour; underpinning expansionist imperialistic behaviour (2.2.2e); progressively changing from win-win to win-lose exploits. With progressively increasing patho-information engram load accumulation, reduced endogenous energetic efficiency then increasingly results in performance capacity-fast

to low performance capacity-slow LHS trade-off constraints. Progressively slow LHS expression predominates and performance vitality declines, leading to the demise of the imperialistic (clerictocratic) venture.
As derived from the LHS explanatory framework for demographic transitions (), the following phases of clerictocratic imperialism are differentiated: from LHS-mode PM (Axial Age) to LHS mode P > M (triggering and initial phase: c. 700-1000); LHS-mode Pm > pM (1): rising phase (c. 1000-1300); progressing to pM > Pm (2): decline phase (c. 1300-1500). (2.3.3e; Table 2.3.3n)

Ascendancy to clerictocracy (from LHS-mode PM, Axial Age, to LHS mode P > M (triggering and initial phase: c. 700-1000). Initially: *The existence of priests still* in form *resembled that of any farmer, knight or prince. The popes and cardinals in the Gothic period were feudal rulers, military leaders, hunting friends, lovers and pursued family politics* (cited/translated ex Spengler 1923).

Build-up of patho-information-engram loads in individuals transgenerationally subject to urban environments, such as the clergy and court-based aristocracy (affluence and population density stress) led up to emergence of extreme win-lose practices (Sections **2.1.3** and **2.3.2**). The basis for the prevalence of such unbalanced vitality and associated win-lose behaviour for higher ranking clergy and court-based nobility during this era can be traced back to a compromised health vitality due to PIE load accumulations (); as reflected by the prevailing infliction with gout recorded for these leadership groups (Section **2.2.1c**). Hippocrates defined gout as 'arthritis of the rich'. He also recognized that gout depended on social differences as related to better nutrition and living conditions. Gout became known as the disease of 'kings and popes' (De Giorgi et al. 2015). From high vitality competitive performance towards predominance of the low vitality win-lose competitive mode as vitality was compromised by increasing patho-information-engram loading (2.3.2a).

Clerictocratic Imperialism (LHS-mode Pm > pM (1): rising phase: c. 1000-1300).
The period 1073-1517 (high and late Middle Age), is here designated as a phase of Clerictocratic Imperialism; with instilling fear as the central mode of assertion and maintenance of power (Table 1.1a). The priesthood was no longer *in form* (vide Spengler 1923). Win-lose psychology of fanaticism prevailed. Wars conducted as

weapons of religious fanaticism during these periods of Christian religious imperialism were particularly atrocious in comparison with those during the the eighteenth century (Toynbee 1946). During the period 1073-1517 (for approximately four centuries), the papacy freed itself from secular rule and the Roman Catholic Church emerged as the dominant force in European politics and religious life (Arnold 1999).

Clerictocratic exercise of dominant worldly power by the Latin Church under papal authority resulted in *inter alia* crusades (religious imperialistic wars), religious wars against pagans and heretics, the inquisition, the practice of fear-inducing practices in order to keep the people in check (from excommunication to burning to death); and shifting alliances and conflicts with the aristocracy for wordly power and influence. Height of the Papacy was under Pope Gregory VII (Hildebrand). TOYNBEE Selling of indulgences: 1119. Inquisition instituted by Pope Gregory IX (1227-1241) in order to subdue heresy (12th to mid 15th centuries: punishments included death by burning and torture). Ban on marriage of clerics (celibacy 1079). The first crusade, prompted by Pope Urban II, started in 1096 and captured Jerusalem in 1099 (Arnold 1999). The only somewhat successful crusade in that it achieved its objective in freeing Jerusalem from the Seljuk Turks. However, the crusaders were defeated by the Ayyubid army under the command of Salah-Ed-Din at the Battle of Hattin in 1187, whereafter the control over Palestine, including the city of Jerusalem, was wrested from the crusaders. Crusades were generally conducted brutally (pillage and massacre). Numerous religious wars (crusades) continued to take place during this period, notably also targeting pagan people or communities/states within Europe (Arnold 1999). Toynbee (1957): '*Yet these signs of vitality in a tenth-century Western Christendom seem hardly adequate to account for the amazing outburst of Western energy in the eleventh century, an outburst in which an outbreak of aggression against two neighbouring societies was one of the less creative and less admirable episodes*' (Scandinavians, Hungary/Poland).

MS Inquisition

MS Investiture controversy

Waning of clerictocracy (LHS-mode pM > Pm (2): decline phase: c. 1300-1500).

Decline of the papacy (1305-1517): rise of national monarchs and a decline of feudalism, increasing spirit of nationalism and increased loyality of people to their secular rulers (Arnold 1999). Opposition and dissent against the Inquisition. Opposition

to and declining support for crusades. After the events which took place during the Papal schism (1378-1417), the power seated in Rome was substantially diminished. The Church progressively descending into corruption and chaos and immorality, especially towards the 15th century (Arnold 1999). The Renaissance (14th to 17th century) marked the rise of a wealthy middle class and in general a new spirit of independent inquiry, challenging the authority of the Church. The Protestant Reformation then took place in the 16th century (Luther, Calvin, Zwingli).

Hildebrand – Emperor Henry IV
Innocent IV – Frederick II
Popes – Hohenstaufen MS Hohenstaufen
Staat und Kirche sind nie zu einem Ausgleich gekommen und dieser Gegensatz hat sich im Kampf zwischen Kaisertum und Papsttum zu einer besonderen Höhe gesteigert.
Christian Religious Imperialism (yang expansion) Clerictocratic imperialism
Christianisierung: 700-1200-1500. Germanic tribes: Early Middle Ages; Northern tribes by 1200.

Baroque Period (1500-1800)

(Wende des 15. Jahrhunderts mit dem Hervortreten der Ideen der Renaissance, Reformation und Revolution; Aufstieg 1500-1900, dann Absturz).

Vierhaus (1984): 'Allerdings ist die Politik von Fürsten, die absolute Herrschaft in Anspruch zu nehmen, die dynamischte politische Kraft der Zeit gewesen'. Ansätze der Ausübung solcher Gewalt schon vor der Mitte des 17. Jahrhunderts. Monarchischer Absolutismus keineswegs zuende nach 1763. Vierhaus (1984) considers the term Absolutism as era descriptor to cover the time period between the end of the thirty years war and the seven year war (1648-1763 in central Europe, *sensu stricto*).

Thirty Year War (1618-1648): much devastation caused by pillaging, poorly or unpaid mercenary soldiers in the final phase of this war. Pest 1636-1640. Substantial population reductions. Vierhaus (1984) In dieser Situation ist es von grosser und folgenreicher Bedeutung gewesen dass die Landesherren und ihre Regierungen wirtschaftspolitisch aktiv wurden. Es setzte eine Phase des Merkantilismus und Kameralismus ein, einer politischen Praxis, die mit der Förderung der Wirtschaft vor allem die Stärkung der Staatsmacht anstrebte. Das 16. Jahrhundert hatte, aufs Ganze gesehen, steigenden Wohlstand gebracht. Am stärksten ist die merkantilistische-kameralistische Politik in Brandenburg-Preussen zur

Wirkung gekommen wo die wirtschaftliche Entfaltung in den Dienst der staatlichen Machtsteigerung, der Rüstung und der Sozialdisziplinierung gestellt worden waren.

Wilson (2008): Difficulty in separating religious and political motives. Differentiation between overall aims and immediate objectives. The former always included the advancement of faith with the hope that victory would restore the lost Christian unity, either by reforming Europe according to Prostestantism or exterminating heresy and bringing Gods flock back into the Catholic fold. Material advantages loomed larger in more immediate aims in the form of dynastic status, territorial aggrandisement and the neutralisation of threats. Seventeeth century militants could draw upon the legacy of the crusades in their bid to relate events to their beliefs. By shattering universal Catholicism, the Reformation unintentionally promoted state development. Wilson (2008): While related to other European conflicts, the Thirty Years War was primarily a struggle over the political and religious order within the Empire (Holy Roman Empire). It stemmed from a coincidence of tension within the Empire with a political and dynastic crisis within the Habsburg monarchy that undermined confidence in the Emperor's ability to resolve long-standing constitutional problems (Wilson 2008).

Wars conducted as weapons of religious fanaticism during the periods of Christian religious imperialism were particularly atrocious in comparison with those during the the eighteenth century (Toynbee 1946). *The royal players knew quite well the degree of licence that their subjects would allow them, and they kept their activities well within these bounds. Their armies were not recruited by conscription, they did not live off the country they occupied like the armies of the Wars of Religion, nor did they wipe the works of peace out of existence like the armies of the twentieth century. They observed the rules of their military game, set themselves moderate objectives and did not impose crushing terms on their defeated opponents. Royal wars and royal marriages were the two procedures through conveyances of such estates, or parts of them, from one dynasty to another were brought about about, and, of the two methods, the latter was obviously preferred* (cited from Toynbee 1947). Clerictocracy manifesting in win-lose mode in comparison with aristocracy in win-win mode.

With reference to Germany, Vierhaus (1984) emphasized the continued influence of the landed nobility: 'Der ältere norddeutsche Adel war Landadel; auf dem ländlichen

Güterbesitz beruhte die Landstandschaft, die Zugehörigkeit zur Ritterschaft. In der Hierarchie der politischen Ordnung hat der Adel seine Rolle als Herrschaftsstand in vielfältiger Form wahren können. Zwar hat der Absolutismus die überkommenen intermediären Gewalten weitgehend ihrer autonomen Rechte und Funktionen entkleidet; als strukturell soziale und mittelbar politische Ordnungselemente aber hat er sie konserviert'.

(Absolutismus Die absolute Monarchie ist eine Herrschaftsform bei der ein Adliger das Staatsoberhaupt ist, den Staat nach aussen und innen repräsentierent. Im Absolutismus ist folglich eine einzige Person der Träger der Staatsgewalt. Der Absolutismus war zwischen den Ende des *Dreissigjährigen Krieges* (1618-1648) und der *Französichen Revolution* (1789) die verbreiteste Herrschaftsform in Europa Diese Herrschaftsform kristallisierte sich vor allem zwischen dem Übergang vom Mittelalter zur Früher Neuzeit heraus, und ist dann vor allem im Barock und der Aufklärung die bestimmende Form der Herrschaft. Wobei es mitunter schwierig ist die Monarchien im Mittelalter vom folgenden Absolutismus abzugrenzen.)

AS Vitality decline has set in re court nobility increasingly challenged by socialist revolutionaries, collapse of monarchies by 1900. Court nobility (Hofadel) versus landed nobility (Landadel).

Bring in Prussian scenario; vitality of landed nobility (Von Bismarck)

Prussian aristocracy

The descendants of medieval colonists who occupied (Brandenburg, Pomerania and Eastern Prussia) these 'bad lands' have payed an exceptional part in the history of our Western Society. It is not only that in the nineteenth century they mastered Germany and in the twentieth led the Germans in a strenuous attempt to provide our society with its universal state. The Prussian also taught his neighbours how to make sand produce cereals by enriching it with artificial manures; how to raise a whole population to a standard of unprecedented social efficiency by a system of compulsory education and of unprecedented social security by a system of compulsory health and unemployment insurance (cited from Toynbee 1946). Stein, Hardenberg, Humboldt to Bismarck: Prussian professional value system and its mimesis by the population (e. g. Prussian ethics: sense of duty and justice, diligence, integrity, incorruptibility, reliability).

Civilization

Spengler (1923): 'The body of the people (Volkskörper), now essentially of urban constitution, dissolves into formless masses. Megalopolis and Province. The fourth class: 'masses' (anorganic and cosmopolitan)'.

Civilization 1 (1800-2000) From Aristocracy to Plutocracy
Rule of money (of "Democracy"). Economic powers permeating political forms and authority. XIXth century: From Napoleon to World War I. System of Great Powers, standing armies, constitutions. XXth century: Transition of constitutional to formless individual authority, wars of destruction, imperialism (Spengler 1923).

Schon Spengler erkannte dass die Herrschaft des Geldes (Plutokratie) durch Massenbeeinflussung (Meinungsmanipulation und Ausrichtung durch die Medien) und Staatsverschuldung in Demokratien vorprogrammiert ist. Classically functional democracies were of a transient nature, then essentially transforming into plutocracies (pluto-democracies).
Demographically, the Industrial Revolution (1760-1840), taking its course in Western Europe through the harnessing of new energy sources and technological improvements in industrial production, brought rising standards of living and set into motion what is known as the demographic transition (Demeny 2011). In the initial phases of this transition, birth rates remained relatively high and population growth rates were comparatively high (2.3.3: Table 2.3.3n).

In Win-win Imperien vitaler Aristokratien kann es den intaktbelassenen Völkern durchaus zeitweilig besser gehen im imperialen Zusammenschluss als wenn getrennt existierend. Unter Win-lose Imperialismus vitalgeschwächter Elitokratien (spätaristokratischer Formenkreis oder unter kleriktokratischer Dominanz) ist dies eher nicht zu erwarten. Insbesonders im 19. Jahrhundert hat sich die die zunehmende Vitalschwäche des Adels (nobility) bisweilen gezeigt in der Brutalität mit der unterliegende Gegner, unter anderem in den Kolonien, behandelt wurden (win-lose mode). Toynbee (1957): *In the Late Modern Age the English-speaking Protestant West European pioneers of a Western society's overseas expansion had been the worst offenders in committing the Nomad empire-builders' sin of making 'Natives' out of*

human souls; and in this repetition of an old crime the most sinister feature had been the proneness to go over the edge of a further downward step to which the 'Osmanlis never descended, and to clinch their assertion of the Natives' political and economic nullity by stigmatizing them as the spawn of 'inferior races' (Toynbee 1957).

Das Bestreben volkszentrierten Eliten um Sicherheit und Fortschritt ihres Volkes zu gewährleisten kann nicht erfolgreich sein im Win-lose Modus (kompromittierte Evolutionskompetenz). Of relevance here is the central systems-ecological rule/cosmic law is that freedom can only be sustained by those who refrain from denying freedom to others (win-win mode). Das nationalsozialistische Deutschland im Zweiten Weltkrieg führte diesen in Osteuropa im Win-lose Modus. Sie kamen als Sieger (Lebensraum) und nicht als Befreier der dortigen Völkerschaften von kommunistischer Herrschaft in der Sowjetunuion. Der Rest ist Geschichte.

Civilization 2 (2000-2200) Plutocratic imperialism

During this phase plutocratic imperialism continues to aspire towards and basically achieves world domination. This era is thus characterized by continuing fundamental confrontations between win-lose plutocratic imperialism and nationalist self-preservation (conservatism; ethnic survivalism): (Plutocracy versus Aristocracy: protection imperative; Table 1.1).

Spengler (1923): Formation of Caesarism. Victory of force politics over money. Increasingly primitive character of political forms. Inward disintegration of nations into formless populations. Uniting such populations into imperiums of gradually increasing primitive-despotic character (2000-2200).

Governments move farther from the people. Issues have to be settled by force. Long-term objectives are abandoned as people live more for the moment (cited from Pendell 1977). Wie im alten Rom Sichelschmidt. Emergence of populism *sensu* Krastev (2008): opposition to the establishment pursuing liberalistic (AS: plutocratic) aims while ignoring existential concerns (AS: conservative) of the people.

Diese von Spengler (1923) projektierten Szenarien ab 2000 nehmen schon gestalt an (**3. Europa unter demografischer Invasion im Zeitalter der Globalisierung: 3.1, 3.1.3: Demographic colonization of Europe; 3.2**)

Demographic colonizations

State of fertility transition

Start of a long-lasting depopulation of Europe following the demographic transition as predicted by Spengler (1923). *The turning point emerges when the attitudes of a highly civized population requires 'reasons' for children* (cited/translated ex Spengler 1923). As opposed to being a matter of instinct as in original populations with undiminished vitality. *At this stage there is an onset in all civilizations of a phase of depopulation lasting for centuries. The whole pyramid of the highly cultured disappears* (cited/translated ex Spengler 1923).

Resource exploitation by multinational corporations in win-lose mode.

Plutocratic imperialism. Plutocratic control in Pluto-Democracies is furthermore achieved through politics of divide and rule. Ethnic and religious heterogeneity of countries is promoted, and the infiltration of opposing groups then allows win-lose polarisation manipulated to entranch plutocratic control. A typical example would be the induction of right-wing extremists to commit acts of aggression towards Islamic communities. Or by inducing rightwing-conservative parties to operate under an anti-Islam program, distracting from and confusing the real survival and peace-threatening issues concerning migrant invasions; irrespective of religion (3.2). In Plutokratien werden volksverbundene Gruppierungen infiltriert um sie zu Win-lose Verhalten zu verleiten um so kontraproduktive Polarisierungen zwischen diesen Gruppierungen und der Volksmehrheit, volkseigenen Sozialisten oder Religionen (Christentum/Islam) zu veranlassen. Zweckallianzen: In Plutokratien (Kapitalismus) werden auch linke Sturmtruppen (Sozialismus) gebraucht um volkskonservative Gruppierungen zu beeinträchtigen. Trotz grundsätzlicher Feindschaft zwischen Plutokratie und Kleriktokratie, wird opportunistisch von kleriktokratischen Kräften (IS) in bedeckter Weise gebrauch gemacht als Zweckalliierte zur innerstaatlichen Polarisierung (Islam *versus* Christentum) und Bekämpfung von volkskonservativen Gruppierungen und um volksschutzverplichtete Elitokratien zu bekämpfen (regime changes; z. B. im Mittleren Osten: 1.3).

Eine Plutokratie besteht aus drei Schichten: Eine Finanzoberwelt (including the bank sector and multinational corporations), darunter die Regierungsstrukturen des relevanten Landes und zu unterst eine kriminelle Unterwelt. Die Finanzoberwelt ist

dominant. Ein unentschiedenes Machtgleichgewicht zwischen Regierungskräften und der kriminellen Unterwelt besteht fort. In der Geschäftswelt von Plutokratien besteht ein Zustand gegenseitiger Duldung und sogar opportunistischer Zusammenarbeit zwischen der Finanzoberwelt, korrupten Regierungen und der kriminellen Unterwelt (Zunehmende Dominanz des Profitmotivs in verflachten Wertesystemen in allen drei Schichten; value systems predominated by notions of using power to gain money and using money to gain power). The boundaries between the three layers of plutocratic endeavour become progressively indistinct. The fight against crime is characterized by sustained lack of success (against *inter alia* mafia-type syndicates, drug cartels, human trafficking syndicates, refugee smuggling rings). Mit fortschreitendem Verfall und zunehmender Anarchie in spät- und nachplutokratischen Zeiten treten unvorausberechenbare Verschiebungen ein in den Machtverhältnissen zwischen diesen Machtgrupierungen; mit auswuchernder Korruption und Kriminalität. Ein entscheidender Machtvorteil gegenüber kriminellen Gruppen kann nicht in Plutokratien erreicht werden, sondern nur in Staaten mit aristokratischer bzw. volkselitärer Führungspotenz (Wertesystem: Schutzpflicht: Aristocratic value system: in honour bound to the protection imperative; Table 1.1a).

Inward disintegration of nations into formless populations (cited/translated ex Spengler 1923: Table).

Innerhalb von Plutokratien stehen zwei Wertesysteme im Gegensatz: Liberalismus (as capitalist or socialist variants). (Kapitalismus, Sozialismus Variante) und volksverbundener Konservatismus. Furthermore, there is tension between capitalism, a driver of wealth creation, but also of exploitation, and socialism, manifesting in reality as the re-distribution of poverty, especially in countries with low capacities for wealth creation.

Rise to greater prominence of those with liberalistic life modes relative to to those still tending to have some conservative values. Increasing polarisation within populations in alignment with liberalistic *versus* conservative values (conservatives, consciously or subconsciously, tending towards a more rural rather than an urbanised mentality; maintenance of family values); ethnocentrism *versus* cosmopolitan; value systems placing focus on **duty** in respect of group persistence (ethnic survivalism) rather than on **rights** for individual self-realisation; ideological focus on ethnic self-determination/identity politics within a long-term context *versus* focus on human rights

in a short-term context; goup survival instincts present *versus* such instincts weak or being absent). Link to second/secondary demographic transition

Eine Unabhängigkeit von Geldmachtgruppierungen, das heisst, Volkssouveränität kann nur existieren in Ländern mit Führungen mit einem aristokratischen Wertesystem (Schutzfunktion: Aristokratischer Machtausübungsformenkreis; Tabelle 1.1a). However, only intact elites can perform this role; once they have lost intactness (lacking an aristocratic-type value system, emerging corruption and incompetence, repressive win-lose tactics), their claim to lead is no longer accepted by the population and they will be challenged by oppositonal forces with secular or sectarian agendas. Geldmachtgruppierungen haben auch nur beschränkte Einflussmöglichkeiten in aristokratischen und kleriktokratischen Staatsgebilden. Daher die fundamentale Feindschaft zwischen Plutokratie und Aristokratie; sowie zur Kleriktokratie (Tabelle 1.1a). The conflict between forces of Plutocracy versus Aristocracy currently manifests in win-lose conflicts between plutocratic imperialism and forces pursuing conservative-ethnic sovereignity/survival (survivalist nationalism). Zur Zeit: Win-lose plutokratischer Imperialismus vs volkskonservativen Selbsterhaltungsbestrebungen. As a result, ethnic survivalist concerns are suppressed and remain unresolved, resulting in the mainstreaming of existential fears as the colonization of Europe by foreigners progresses; leading to systemsecologically unavoidable inter-ethnic conflict.

During this late phase of plutocracy, entering the phase of disintegration, Toynbee (1946) observed a failure of self-determination. Toynbee (1946): *Growth is the work of creative personalities and creative minorities; they cannot go on moving forward themselves unless they can contrive to carry their fellows with them in their advance. The leader's task is to make his fellows his followers; and the only means by which mankind in the mass can be set in motion towards a goal beyond itself is by enlisting the primitive and universal faculty of mimesis* (imitation). *The condition which is required for the maintenance of growth is a perpetual flexibility and spontaneity, whereas the condition required for effective mimesis, which is itself a prerequisite of growth, is a considerable degree of machine-like automatism. When the leaders cease to lead, their tenure of power becomes an abuse. The rank and file mutiny; the officers seek to restore order by drastic action. It is that 'disintegration' of a broken-down civilization which declares itself in the 'secession of the proletariat' from a band of leaders who have degenerated into a 'dominant minority'. This secession of the led*

from the leaders may be regarded as a loss of harmony between the parts which made up the the whole ensemble of the society. Corresponding loss of self-determination (progress towards self-determination is the criterion for growth).

Increasingly taking effect in this phase, Spengler (1923) predicted the ongoing and long-term depopulation of Europe. Fertility and mortality were high in traditional societies, changing to low fertility and low mortality/higher longevity in modern societies: demographic transitions (Demeny 2011); described in more detail in section **2.3.3**.

DL DT-coleman ref

Link to third demographic transition Coleman (2006) DL DEMOGRAPIC TRANSITION-coleman-third Migrations and its consequences COLEMAN

Demographic colonization of Europe (**3.1.3**).

Civilization 3 (2200+) Disintegration

Maturing of the final form: Private and family politics of individual leaders. The world as spoil. (Egyptionism, Mandarinism, Byzantinism). Paralysis and impotence also of the imperial machinery facing younger peoples (Völker) eager for spoil, or foreign conquerers. Progressive emergence of primitive conditions into a highly-civilized mode of living (after 2200).

The civilization may then be overcome by conquering invaders or sink into a self-created dark age (cited from Pendell 1977). Toynbee (1946): *The cause of the breakdowns (the termination of the period of growth) is not to be found in the loss of command over the human environment as measured by the encroachment of alien human forces upon the life of any society. The most that an alien enemy has achieved has been to give an expiring suicide his coup de grâce. A society does not die from natural causes, but always dies from suicide or murder; nearly always from the former* (cited ex Toynbee 1946).

The breakdown of civilizations can be summed up in three points: a failure of creative power in the minority, an answering withdrawal of mimesis on part of the majority and a consequent loss of social unity in the society as a whole (cited ex Toynbee 1946; also

Toynbee 1957). *We have also described the nature of these breakdowns in non-material terms as a loss of creative power in the souls of creative individuals or minorities, a loss that divests them of their magic power to influence the souls of the uncreative masses. Where there is no creation there is no mimesis. We have seen when in the history of any society, a creative minority degenerates into a dominant minority which attempts to retain by force a position that it has ceased to merit, this change in the character of the ruling element provokes the secession of a proletariat which no longer admires and imitates its rulers and revolts against its servitude* (Toynbee 1946).

Further playing out of confluent global conditions: demographic transitions, global overpopulation, socioeconomic collapse, unprecedented decline of vitality and health.

The Spenglerian phase sequence (Phasenabfolge) of the rise and fall of civilizations progresses from intact aristocracy, through clerictocracy, re-asserion of aristocracy (but progressively losing vitality intactness), plutocracy, followed by disintegration (Table 1.1c).

Table 1.1c The Spenglerian Phase Sequence

Aristokratischer Formenkreis	**Kleriktokratischer Formenkreis**	**Plutokratischer Formenkreis**
Clan Führungseliten		
Clanfürsten (als Proto-Aristokratie)		
Aristokratie		
	Anstreben und Ausübung weltlicher Macht unter religionsfundamentalistischen Vorzeichen	
	Christlicher Religionsimperialismus	
Aristokratie (Monarchien)		
		Plutokratischer Imperialismus (USA mit westeuropäischen Demokratien/Plutokratien)
Spenglers phase sequence: **Aristocracy – Clerictocracy – Aristocracy – Plutocracy – Disintegration**		
Globale Gleichzeitigkeit Global concurrence manifesting in the Middle East		
Monarchien Aristo-Theokratien Volksbezogene Elitokratien Volkszentrierte Eliten Stammesgebundene Eliten Elitäre Autokratien	Islamischer Staat (IS)	Plutokratischer Imperialismus (USA mit westeuropäischen Demokratien/Plutokratien)

The disintegration of civilization unfolds through a series of demographic transitions/transformations (1.2): fertility decline during the first demographic transition (2.3.3e), dysgenic reproductive patterns culminating during the second demographic transformation (2.3.3f) and genetic replacement through demographic colonization by foreigners (3.1.3). Concomittant loss of evolution-competent behaviour and leadership due to diminishing instinct vitality; associated with conduct in an increasingly win-lose mode (loss of win-win vitality).

Win-win vitality. Cosmic causality manifesting through kharmic laws of cause and effect in the four-dimensional world. Diese Interpretation im Rahmen dimensionenübergreifender kharmadynamischer Funktion kann natürlich nicht wissenschaftlich bewiesen werden (?) sondern nur intuitiv erahnt sein. Wissenschaft kann nur zur Anwendung kommen in unserer irdischen vierdimensionalen Welt (drei Raum- und eine Zeitdimension). Kharma dynamics manifests itself during incarnation in our world according to natural laws of cause and effect, identifiable through science. Ursache und Wirkung kann sich aber nur manifestieren wo Raum- und Zeitdimensionen existieren (irdische, vierdimensionelle Welt).

An in-depth understanding of win-win/win-lose dynamics is facilitated by an awareness that reality embraces both cosmic (kharmic cause-and-effect law) and terrestrial dimensions (natural cause-and-effect laws). In the cosmic dimension (spatiotemporal concurrency/ubiquity of information) we exist as information entities, whereas in the four-dimensionsional world (three spatial dimensions and time as the fourth dimension) we exist as incarnate beings; subject to the realization of both kharmic and natural laws. In the context of kharma dynamics (interacting cross-dimensional information effects), spatiotemporally unrestricted information availability applies, *inter alia* in respect of information entities (genetics, epigenetic engrams, including accumulated patho-information-engram loads; and transgenerational kharmic credits and debt) and allied circumstances (aspirations, social class environment, character, personality). The realization of kharma dynamics involves construeing optimised conceptual fates on the basis of ubiquitous information availability, as interacting with other information entities and circumstances; subject to cause-effect constraints and possibilities.

Win-lose Imperialismus plutokratischer und kleriktokratischer Art.

Win-win Imperien vitaler Aristokratien: intaktbelasserner Völker denen es besser geht im imperialen Zusammenschluss als wenn getrennt existierend. Win-lose Imperialismus vitalgeschwächter Elitokratien (spätaristokratischer Formenkreis). Im 18. und 19. Jahrhundert hat sich die Vitalschwäche des Adels (nobility) bisweilen gezeigt in der Brutalität mit der unterliegende Gegner, unter anderem in den Kolonien, behandelt wurden. Es wurden Win-lose Kriege geführt und damit kharmapositive Prinzipien der Kriegsführung *vide* Sun Tzu missachtet (Tabelle 1.1d).

In contrast, for example, Fürst Otto von Bismarck (1815-1898; German chancellor and prime minister): *A statesman must wait until he hears the step of God sounding through events, then leap up and grasp the hem of His garment.* Sun Tzu (): *The good fighters of old first put themselves beyond the possibility of defeat, and then waited for an opportunity of defeating the enemy.* Then proceeding to leave the defeated undestroyed and in dignity, treated in win-win mode according to the take-whole principle (Table 1.1d). During encounters conducted under **the win-win mode** the predominating strategic focus is fighting **for something** rather than fighting **against somebody.**

Table 1.1d Kharma-positive Life Mastery (Warfare)
Kharma: The cosmic law or principle of cause and effect governing the future, involving reward and punishment for the acts performed during succeeding incarnations. Actions that generate a force of energy which returns in kind: Win-win approaches beget Win-win responses. The totality of potential/weaknesses and actions/conduct during successive incarnations, causally influencing his or her destiny.
Sun Tzu (Chinesischer Strategist und Philosoph 544-496 BC). *Invincibility/take whole*; Win-win Strategien; Kharmischer Schutzschirm: Aufbau von Invincibility (Unüberwindlichkeit) der eigenen Position an Stelle von ad hoc Aggression; *Take whole*: Nimm Ganz (Gegner bleibt unzerstört). Kriegsziel nicht die völlige Vernichtung des Gegners sondern eher die Vorbereiting zukünftiger Partnerschaft zum nachhaltigen Frieden und genereller Zusammenarbeit zu beiderseitigem Vorteil. Kharmapositive Win-win Strategie: das Anstreben von Konfliktbeilegung mit unterhandelten Lösungsansätzen beiderseitig akzeptierbar, dass heist mit welchen beide Parteien leben können. Invincibility: **Unüberwindlichkeitspotenz**: Grundlage zum Handeln aus einer Position der Stärke, d.h. kharmapositives Handeln im Win-win Modus. *Invincibility lies in the defence; the possibility of victory in the attack*. *He will win who knows when to fight and when not to fight*. Sun Tzu places *Invincibility* before war; preferring to not have to wage war at all. *The supreme art of war is to subdue the enemy without fighting*.
Kharmadynamik LASZLO
Im Bereich kosmischer Dimensionen (existiert eine raum-zeitliche Gleichzeitigkeit) gibt es keine Realisierung einer Kausalitätsabfolge. Im irdischen Leben (Inkarnation in zeit-räumlichen Dimensionen) wird Kausalität gelebt. Kharmadynamik gestaltet sich in kosmischen Dimensionen in raum-zeitlicher Informationsgleichzeitigkeit und

wird gelebt in der irdischen Dimension (drei räumliche und eine Zeitdimension: die Entwicklung systemökologischer Perspektiven wird angestrebt auf naturgesetzlicher Grundlage mit Gültigkeit in dieser vierdimensionalen Welt).
Universal consciousness: the infinite mind within which the entire universe is conscious. Every action and thought of every individual makes an impression on the Universal Consciousness. Equated with the Hindu concept of an Akashic Record. All forces and activities are manifestations in relation to the first cause (God). The law of cause and effect in material things.

1.2 Loss of evolution-competent behaviour

Toynbee (1946, 1957) vs Knaul (1985) who attributes cultural decline to the degeneration of elites and their reduced fertility under conditions of population density stress.

Pendell (1977) Dysgenetisches Reproduktionsverhalten. Civilizations fall because the less capable part of the population outbreeds the more capable. As intelligence rises, the fixed processes of instinct dissolve. Intelligence is the ability to solve problems. Civilization is an accumulation of improvements. Gradually a weakening of average intellectual capacity sets in. Cooperative living becomes highly developed. The strong create living patterns/conditions that protect themselves, but also protect the weak and uncooperative. Service to others, and especially to the helpless, is recognized as the primary moral imperative. Then adverse birth rate differences take effect. The less intelligent multiply more rapidly than the more intelligent. Evolution goes into reverse. Gradually a weakening of of average intellectual ability sets in (wisdom no longer available). Judgements become more ill-advised. Governments move farther from the people. Issues have to be settled by force. Long-term objectives are abandoned as people live more for the moment. The civilization may then be overcome by conquering invaders or sink into a self-created dark age.

Knaul (1985) also interpretes the fall of civilizations as resulting from the disproportionate increase of the less competent part of the population relative to the more competent due to more favourable conditions created by the the latter. At some point of such dysgenic reproductive patterns, leadership and other functional capacities diminish while at the same time the population is progressively replaced by foreigners and the civilization collapses. This interpretation is also congruent with Spengler (1923) for the period > 2200 (Table **1.1c**); although no reference is made by to any possible biological causes, as Pendell (1977) and Knaul (1985) have attempted.

Population density effects, as comprehensively studied and observed (Table 1.2a), also apply to human demographic population dynamics, as recognized by Knaul (1985).

Table 1.2a Synopsis of population density stress symptoms

Abridged summary according to Knaul (1985): based on animal experimental studies and observations in the wild

1. Changes in social behaviour

a) Disintegration of hierarchy and therewith the collapse of a necessary basic order for coexistence within a society. No property rights, no permanent sexual partners and no orderly rearing of offspring.
b) Freedom of movement is restricted; with a tendency to flee from crowded conditions.
c) Individuals of a particular group suffer from nervous irritation and aggression against conspecifics.

2. Health disorders and and autonomic dysfunction

a) Hypertension and arteriosclerosis (*inter alia*).
b) Stomach- and intestinal ulcers; ovarian and diseases of the uterus.
c) Hormonal disturbances (regression of sexual glands and enlargement of the adrenal gland: aggression hormones).
d) Depression and chronic fear.
e) State of nervous exhaustion.

3. Phenomena curbing population size increases

a) Gender differences in sexual behaviour and phenotypes declining.
b) Decreased sexuality (impotenz; infertility).
c) Generally rejecting behaviour towards offspring. Neglect of progeny.
d) Declining birth rates; increasing incidence of miscarriages, pre-term births and births of deformed babies.

Social transformation associated with high population density stress of late-stage civilizations was characterized by Knaul 1985 (also Sichelschmidt 1973: *Wie im alten Rom*). Weakening of social hierarchical order. Hierarchical order is now longer accepted and the mindset becomes progressively more anti-elitist. Everybody is considered equal and individuals with special competencies, skills or moral standing no longer receive due respect. Gender differences in roles and behaviour are reduced (reduced secretion of sex-specific hormones results in a reduction of gender-specific appearance and behaviour, reduced offspring being born and finally a complete disregard for having children at all). Family aspirations and the rearing of children are no longer of high priority. Increasing aggression levels within society. Social disorders (as mentioned) and declining reproductive success are particularly prominent in higher

social classes. Many diseases of zivilisation, especially psychological disorders, are more prevalent in urban environments, as would be expected from intensified population density effects prevailing under urbanized conditions; as paralleled in animal studies observed under conditions of space deficit (Table 1.2a: Knaul 1985).
Diseases of civilization develop over longer time spans, even over generations and manifest earlier in the lives of individuals from generation to generation. Engrammatically pre-programmed already in parents and grandparents subject to population density stress, notably in urban centers (Knaul (1985).

Chronic exposure to stress results in chronic engagement of the fight-flight mechanism (Selye 1953, 1978). The associated effects, linked to chronic overreaction of the sympathetic nervous system, induce the increased secretion of stress hormones (cortisol, epinephrine). Complex interactions between between the nervous and endocrine systems then manifest in the stress adaptation response (Selye 1953, 1978). The hypothalamus responds to stress by releasing the cortico-tropin-releasing factor (CRF), in turn signalling the pituitary gland to release adrenocorticotropic hormone (ACTH). This hormone stimulates the adrenal glands to release cortisol. Rising levels of stress hormones then set in motion mechanisms of feedback control, eventually leading to the cessation of CRF production by the hypothalamus. For cortisol to fulfil its health-maintaining role, levels must be maintained within fairly narrow ranges. When below optimal signs and symptoms of adrenal fatigue will manifest and if above-optimal levels persist disturbances of metabolic syndrome will ensue (Wilson 2014). Following Knaul (1985), the enlargement of adrenal glands and associated increased corticosterone secretion due to persistent chronic stress is implicated to result in early sexual maturity and equalizing orientation of male and female phenotypes (physical and psychological mascularization of females and feminization of males), *inter alia* resulting in declining reproductive output (and other dysfunctionalities as listed in Table **1.2a**).
The disappearance of elites is attributed to these being more vulnerable to population density stress. AS: functionality/performance based on enhanced sympathetic nervous system functionality. Good thyroid glandular functionality supports high metabolic performance and behavioural competence (wakefulness, diligence, enterprising, resourcefulness, imaginative, positive). When subject to population density stress, requiring constant defence of positioning in respect to others, thyroid functionality is

over-activated, resulting in a state of permanent sympathetic overarousal (restlessness, irritability, anxiety, loss of libido, impotence, menstrual disorders). Adaptation to such impacts may then result in hypothyroidism, with its own pathological consequences (from hyper- to hypothyroidism).

Talents, skills, competencies, value systems and aptitudes gained through the course of life (engrams: adaptations to changing circumstances) are transmitted to following generations; but if not re-inforced, are lost again over time (generations), as talents no longer used/gefordert are lost over generations (Knaul 1985). This is consistent with the notion of transgenerational carry-over of phenotypic memory (Jablonka et al. (1995; Jablonka & Lamb 2014). Controversy over whether learning represents the recognition of engram information or is based on new experiences. Knaul (1985) contends that it is probably both. Jablonka & Lamb 2007; 2014.

Greek and Roman civilizations collapsed when those families which traditionally provided the leaders had fewer and fewer children and those with lower cognitive abilities and ethics (including former slaves and workers from foreign countries) replaced them in holding leadership positions. The engram memory contains subconscious adaptive information (Adaptionsengramme) as accumulated over generations (traces of observations, emotions, experiences, experience, skills, insights, talents, customs and traditions; value systems); as well as the genetic blueprint. (AS: Unresolved pathological traumata are similarly added to the engram memory as part of an adaptation process to cope with anticipated environmental conditions). Hormonal activation under acute stress (alarm phase *vide* Selye), supporting survival under acute challenges, transforms into a persisting state of of sympathetic nervous system arousal under population density stress. Associated hormonal overactivation and dysregulation then results in decreased gender differentiation, sterility, loss of rearing instinct, aggression and disease; ultimately leading to population density reduction (seen as an adaptive population-reducing mechanism). Knaul (1985) also refers to the derailment of the biochemical equilibrium of one or more neurotransmitters under prolonged population density stress. Associated states of depression and aggression result in a psychosomatic syndrome manifesting in psychological (sadness, fear, apathy, mental decline), somatic and organ-linked nervous and functional disorders. Depression can be grouped into those with serotonin deficiencies and those with noradrenalin insufficiencies. The sister of depression is aggression; the former associated with noradrenalin insufficiency and the latter with noradrenaline surplus. Adaptation to

persistence of aggressive behaviour has prolonged consequences and is transmitted across generations, resulting in progressively increasing aggressivity levels from generation to generation (Knaul 1985).

According to Knaul (1985), more competently performing people are more vulnerable to these population-reducing stress impacts (Sections 2.2.2j/j). Implying that the less competent are better adapted to high population stress, at least transiently and therefore sustaining their fertility disproportionately relative to the more competent; eventually leading to functional disintegration and collapse of the so affected civilizations. Invoking that population stress = dysfunctionalities = fertility decline = dysgenic population regulation. Collapse because of dysgenic nature of population regulation (Knaul 1985). Space deficit symptoms first become apparent in the talented and intelligent (The fish starts to rot from the top). According to this interpretation we have a phase sequence of selection for competence, rising population densities as a consequence, counterselection of competence in the context of a population regulation mechanisms and collapse/disintegration of civilization; frequently involving the genetic extinction (invasion, annihilation, assimilation) of the population entity which originally created the civilization.

The mechanism for the fall of civilizations proposed by Knaul (1985) focused on dysgenic reproductive patterns as a result of high population density stress effects; i.e. civilization must inevidably end up in the extinction of those more competent positively selected for during pre-late civilization phases. This represents an evolutionary *cul-de-sac*. From an evolutionary perspective this appears inconsistent. The explanatory framework for the rise and fall of civilizations as presented by Knaul (1985) is therefore considered systems-ecologically incomplete in terms of ultimate causality for the fall of civilizations.

Animal population densities are generally controlled by the availability of food resources (). Prolonged spatiotemporal cicumstances of high population densities of animals in the wild are accordingly the exception. For human populations, in the context of creating civilizations, conditions of high population densities are reached and prolonged; with the consequences of high population density stress taking effect. Unlike in the case of animals, which are usually subject to alternating feast-famine conditions of food supply, in high density human populations adequate/excess food supply is generally sustained. This is even more applicable for higher social classes; uninterrupted affluence being secured earlier in the generational sequence (**2.2.2j**).

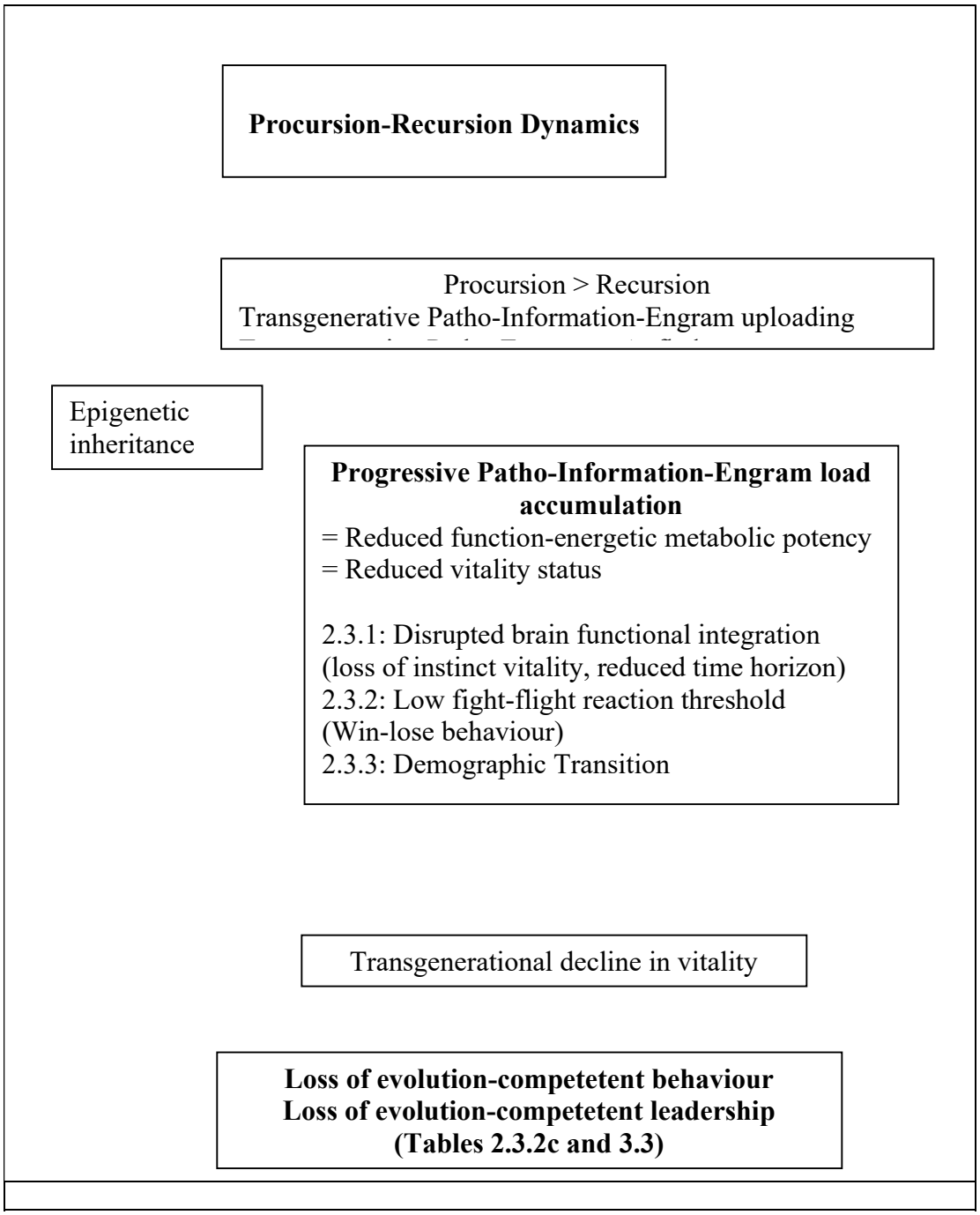
Susceptibility to degenerative diseases increases concurrently with rising living standards (levels of affluence). Independently from environmental and dietary factors, caloric intake alone (as reflected in body size) apparently accounts for much of the differential risks in this context for inter-population differences in humans (Frame et al. 1998). Research results suggest that caloric intake acts as primary effector for many hormonal, metabolic, physiologic and behavioural responses coordinating reproductive strategy with prevailing food availability (Frame et al. 1998). Caloric intake under conditions of resource abundance, physiologic priorities are set for body growth and fecundity (P: production) rather than survival capacities (S: healing processes, longevity); the converse occurring during periods of famine (improved functional profile for the handling of stress). Feast-famine; P *versus* S trade-off relationships. After taking other influential factors, such as genetics, into consideration, dietary caloric consumption remains one of the most important risk factor for a spectrum of human degenerative diseases and studies have established that increased body weight or body mass index (BMI) is positively correlated with a number of morbidity/mortality indices (Frame et al. 1998). (2.5.1.4: Feast-famine dynamics at multiple temporal scales).

Statistiken die eine negative Korrelation andeuten zwischen Begabungskompetenzen (unterschiedlicher Art: schulische/akademische Ausbildung; Ausbildungsgrad; verschiedene Wohlstandsanzeiger) und Kinderzahl stehen weitläufig zur Verfügung für derzeitige europäische (Schade 1974; Knaul 1985) und nordamerikanische Kaukasier. Mit diesen Negativkorrelationen sind deren Ursächlichkeit hingegen noch nicht erfasst. Dysgenetische Reproduktionsmuster sind bereits symptomatisch für ein Versiegen evolutionskompetenten Verhaltens. Nobelpreisträger Bertrand Russell sprach 1957 vom Aussterben der besten Erbstämme der abendländischen Völker. Progressive Abnahme der Kinderzahl über Folgegenerationen, vor allem in begabten, erfolgreichen Familien in Europa. Progressively increasing affluence in earlier generations of aristocrats/successful families. Thus earlier generational onset of negative impacts due to the inefficiency of dealing with procursive impacts (Accumulating patho-information-engramme load Table ; e.g. absence of intermittent fasting and urbanization: population density stress).

Eskalierende Patho-Information-Engramm-Anhäufung über Generationen. Personen in höheren, wohlhabenderen Gesellschaftsschichten (mit Kompetenz in diversen Lebensbereichen) sind schon früher in ihrer Generationsfolge an Prokursionsstress unterworfen gewesen (Landentfremdung, Wohlstandsüberfluss/affluence, Verstädterungsfolgen, Dichtestress). Progressive Abnahme der Kinderzahl über Folgegenerationen, vor allem in begabten, erfolgreichen Familien in Europa. (Alexis Carrel). In die Stadt einwandernde Familien im Durchschnitt nach der dritten Generation ausgestorben (). Derzeit ist das städtische Bürgertum mehr Patho-Information-Engrammverschlackt als Teile der auf dem Lande lebende Bauern.
GAVRILOV

Causality of the rise and fall of civilizations is thus identified as the disruption or dysfunctionalization of feast/famine metabolic performance dynamics (and associated health maintenance: 2.5.1.4) during the lifespan of individiuals when sustained transgenerationally; resulting in the accumulation of patho-information-engrams within the biocybernetic system of the body (2.1.2); leading to loss of health and vitality of survival instincts (Table 1.2b; Section 2).
The disintegration of civilization thus unfolds through a series of demographic transitions/transformations (2.3.3): fertility decline during the first demographic transition (2.3.3e), dysgenic reproductive patterns culminating during the second demographic transformation (2.3.3f) and genetic replacement through demographic colonization by foreigners (3.1.3); concurrently manifesting in the loss of evolution-competence (Table 1.2b).

Table 1.2b Declining Evolution-competence in Behaviour and Leadership (Loss of vitality)
Epigenetic inheritance of cumulative Patho-Information-Engram-load accumulation (Procursion-Recursion dynamics), Transgenerative Patho-Information-Engram loading ≈ reduced function-energetic potency = declining vitality status. 2.3.1: Disrupted brain functional integration (loss of instinct vitality, reduced time horizon; lack of long-term thinking); 2.3.2: Low fight-flight reaction threshold (Win-lose behaviour) and 2.3.3: Fertility decline. As Patho-Information-Engram accumulation predominates (Procursion) relative to recursive pathogram deletion of these in the biocybernetic system of the body, progressive Patho-Information-Engram accumulation occurs (Procursion: Sections 2.1.2a; 2.1.3).



Proto-Aristokratie (Clanfürsten), Aristokratie (intakt und landgebunden) → Kleriktokratie → Aristokratie (intakt und landgebunden) → (progressiv vitalgeschwächte) Spät-Aristokratie → Plutokratie → Anarchie.

(Spengler-Abfolge): progressives Vitalversiegen im Win-lose Modus

1.3 Contemporary Win-lose imperialism in the Middle East (2014-2019)

In diesem Jahrhundert (2001-2100) finden entscheidende Auseinandersetzungen statt mit schicksalhafter Bedeutung für die Völker des Mittleren Osten und Europa. (Spengler-Abfolge: 2001-2200: Table). Ethnozentrische Elitokratien führen einen existentiellen Abwehrkampf gegen Mächte des plutokratischen und des kleriktokratischen (IS) Imperialismus. Des weiteren befinden sich die letzteren zwei Imperialismen ebenfalls in fundamentalistischer Auseinandersetzung (beide im Win-lose Modus).

Table 1.3a Fundamental forms of rulership in the Middle East (2015-2018)

		Aristokratischer Formenkreis	**Kleriktokratischer Formenkreis**	**Plutokratischer Formenkreis**
		1 Monarchien 2 Volksbezogene Elitokratien 3 Stammesgebundene Eliten 4 Elitäre Autokratien 5 Volkszentrierte, teils theokratische Eliten	Sunni clerictocratic imperialism: Islamischer Staat (IS)	Plutokratisches Imperium (USA mit westeuropäischen Demokratien = Plutokratien, Türkei)
Machtschwerpunkte/Machtzentren	1	Saudi-Arabien mit allierten Golfstaaten [1] Ägypten (Sisi) [4] Pakistan [4]	Sunni clerictocratic imperialism	Zweckallianz mit Plutokratien
	2	Iran mit allierten Shia-Milizen [5] Stammesgebundene Eliten [3] Syrien [4] (Assad Dynastie) Kurdische Volksgruppen [3] Houthis/Saleh (Jemen) [3]	(Shia)*	
	3	Israel [5]	(Judaismus)*	Israel (eingebettet im Plutokratischen Imperialismus)
			* Keine Kleriktokratien, aber Win-lose konflikt-verschärfend	
		Partly/variably win-lose	Win-lose	Win-lose

Mächte verbunden mit einem von allen drei Machtausübungsformenkreisen liegen gegenwärtig (2014-2019) im kriegsartigen Wettstreit (Tabelle 1.3a). Plutokratie (Formenkreis 3) versus Aristokratie (Formenkreis 1: Volksbezogene Elitokratien, Stammesgebundene Eliten, Elitäre Autokratien, Volkszentrierte, teils theokratische

Eliten) und Kleriktokratie (Formenkreis 2: IS); sowie Aristokratie (Formenkreis 1: Gruppe 2) versus Kleriktokratie (Formenkreis 2: IS) und Plutokratie (Formenkreis 3).
Win-lose Imperialismus vitalgeschwächter Elitokratien (spätaristokratischer Formenkreis 1). Wenn gleichgeschaltet mit religiösem Imperialismus (z. B. Shia versus Sunni) geht das einher mit einer Verschärfung des Win-lose Verhaltensmodus.
Saudi-Arabien (Monarchie) und Israel (eingebettet im Win-lose plutokratischen Imperialismus versus Volkszentrierte Eliten) befinden sich im Ineressenkonflikt zwischen Dynastieschutz, bzw. Volkserhaltungsbestrebungen und Zweckallianzen mit dem Win-lose plutokratischen Imperialismus (USA).

The resolution of the Israel-Palestine conflict is a pivotal issue in overcoming the prevalence of win-lose imperialistic proxy-wars in the region. Die Handhabung der längerfristigen genetischen Identität des Jüdischen Volkes ist bedroht durch kosmopolitische Dominanz und progressivem Vitalitätsverlust (Versiegen evolutionskompetenten Verhaltens; genauso wie für die europäischen Völker) in typischerweise kosmopolitischen Plutokratien (schleichende Vermischungstendenzen gefördert durch Zivilisatose). Theodor Herzl erkannte dies und zweifelte an der Möglichkeit einer jüdischen Volkserhaltung unter den modernen Weltverhältnissen (und internationaler Volkszerstreuung) und strebte eine landgebundene, bäuerliche Regeneration des Judentums an (Sanden 1971) und proklamierte als Ziel des Zionismus '*die völkerrechtlich gesicherte Souveränität auf einem für unsere gerechten Bedürfnisse ausreichenden Landstrich'* (op. cit. Sanden 1971). Die Gründung des Staates Israel erfolgte im Jahre 1948. Israeli prime minister Yitzhak Rabin embraced the Iraeli-Palestinan peace process, also in the context of the Oslo Accords (Israel-Palestinia two state solution). After his assassination in 1995, the government of Israel pursued the expansion and safe-guarding of Israel in an increasingly win-lose mode. According to kharmic law the persistent pursuit of objectives in win-lose mode is ultimately suicidal. The pursuit of long-term survival and safety of Israel would therefore be better served by following the rules of *Art of War* (Sun Tzu), that is, in Win-win mode. This would require Win-win regional alliances rather than reliance on the United States of America for protection.
Win-lose or win-win strategies for the long-term survival of Israel ? In this context a two-state solution is being championed (independent states of Israel and Palestine existing side by side). A one-state solution where Jews, Palestinians and other

minorities would exist in a democratic state in a country embracing both Israel and Palestine land would seem the only realistic alternative to the two-state solution. However, as the leadership of Israel is well aware, an ethnically heterogenous state represents a demographic time bomb, and could therefore not serve the interests of the long-term safety and survival of Israel as a country for Jews. In the mean time, the two-state solution is being compromised by continuing Israeli settlements on Palestinian land and far-reaching claims for security-based dominance of Israel over the to be created Palestinian state, hardly leaving much sovereignity for the latter. The viability of the two-state solution is progressively eroded away by continued Israeli settlements on Palestine land. Win-lose strategies seem to have ended in a *cul-de-sac*.

As a rule, the long-term survival of ethnic states cannot be achieved through reliance on protection by extra-regional powers. The long-term threat to all three of the main regional power nodes (Israel, Iran, Saudi-Arabia) emanates from IS clerictocratic imperialism rising to regional dominance. Whilst embedded within plutocratic imperialism of the United States of America (Table), Israel is confronted with a conflict of interest: reliance on protection by the USA, following a win-lose strategy against its regional opponents; as against win-win alliances with regionally effective anti-IS forces (tripartite alliance between Israel, Iran and associated Shia/Kurdish forces, Saudi-Arabia and associated Golf states; Table).

Given the anticipated disintegration of Plutocracy according to the Spengler sequence () and ongoing demographic shifts within the USA, protection of Israel cannot be taken for granted to last into the long-term future. Demografische Verschiebungen zwischen den drei verschiedenen Populationssegmenten in der USA, Weiss-Amerikaner, Afro-Amerikaner und Latino-Amerikaner (Hispanic Americans), laufen an. Längerfristig wird das dazu führen dass die Weiss-Amerikaner in vielen Teilen der USA ihre Machtdominanz verlieren werden. However, as a general systems-ecological rule, peaceful coexistence can only be achieved and sustained under conditions where divergent group entities do not feel threatened by one another. Aus systemökologischer Perspektive würde das einen Zustand soziopolitischer und sozioökonomischer Unstabilität darstellen. Wohlfahrtshandhabung/Schutz und ausreichender Personenschutz wäre damit für Weiss-Amerikaner nicht mehr gegeben (Vom *melting pot* in die *melt-down* Phase. A *melting pot* can only have one of two outcomes: progression into the *smelt-down* phase = chronic geno-suicide or progression towards

the *melt-down* phase = escalating inter-ethnic conflict). Segretative Fragmentation der USA, sodass Besitz und Machtmonopol der Staatsführung wieder raum-gruppenkonform konsolidiert wird (Territorialität), ist folglich systemökologisch zu erwarten. Aus einer systemökologischen Perspektive würde dies erwartungsmässig hinauslaufen auf eine Re-Territorialisierung der Weiss-Amerikaner in nördlichen Bereichen der heutigen USA (Latino-Amerikaner im Südwesten/Afro-Amerikaner im Südosten). Die zur Zeit noch gegebene Schutzfunkion für Israel durch den Westen würde damit längerfristig wegfallen.
The long-term security and survival of ethnic states can only be achieved through win-win strategies (refer also to Sun Tzu *The Art of War*). Persistently pursuing win-lose victories invidently results in suffering defeat in the long-term (kharmic backlash). As the real long-term threat to Israel, Iran and Saudi-Arabian/Golf state monarchies resides in IS clerictocratic imperialism, win-win strategies would dictate a tripartite alliance between the former three. The Iran-Shia axis, together with other ethnocentric forces (the Kurdish people) have proven to be most effective in counteracting IS forces. The leadership of Iran has shown some capacity for win-win strategies (nuclear deal with USA, UK, Russia, France, China and Germany). The leadership of Iran is aware that nuclear weapons really serve no purpose for them (using such against Israel would be suicidal and using them against IS, their real enemy, would be counterproductive). For the leadership of Israel to cling on to the perception that Iran is continuing towards nuclear military capacity in order to destroy Israel, is disingenuous. In any event achieving win-win solutions would require considerable win-win capacities in the leadership of all three parties concerned (Gandhi: The weak can never forgive. Forgiveness is the attribute of the strong).

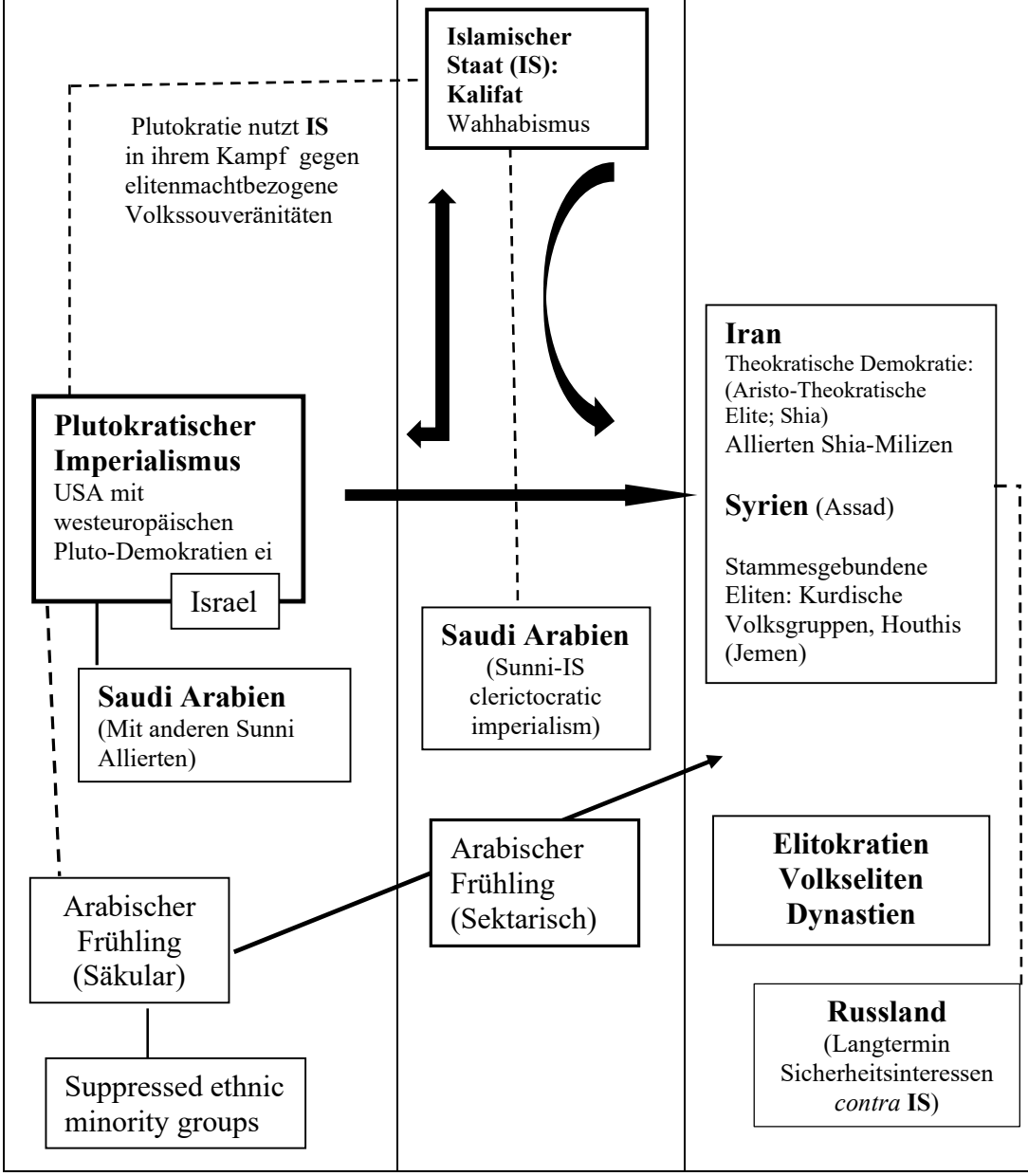
Mit einem Verharren im Win-lose Modus der stärkeren Kontrahenten (lacking the capacity for win-win statemanship) gelang es nicht, selbst über einen längeren Zeitraum (Jahrzehnte), Lösungen zu finden für eine friedliche Koexistenz und sinnvolle Allianz gegen IS: Türkei gegen die Kurden, Israel gegen die Palestinenser und Saudi-Arabien gegen die Houthis in Jemen. Win-lose conflict between Saudi-Arabia and and Iran; and Israel and Iran. Eine Win-win Lösung für die Kurden durch die Etablierung regionaler Autonomie oder eines Volksstaates für die Kurden (Kurdistan) könnte einen wesentlichen Beitrag darstellen für eine regionale Stabilität und der längerfristigen Eindämmung von IS. Die syrische Regierung (Assad Dynastie

und Teile der syrischen Bevölkerung die eine post-Assad IS-type dominance befürchtete) verteidigte sich gegen die Versuche des plutokratischen Imperialismus (regime change agenda) diese zu vernichten (Table 1.3b).

Die syrische Regierung konfrontierte oppositionelle Kräfte in der Bevölkerung im Win-lose Modus welches dann eine offene Rebellion geradezu heraufbeschwor. Es muss aber auch in Betracht gezogen werden dass sektarische Kräfte (z. B. *El Nusra*) die Machtdominanz hatten in der rebellierenden syrischen Opposition. Damit war die Erhaltung ihrer Macht für die syrische Regierung eine Existenzfrage. However, in the attempt to retain power the Syrian governmemt resorted to win-lose suppressive strategies against oppositional forces which counterproductively resulted in a stronger alliance between sectarian and secular elements (such as ethnic minorities) of the rebellion. Obwohl propagandistisch auf die Person Assad eingeschossen, wird vergessen dass die Regierung Syriens Teile der syrischen Bevölkerung vertritt welche besorgt waren über ein Nach-Assad Machtvakuum und damit eine einhergehende Dominanz von IS. More or less clandestinely supported by Western plutocratic imperialism (Table 1.3b), the Syrian opposition challenged the Syrian government following a Syria-lose endgame: that is, either a state of IS-type dominance or Syria as a United States of America protectorate against IS (since IS-type forces usually dominated in Arabian Spring-type rebel groups). Either outcome would be associated with continuing conflict and suffering of the people of Syria. Als grosse Teile der Bevölkerung Syriens die militärische Dominanz ihrer Regierung im Niedergang erkannte und aus Europa (Deutschland) Einladungssignale für die Aufnahme von Kriegsflüchtlingen abgegeben wurden, begann der Flüchtlingsstrom aus Syrien nach Europa anzuschwellen. Eine damit einhergehende, planmässige Einschleusung von potentiellen IS Kämpfern nach Europa konnte nicht ausgeschlossen werden.

Saudiarabien (Crooke 2014). ISRAEL

Table 1.3b Imperialisms in conflict (Middle East: 2015-2019)		
Plutokratischer Imperialismus	**Kleriktokratischer Imperialismus**	**Spät-Aristokratischer Formenkreis: Ethnozentrische Eliten Elitenmachtbezogene Dynastien/ Autokratien**
		Auch Arabische Monarchien und Israel
Plutokratisches Imperium (USA mit westeuropäischen Pluto-Demokratischen Vasallen) Rebellierende unter dem Arabischen Frühling	Islamischer Staat (IS): Wahabismus	Iran (Theokratische Demokratie) mit allierten Shia-Milizen Stammesgebundene Eliten Syrien (Assad Dynastie) Kurdische Volksgruppen Houthis (Jemen)



REGIME CHANGE DYNAMICS Coalition between Sunni clerictocratic imperialism championed by Saudi Arabia and US-led plutocratic imperialism

Plutokratische Imperialisten, im Zuge ihrer Win-lose Vernichtingsstrategien gegen elitär-autokratische Machtzentren (Tabelle : Gruppe 2), hinterlassen Machtvakuen zum Vorteil von IS. Damit verfallen die betroffenen Länder in (Protektions-) Abhängigkeit von Mächten des plutokratischen Imperialismus (Zugang zu Öl und Absatz für die Waffenindustrie). Wenn die dominante Shia Machtgruppe (Aristokratischer Formenkreis: Machtgruppe 2; Tabelle 2) die Überhand in Syrien verliert wird das entstandene Machtvakuum durch IS eingenommen werden. Die Russen verstehen das. Amerika als Führungsmacht des plutokratischen Imperialismus will hingegen erst von der IS Gebrauch machen um ihre Gegner aus dem Aristokratischen Formenkreis zu vernichten. Perpetuation of conflict and suffering in the Near/Middle East.

Bei sich ausbreitender regionaler Dominanz von IS (Kleriktokratie) sind die Volkssicherheitsbestrebungen (Aristokratischer Formenkreis) der arabischen Monarchien (Saudiarabien), volksbezogener Elitokratien (Iran, Kurden, stammesverbundene Shia Milizen) und volkszentrierter Eliten (Israel) langfristig gleichermassen äusserst gefährdet. The Saudi monarchy does not appear to be concerned about the expansion of IS in the region. This is at odds with the fundamental conflict between aristocratic and clerictocratic power expression.

Verlängerung des Syrienkrieges durch Win-lose Modus gegen das Assad Regime und assozierte Shia Gruppierungen die einen existenziellen Überlebenskampf gegen IS führen.
Eine grundlegende Feindschaft existiert zwischen der Plutokratie und der Kleriktokratie und der Plutokratie und der Aristokratie (1.1: Tabelle). Eine ethnisch-religiös überlagerte Konfliktsituation (Erhaltung ethnischer Souveränität, sowie Sunni versus Shia).
Obwohl selbst in Gegnerschaft zu IS (Plutokratie versus Kleriktokratie) wird diese (IS) gebraucht von plutokratischen Imperialisten zur Vernichtung von volksbezogenen Elitokratien und elitäre Autokratien (Plutokratie versus Aristokratie); obwohl gerade diese vorort die effektivsten Kämpfer gegen eine IS Ausbreitung darstellen (Aristokratie versus Kleriktokratie). Verdeckte Unterstützung von oppositionellen

Kräften des Arabischen Frühlings (inklusive der IS) durch plutokratische Imperialisten in ihrem Kampf gegen Elitär-Autokratien (Tabelle 1.3a: Gruppe 2, auch Gruppe 1). In the context of plutocratic imperialism we have the opportunistic use of Arab Spring dissident groups, challenging autocratic governments, for regime change purposes by the United States of America and its Western allies. Durch die Einführung demokratischer Staatsgebilde in welchen ethnozentrische/dynastische Eliten entmachtet werden entstehen Machtvakuen welche durch IS dann gefüllt werden. (siehe auch Irak, Jemen, Syrien).
In pursuit of regime change the US uses the allegation that the targeted countries support terrorist groups. Paradoxically, however (*vide* Cockburn 2015), the interference of the US in the region (e.g. Iraq) resulted in the emergence of IS-type terrorist forces in the first place, which were then supported and used for regime change (e.g. against Syria) and their prolonged survival in the region facilitated by targeting and weakening those forces on which the sustained containment of clerictocratic IS terrorism in the region would depend (Table 1.3b: Iran, Shia militias, ethnocentric forces such as the Kurdish people, Houthis and others). EXPLAIN STRATEGY OF PLUTOCRATIC IMPERIALISM

Win-lose Rhetorik zwischen Iran und Israel hat deren Gegnerschaft unnötigerweise verschärft. Inzwischen (2015/2016) ist bei Iran ein Übergang zum Win-win Verhalten zu beobachten (u.A. Nuklearabkommen). Verschärfte Win-lose Gegnerschaft zwischen den Machtzentren 1 () und 2 () auf Grund religiöser Sunni-Shia Polarisierung.

Iran A vs K intern vs P
Saudiarabien A vs K intern (Allianz mit P, aber P vs A) Ali Abdullah Saleh (Formerly President of Yemen): Saleh has been a behind the scenes leader of the Houthi takeover in Yemen led by Shia Houthi forces. Tribesmen and government forces loyal to Saleh joined the Houthis in their march to power. (Republican Guard)
Israel (in P eingebettet) P vs A, P vs K

Win-lose plutokratische Imperialisten schrecken nicht davor zurück Völker blosszustellen an destruktives Win-lose Verhalten ihrer Zweckalliierten (Kommunistische Diktaturen, IS). Violation of the Take Whole principle (Sun Tzu). Win-lose Imperialismus verhindert eine Befriedung im Mittleren Osten. Im Zuge einer

Dreiecksauseinandersetzung zeigen sich zwei Hauptfronten. Auf der einen Seite plutokratischer und kleriktokratischer Imperialismus. (Formenkreis 3: USA und alliierte Pluto-Demokratien, Saudiarabien/Sunni in Zweckallianz mit den USA, und Israel durch Einbettung im plutokratischen Imperialismus, Tabelle). Auf der einen Seite Plutokratischer Imperialismus in verdeckter Zweckallianz mit dem kleriktokratischen Imperialismus (Formenkreis 2: IS, Tabelle) und auf der anderen Seite volksbezogene (autokratische) Eliten (Formenkreis 1: Volksschutzimperativ, Gruppe 2, Tabelle) im Überlebungskampf. Letztere sind aber gerade auch die Kräfte die am effektivsten sind im Kampf gegen IS. Hiermit besteht ein fundamentaler strategischer Interessenkonflikt in Bezug auf langfristige Volksschutzinteressen von Israel. Auch für die arabischen Monarchien besteht ein gleichgearteter Interessenkonflikt da das Überleben dieser Monarchien grundsätzlich durch IS bedroht wird (Crooke). PRINCIPLES art of war in conflict non-alignment

The win-lose dynamics in the Middle East results in much collateral damage, causing not only much human suffering for the populations concerned; but is also generally threatening peace regarding the future, in the region and beyond (especially alsi in respect of Europe). One could interpret the situation in the Middle East contending that the Third World War is already ongoing, presenting itself as a fundamental conflict between plutocratic and clerictocratic imperialisms and their opposing forces (Table 1.3b). Somewhat more than a century ago, monarchies (aristocracy) were on the regime change list of the rising plutocratic imperialism (1.1: Civilization 1: 1800-2000: from Aristocracy to Plutocracy). During the phase Civilization 2 (2000-2200; 1.1), US-led plutocratic imperialism continues to aspire towards and basically achieves world domination. This era is thus characterized by continuing fundamental confrontations between win-lose plutocratic imperialism and forces of nationalist self-preservation (conservatism; ethnic survivalism: protection imperative; Table 1.1); and further escalation of the Third World War, as regime change pursuits of US-led forces of plutocratic imperialism advance in the Middle East (Afghanistan, Iraq, Syria, Iran), and elsewhere. As the conflict in the Middle East escalates, win-lose imperialisms (US-led plutocratic imperialism colluding with Saudi Arabia-led Sunni clerictocratic imperialism: Table 1.3b) may possibly achieve initial pyrrhic victories, but the demise of plutocratic imperialism is nevertheless to be anticipated (1.1).

2. SYSTEMS-ECOLOGICAL HEALING

2.1 Healing and disease management

2.1.1 Symptoms management and causality-based healing practices

Therapies of conventional modern medicine, involving operations, pharmacological and specialist interventions, have reached unprecedented levels of scientific sophistication and play an important role in the medical care of people (notably in the context of symptom-linked crisis management).

Progressing developments in the domain of holistic integrative medicine have been emerging (Popp 1987; Reckeweg 1986; Preusser 1987; Langreder 1991; Mennerich 1979; Rusch 1979; Rusch et al., 1985; Pischinger 1989). Holistic insights about health and healing are emerging (*inter alia* Mennerich 1979; Köhnlechner 1980; Weil 1985; Weil 1995; Goswami 2004). Insights of relevance to health and healing from the field of quantum physics are being acquired (Citro 2011; Laszlo 2014a; Goswami 2004).

Conventional treatment of symptoms represents a treatment approach with the objective of alleviating the consequences of a disease and to resolve any acute dangers to the health of the patient. However, an increased incidence of chronic disease states is being registered (termed “Zivilisatose” by Jentschura & Lohkämper 2014). In contrast, with systemsecological healung the achievement and maintenance of health is pursued by supporting or harnessing of self-healing processes operative at the causative level (2.1.2: involving the ultimate causality of disease: patho-information-engram loading of the biocybernetic system of the body). Symptoms are already/also manifestations of body-own healing processes (e.g. Reckeweg 1986). Suppressive treatment of disease symptoms therefore often result in disruption or blockage of recursive healing processes, thereby leading towards an increasing chronification of disease states (Procursion: further patho-information-engram uploading).

2.1.2 Pathogenic-information-engrams (PIE) and recursion-healing

a) Dynamics of patho-information-engram loading

It is here presumed that the functionality of any organism is being controlled within the context of a biocybernetic system (according to an information/intelligence blueprint). During the course of life any traumatic impacts (of a psychological or physical nature) not successfully warded off or processed becomes imprinted into the biocybernetic system of the body in the form of pathogenic-information-engrams (also in the context of epigenetic adaption to environmental impacts/influences: 2.1.3). The effectiveness of body functional control is increasingly impaired/reduced by such up-loaded patho-information-engrams. This is associated with reduced body functional efficiency (vitality impairment = lowered functional-energetic potency) and thus with chronic disease states. Self-healing processes of the body attempt to delete the uploaded patho-information-engrams in reverse chronological order of their incorporation into the biocybernetic system (Baur 1982; Buchinger op. cit. Fahrner 1985; Mennerich 1979; Pischinger 1989): **recursion healing**. This is also in agreement with cosmic-multidimensional information dynamics (Laszlo 2014a: Table 2.1.2a).

Laszlo (2014a): The human body consists of trillions of cells, and each cell produces thousands of bio-electrical-chemical reactions every second. This enormous "living symphony" is precisely governed and coordinated, focused on the paramount task of maintaining the organism in its physically improbable living state. Governing and coordinating the reactions that enable the organism to stay alive is the function of the information that pervades the body (**AS: Table 2.1.2a: Laszlo 2014a**). Information in this context is not a peripheral adjunct to biochemical processes but that which governs and coordinates those processes. The information that governs the organism is what differentiates *inter alia* one individual from another and a healthy individual from a sick one.
It was believed that information in the body is limited to genetic information, and that genetic information is fixed for a lifetime. Current findings in biology and medicine indicate that this is not the case. The information that governs organic function is more complex and comprehensive than the genetic code in the DNA, and it is not rigidly fixed but open to adaptation and modification. Even genetic information is modifiable. Although the sequence of genes in the DNA is fixed, the way that sequence affects the body is flexible: it is governed by the epigenetic system, and the epigenetic system is adaptive (**AS: dealt with in more detail in sections 2.1.3.1 and 2.1.3.2**).

Table 2.1.2a Cosmic-multididimensional information dynamics
Cited from Laszlo (2014a)

Governing and coordinating the reactions that enable the body to stay alive is the function of the information that pervades the body. Information in this context governs and co-ordinates functional processes (e.g. biochemical processes). According to the Akasha paradigm the information that coordinates the functions of a living organism is a specific pattern in the living sea of A-dimensional information. This corpus of information governs action, interaction and reaction throughout the manifest world. It also governs the functions of the living organism (a blue print of normal organic functioning). The blue print of organic functioning for living organisms emerged in the course of interaction between the M (observable dimension) and A (the deep dimension, the Akasha) dimensions. The A-dimension interacts (informs systems in the M-dimension) with the M-dimension. The information generated in this interaction is conserved in the A-dimension. The A-dimension is the memory of the M-dimension; it is the manifest Akashic Record in the universe. The sea of Akashic information includes the species-specific pattern that is the natural attractor of healthy functioning in the organism. This pattern results from the long-term interaction of a species with the A-dimension; it is the enduring memory of those interactions and it codes the the generic norms of viability. For human beings it is the equivalent of Qi, prana or the *life energy* of traditional Western healing arts. Without acces to this life energy, errors in cellular and organic interactions, reaction, and transcription would accumulate in the body leading to ever more serious malfunctions. Prior to manifestation of disease there is a breakdown or blockage of information in the organism and these conditions can be treated by re-establishing resonance with the organisms's life energy. Doing so is to treat the cause of the malfunction rather than its manifestation. The Akasha paradigm suggests that the first task of the medical practitioner is to adapt the M-dimensional interactions of the organism for optimal conformance with the A-dimensional information. Impacting stresses and strains (procursive impacts) interfere with the ability of the organism to cope with adverse conditions and toxic substances in its environment. They interfere with its conformance with Akashic information and thus (thereby) diminish its vitality.
In today's world there is an urgent need to regain contact with the A-dimension. The fuller our body's **conformance with the relevant Akashic blueprint for optimal functioning**, the more robust our health and capacity to resist negative influences.

During the course of life the body is exposed to an onslaught of procursive impacts/insults (procursive patho-information-engram uploading) with phase-variable intensity (toxic effects, traumata, stress effects, challenges, unresolved conflicts); which may partially block recursion healing. Accordingly, causes of disease are patho-information-engram-specific dysfunctionalities which then manifest during self-healing processes as disease symptoms. Symptoms are a reflection of attempts of the body to overcome the disease or regulate associated physiological disequilibria (healing-directed dynamic processes). During phases of reduced incidence of procursive insults, and in the context of recursion self-healing processes, functional disturbances primarily linked to the most recently imprinted/uppermost patho-information-engram layer, become manifest (e.g. acidosis, milieu changes promotive for endogenous and external pathogenic microbes and associated relevant symptom complexes. This involves the exposure of patho-information-engrams to immune system interactive deletion in the context of recursion-healing attempts. Symptoms thus reflect subacute/akute states in the context of recursive self-healig attempts. Symptom

suppression then results in progressive chronification (procursion); In other words, if recursion healing processes of the body cannot neutralise an ongoing patho-information-engram up-loading, a progressive accumulation thereof occurs (procursion). Central to the elimination and prevention of the accumulation of patho-information-engrams are autophagous maintenance processes (catabolic) which cannot occur under conditions of chronic overfeeding (feast > famine conditions) and stress impacts. Circumstances of uninterrupted food availability and increased population density stress generally co-occur, resulting in ***procursive overload*** (including allostatic overload: Table 2.1.2b) and associated reduced metabolic functional efficiency.

McDade et al. (2016): Chronic inflammation has been implicated in the etiology of diverse chronic degenerative diseases (e.g. Ridker et al. 2003, op. cit. McDade et al. 2016; Kuo et al. 2006, op. cit. McDade et al. 2016). The critical role of inflammation as part of the innate immune defenses has been known since 2000 years ago (Rather1971, op. cit. McDade et al. 2016), but only relatively recently has inflammation been pathologized and its importance for survival disregarded (McDade 2012).

McDade et al. (2017): Chronic inflammation contributes to a wide range of human diseases. Environments in infancy and childhood are important determinants of inflammatory phenotypes. Evidence was found that that nutritional, microbial and psychosocial exposures in infancy and childhood predict adult levels of DNA methylation in inflammation-regulating genes; suggesting that epigenetic mechanisms have lasting effects on inflammation and inflammation-related diseases. Analyses across nine genes revealed that the level of DNA methylation was predicted by the following variables: household economic status, extended absence of a parent during childhood, exposure to animal faeces in infancy and duration of exclusive breastfeeding. Individuals born at lower birth weight and infants breastfed for shorter durations have higher concentrations of C-reactive protein (CRP: biomarker of inflammation) as adults (Danese et al. 2007, op. cit. McDade et al. 2017; Tzoulaki et al. 2008, op. cit. McDade et al. 2017; McDade et al. 2010, op. cit. McDade et al. 2017; McDade et al. 2014).

McDade et al. (2010): Microbial exposures in infancy predict lower levels of C-reactive protein (CRP) in adulthood. Lower birth weight was associated with increased CRP. Higher levels of microbial exposure in infancy were associated with lower CRP in adulthood. We conclude that measures of microbial exposure and nutrition during the prenatal and early post-natal periods are important predictors of CRP concentration in young adulthood. We speculate that the development of anti-inflammatory regulatory networks in response to early microbial exposure represents plasticity in the development of anti-pathogen defences, putatively explaining low CRP levels in such populations.

Bach (2002): Infectious agents can induce autoimmune diseases in several experimental settings and a variety of mechanisms have been invoked to explain these observations (Olson et al. 2001, op. cit. Bach 2002). Paradoxically, infectious agents can also suppress allergic and autoimmune disorders. A summary is presented of the evidence that a main factor of these diseases in industrialized countries is the reduction in the incidence of infectious diseases in those countries over the past three decades. Epidemiological data provide strong evidence of a steady rise in the incidence of allergic and autoimmune diseases: allergic diseases: asthma (Woolcock & Peat 1997, op. cit. Bach 2002), rhinitis (Upton et al.2000, op. cit. Bach 2002), atopic dermatitis (Williams 1992, op. cit. Bach 2002) and autoimmune diseases: multiple sclerosis (Poser et al. 1989, op. cit. Bach 2002), insulin-dependent diabetes mellitus and Crohn's disease (Swarbrick et al. 2001, op. cit. Bach 2002). Concomittantly there has been a decrease in the incidence of many infectious diseases (rheumatic fever, measles, mumps, hepatitis A) in developed countries as a result of antibiotics, vaccination, generally improved hygiene and better socioeconomic conditions.

The frequency of intestinal infections has notably decreased in developed countries. Furthermore, the age at which colonization of intestinal flora (e.g. gram-negative bacteria) occurs is later in developed countries, both quantitatively and qualitatively (Adlerberth et al. 1991, op. cit. Bach 2002). A latitudinal distribution gradient of disease was established: one is the north-south gradient; the incidence of disease decreases from north to south in the Northern Hemisphere (and reciprocally from south to north in the Southern Hemisphere). (**AS: refer to 2.3.3d for underlying mechanisms**).

A positive correlation exists between the gross national product and the incidence of asthma, type 1 diabetes, and multiple sclerosis across 12 European countries (ex Kurtzke 2000, op. cit. Bach 2002; Green & Patterson 2001, op. cit. Bach 2002; Stewart et al. 2001, op. cit. Bach 2002). In regions of Yorkshire (Staines et al. 1997, op. cit. Bach 2002) and Northern Ireland (Patterson et al. 1996, op. cit. Bach 2002), a significant positive correlation between the low incidence of type 1 diabetes and low socioeconomic status was confirmed. (**AS: low SES of more rural origin, see op. cit Staines et al. 1997; transgenerational effects of affluence affecting individuals of higher SES more/earlier than poorer people: 2.2.2j**).

The administration of antibiotics to children has been suspected to increase the risk of asthma and allergy. The use of antibiotics in the first year of life increased the risk of asthma or other allergic diseases in children with a genetic predisposition to atopy (Droste et al. 2000, op. cit. Bach 2002). Antibiotics might act by decreasing the number of infectious episodes or by modifying intestinal flora. The composition of the intestinal flora differs between newborns in whom allergy develops at a later age and those in whom atopy does not develop (Bjorksten et al. 2001, op. cit. Bach 2002; Kalliomaki et al. 2001, op. cit. Bach 2002).

Anecdotal evidence suggests that exposure to infectious diseases is associated with decreased manifestations of immune-related diseases. According to a study carried out in Austria, Germany and Switzerland, allergies were less frequent when the children were exposed earlyand for a prolonged period to farm animals and cow's milk (Riedler et al. 2002, op. cit. Bach 2002). Measles has been reported to ameliorate the severity of nephrotic syndrome (Blumberg & Cassady 1947, op. cit. Bach 2002) and atopic dermatitis (Kondo et al, 1993, op. cit. Bach 2002; Biner et al. 1985, op. cit. Bach 2002). The deliberate administration of a non-pathogenic lactobacillus to pregnant women with atropy, and ultimately, to their newborns

significantly decresased the incidence of atopic dermatitis in the newborns (Kalliomaki et al. 2001, op. cit. Bach 2002). Children who received antibiotics during infancy had a higher incidence of allergy and other atopic disorders who had not received antibiotics (Wickens et al. 1999, op. cit. Bach 2002). An association between between allergic and autoimmune diseases in individual patients has bcome apparent: the frequency of atopic diseases is increased in patients with diabetes and rheumatoid arthritis (Kero et al. 2001, op. cit. Bach 2002; Simpson et al. 2002, op. cit. Bach 2002). These observations fit in with the concept of common mechanisms underlying infection-mediated protection against autoimmunity and allergy.
The transfer of maternal antiviral antibodies to newborns may have a role in the susceptibility to autoimmune diseases. Zinkernagel (2001, op. cit. Bach 2002) suggested that the decreased exposure of women to particular viruses before pregnancy may subsequently reduce the degree of protection against these viruses afforded to their newborns.
Some clinical implications. Positive results involving treatment with a mycobacterial extract (Arkwright & David 2001, op. cit. Bach 2002) and probiotics (Kalliomaki et al. 2001, op. cit. Bach 2002; Isolauri et al. 2000, op. cit. Bach 2002) have been reported in patie The deliberate administration of a non-pathogenic lactobacillus to pregnant women with atropy, and ultimately, to their newborns significantly decresased the incidence of atopic dermatitis in the newborns (Kalliomaki et al. 2001, op. cit. Bach 2002). Children who received antibiotics during infancy had a higher incidence of allergy and other atopic disorders than those who had not received antibiotics (Wickens et al. 1999, op. cit. Bach 2002). Vaccination with bacilli Calmette-Guérin has produced encouraging results in patient with multiple sclerosis (Ristori et al, 1999, op. cit. Bach 2002) and should be investigated further once the treatment is found to be safe. Vaccinations may cause immunostimulation and thus have a favourable effect, or they may prevent “protective” infections and thus have an unfavourable effect. In addition to the problem of antibiotic resistance, unnecessary treatment with antibiotics could reduce the degreeof physiological immunostimulation afforded by commensal bacteria.

Staines et al. (1997): Insulin-dependent diabetes mellitus (IDDM) rates were significantly lower in wards of high population density and with many overcrowded houses. The incidence of childhood IDDM was associated with environmental factors including population density and overcrowded homes. A possible inference from these data is that patterns of infection are involved in the occurrence of IDDM. One correlate of household crowding (lower incidence of IDDM) is poverty; implying a lower incidence of IDDM in lower socioeconomic strata. Other studies have found urban rural differences. Bruno et al. (1993, op. cit. Staines et al. 1997) found an excess of IDDM in Turin compared with the surrounding rural areas. Rewers et al. (1987, op. cit. Staines et al. 1997) in Poland found higher rates in the city of Poznan than in surrounding rural areas. (**AS: There sems to be a confoundment of results: lower rates of IDDM in crowded lower socioeconomic strata and in rural areas. Generally, higher rates of such disorders occur in people of lower socioeconomic strata (2.2.2k). These contradictory results may be reconciled by surmising that people of study populations living under crowded conditions in low socioeconomic strata, exhibiting lower rates of IDDM, were people of rural origin (lower rates of IDDM) which had relatively recently immigrated into urban areas**).

McDade (2012): Studies of populations in low-income countries revealed low levels of chronic inflammation later in life (adulthood) in spite of higher burdens of infectious disease during infancy and childhood. Regulation of acute inflammatory responses due to infectious exposures and other early environmental conditions moderated responses to inflammatory stimuli later in life, with implications for the association between inflammation and chronic diseases. Low levels of infectious exposure in infancy have been associated with increases in Th2 cytokine production and total IgE concentration (Matricardi et al. 2000, op. cit. McDade 2012; McDade et al. 2004, op. cit. McDade 2012; Shirakawa et al. 1997, op. cit. McDade 2012), a pattern of immune development promoting allergic, atopic and autoimmune diseases later in life. Research on the hygiene hypothesis has confirmed that microbial exposures in infancy shape the development of immune regulatory networks in ways limiting immunopathological processes and thus chronic disease later in life (Garn & Renz 2007, op. cit. McDade 2012). Human gut microbiota are also implicated to play an important role in this context (Round & Mazmanian 2009, op. cit. McDade 2012). Active engagement with the environment (response to microbial exposures) during critical stages of development is required to achieve such immune regulatory networks (immune/inflammatory systems). (**AS: acute immunological engagement overcoming stressor impacts, type 1 allostatic load, in order to remove chronic pathological imprints, type 2 allostatic load**).

The insights of Bach (2002), McDade (2012), McDade et al. (2010), McDade et al. (2012), as presented above, underpin the fundamental principle of healing according to which chronic disease factors can only be eliminated, and healing achieved, through exposure of these to acute immune interaction (e.g. Pischinger 1989). Patho-information-engram-linked information, as reflected in symptoms of associated health impediments, is exposed to processes of immune interaction at various interfaces: during bacterial/viral infections, immune-interaction with gut microflora, immune-interaction of newborns with epigenetic patho-information contained in mother's milk (breastfeeding), during childhood diseases (*inter alia* measles) and immune system modulation by commensal bacteria (Brestoff & Artis 2013; Artis 2008; Vitetta et al. 2012); and microbe-immune iteractions on the skin surface. As in the case at most of these interfaces, immune interactions take place with microbes thriving in the milieu produced by functional disturbances associated with relevant patho-information-engrams (mostly those most recently embedded into the biocybernetic system of the body). Overcoming of the microbes containing information of the chronic pathology (exposure of chronic patho-information) is then expected to result in self-healing through erasure of associated patho-engram information. Systems ecological healing interventions are aimed at facilitating the exposure and

supporting the overpowering of chronic pathological factors through their exposure to immune interactions and/or autophagy.

These processes of immune interaction are cornerstones of recursion healing. Exposure to active immune interaction is prominently functionalised by fever and autophagy during fasting (2.1.2c/d).

Refer also to CISDS 2.2.2i
Catalysis of immune system interactive self-healing at the exposure interface. Catalytic synergy, clear exposure of successive layers, time, repetition
Catalysis of immune interactions at the exposure interface
Methyl catalysts
Imtermittancy reaching the epigenetic level repeated confrontation
In a recursion-friendly environment – diet lifestyle
Sympathetic parasympathetic state IgA up also meditation
Transcriptional and epigenetic control of autophagy (Füllgrabe et al. 2014)

REFER TO SECTION 2.1.2d
LINK TO EPI
PIEs are lodged at the epigenetic level and thus require to be deleted as such
Seisenberger et al. (2012) Reprogramming DNA methylation

As far as possible (but subject to advice by a medical professional), avoid suppression of acute immune interactions with anti-fever drugs, antibiotics, vaccination and suppressing pharmacological medications (such suppression representing procursive impacts).

The interplay between procursion-recursion dynamics is similarly reflected as outlined by *inter alia* McEwen & Wingfield (2003) with reference to allostasis and allostatic load accumulation (Table 2.1.2b).

Allostasis is a fundamental process through which organisms actively adjust to predictable and unpredictable events; and allostatic load refers to the cumulative costs

to the body of allostasis (responses to procursive impacts) when ineffectively managed by the body. Allostatic overload represents a state in which serious pathophysiology can occur (McEwen & Wingfield 2003). Two types of allostatic overload are defined with reference to prevailing conditions of energy balance. Type 1 allostatic overload occurs when energy demand exceeds supply (**AS: fasting conditions, supportive of healing through recursive processes; 2.1.2**), resulting in the activation of the emergency life stage; establishing a survival mode which decreases allostatic load and positive energy balance is regained. Type 2 allostatic overload results when there is sufficient or excess energy consumption, accompanied by social conflict and other types of social dysfunction (McEwen & Wingfield 2003). (**AS: feast conditions: maximum opportunistic utilization of surplus food availability for reproductive and competitive performance and energy storage: fast-LHS expression; 2.2.2e**). In all cases, secretion of glucocorticosteroids and activity of other mediators of allostasis (autonomic nervous system, CNS neurotransmitters, inflammatory cytokines) wax and wane with allostatic load. Pathologies develop when allostatic load is chronically high (allostatic overload: McEwen & Wingfield 2003). (**AS: high intensity of procursive impacts arising from uninterrupted overabundance of food resources and population density stress; resulting in progressive patho-information-engram uploading/allostatic overload**). Accordingly, allostasis and allostatic states apply to all situations involving physiological and behavioural responses to challenge and associated cumulative costs to the organism depend on the balance between energy supplies and demands and factors involving social competition. (**AS: dependent on the magnitude of procursive impacts associated with uninterrupted utilization of food resource surplus conditions and population density stress: 2.3.3e**).

Allostasis, as manifesting in type 1 overload, is geared to cope with unpredictable environmental events (impacting stressors; e.g. threats to food availability, physiological and social stress); thereby representing a mechanisms of coping with stress (acute responses to stressors in order to re-establish physiological homeostasis). The associated rapid behavioural and physiological changes in response to perturbations termed the emergency life history stage (increased foraging, enhanced restfulness at night, elevated gluconeogenesis and recovery once the perturbation has passed) thereby serve to enhance lifetime fitness (Wingfield et al. 1998, op. cit. McEwen & Wingfield 2003). If the perturbations remain chronic and the emergency

life history stage fails to reduce allostatic load, pathological effects will take effect (Table 2.1.2b). From a state of negative energy balance, the emergency life history stage then facilitates the regaining of a positive energy balance and the re-establishment of physiological homeostasis (McEwen & Wingfield 2003). However, cumulative effects of remaining in a state of positive energy balance then become pathological (type 2 allostatic overload: **AS: representing an allostatic state of accumulated patho-information-engram load which resulted from the failure to adequately overcome stressor perturbations during acute interaction with these**). In modern human societies a state of chronic positive energy balance has resulted in, *inter alia*, pathological states such as abdominal fat accumulation, atherosclerosis and inflammatory disorders linked to oxidative stress (e.g. Bierhaus et al. 2001, op. cit. McEwen & Wingfield 2003; Krysiak et al. 2001, op. cit. McEwen & Wingfield 2003; chronic immune system dysregulation syndrome: 2.2.2i).

McEwen (2016): Resilience to adverse events is here defined as achieving a positive outcome in the face of adversity. The term allostasis, as introduced by Sterling & Eyer (1988, op. cit. McEwen 2016), refers to active processes by which the body responds to daily events in order to maintain homeostasis. Sustained or inadequate allostasis can lead to disease if too much stress or inefficient management of allostasis (e.g. failure to turn off the response when no longer needed) results in allostatic load or overload (McEwen & Wingfield 2003). The brain is central for adaptation to experiences, including stressors, which which are capable of changing brain architexture and altering systemic function through neuroendocrine, autonomic, immune and metabolic systems. Chronic stress can have direct and indirect effects on cumulative allostatic overload (representing costs of adaptation/plasticity costs: 2.2.1d; Table 2.1.2b).

Table 2.1.2b	**Allostasis and allostatic load** **(cited as indicated; predominantly McEwen)**
McEwen & Wingfield (2003): Allostasis is achieving stability through change; i. e. a process supporting homeostasis (maintaining systems in balance) in respect of physiological parameters essential for life, as environmental and/or life history stages change. Allostatic state refers to altered and sustained activity of the primary mediators (e. g. glucocorticosterioids) that integrate physiology and associated behaviours in response to changing environments (food availability) and challenges (social interactions, disease). An allostatic state results in an imbalance of primary mediators, involving excessive production of some and inadequate production of others. The cumulative effect of an allostatic state then is allostatic load. If imbalances continue, independent of maintaining adequate energy reserves, allostatic overload results. Mediators associated with allostasis have protective effects in the short term, but decome damaging over longer time intervals when subject to many adverse life events or hormonal dysregulation in a sustained allostatic state leading to allostatic overload (McEwen 1998a). **McEwen (2007)**: Stress involves two-way communication between the brain and the cardiovascular, immune, and other systems via neural and endocrine mechanisms. Beyond the "fight-or-flight" response to acute stress, there are events in daily life that produce a chronic stress and lead over time to wear and tear on the body (allostatic load). Hormones associated with stress protect the body in the	

short-term and promote adaptation (allostasis). The brain is a target of stress, and and the hippocampus was the first brain region, besides the hypothalamus, to be recognized as a target of glucocorticoids. Stress and stress hormones have effects on the brain region throughout the life course. Early life events influence life-long pattrrns of emotionality and stress responsiveness and alter the rate of brain and body ageing. The hippocampus, amygdala, and prefrontal cortex undergo stress-induced structural remodelling, which alters behavioural and physiological responses.

According to the cumulative advantage/disadvantage hypothesis it is argued that early life events can set into motion a trajectory where advantage /disadvantage is accumulated throughout the course of life (O'Rand & Hamil-Luker, op.cit. Hanson 2013). Sequential exposures to adverse environments may lead to excess stress or exposure to chronic stress that leads to increased risk for disease later in life. Allostasis, the ability to achieve stability through change, is maintained through the autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis and other metabolic and immune systems (McEwen 1998a/b). Allostatic load describes a process through which exposure to chronic stress throughout life can lead to progressive dysfunctionality in these systems and lead to poor health/chronic disease in adulthood/later in life (McEwen 1998a/b). Research in epigenetics has shown that epigenetic modifications occur across the lifespan (Champagne 2010; Montesanto et al. 2012).

McEwen (1998a): Stressful experiences include major life events and trauma. Acute stress (fight-flight or major life events) and chronic stress (cumulative load of minor day-to-day stresses) can both have long-term consequences. Chronic stress effects are exacerbated by a rich diet and toxins such as tobacco and alcohol and reduced by moderate exercise. Whether one perceives a situation as threat, either psychological or physical, is crucial in determining the behavioural response (fleeing, fighting, fear, elevated cortisol levels *versus* calmness, sense of being in control). The physical condition of the individual has implications for the capacity to mount an appropriate physiological response to stressful stimuli. Chronic stress (fatigue, lack of energy, irritability, demoralization, hostility) has been linked to the development of insulin resistance (Raikkonen et al., op. cit. McEwen 1998a), a risk factor for non-insulin dependant diabetes. Deposition of abdominal fat, a risk factor for coronary heart disease and diabetes (Bjorntorp, op. cit. McEwen 1998a) is increased by psychosocial stress (Moyer et al., op. cit. McEwen 1998a). Allostatic systems (most common allostatic responses involve the sympathetic nervous system and the HPA axis) enable us to cope with noise, crowding, isolation, hunger, extremes of temperature, danger and microbial or parasitic infection. Response to a challenge (dangerous situation, crowded neighbourhood) is twofold: turning on an allostatic response initiating complex adaptive pathways and then shutting down the particular response when the threat is past. Activation of the allostatic system involves *inter alia* the release of catecholamines and cortisol, leading to adaptation to the threat condition (danger, infection, poor living conditions). Inactivation returns the system to base-line levels of catecholamine and cortisol secretion once the threat situation is past. If the inactivation is inefficient, overexposure to stress hormones persists and over time results in allostatic load and its pathophysiologic consequences. Four conditions may lead to accumulated allostatic load: repeated multiple stress, lack of adaptation to stressor, prolonged response due to delayed shut-down and inadequate response leading to compensatory hyperactivity of other mediators. If cortisol secretion does not increase in response to stress, secretion of inflammatory cytokines increases (Munck et al., op. cit. McEwen 1998a). Prolonged anxiety and anticipation are likely to result in allostatic load (Shulkin et al., op. cit. McEwen 1998a). Job strain (high psychological demands and lack of control) results *inter alia* in increased progression of atherosclerosis (Everson, op. cit. McEwen 1998a). Results from the MacArthur Studies of Successful Aging showed that subjects with higher levels of physical and mental functioning had lower allostatic load scores (Seeman et al. 1997). Repeated stress affects brain function, especially in the hippocampus, which has high concentrations of cortisol receptors. Impairment of the hippocampus decreases the reliability and accuracy of contextual memories; thereby exacerbating stress by preventing access to decide whether a treat situation is not a threat (Sapolsky, op. cit. McEwen 1998a). The hippocampus also plays a role in regulating the stress response and inhibition of the response of the HPA axis to stress (Jacobson & Rapolsky, op. cit. McEwen 1998a). Early experiences are believed to set the responsiveness of the HPA axis and autonomic nervous system. The systems were found to overreact in animals subjected to early unpredictable stress and underreact when exposed to neonatal handling (maternal care); associated with brain aging being accelerated or reduced respectively (Meany et al., op. cit. McEwen 1998a).
McEwen (1998b): As an essential component of homeostasis, **allostasis** represents a system of adaptation in the face of stressful challenges through the activation of neural, neuroendocrine and

neuroendocrine-immune mechanisms (stability through change; Sterling & Eyer, op. cit. McEwen 1998b). When these adaptive systems are activated and de-activated, but not too frequently, they promote homeostasis and survival. If allostatic systems are over- or underactive, pathophysiological response modes may become entranched, referred to as **allostatic load**. Three types of pathophysiological response modes result in allostatic load: high intensity and repetitive frequency of stress reactions, as such, may induce pathological outcomes, lead to failed shutdown or inadequate response capacities of allostatic systems. Chronic activity and failure to shut down: Persistently elevated blood pressure and glucocorticoids (acceleration of obesity and type 2 diabetes). Failure to respond to a challenge (failure to mount an adequate HPA response) leads increased to vulnerability to autoimmunity and inflammatory disturbances and is associated with inadequate endogenous glucocorticoid responses (chronic fatigue syndrome, also adrenal fatigue).

Seeman et al. (1997): Allostatic load scores were derived as the sum of the number of indicators of high allostatic load (systolic blood pressure ≤ 148 mm Hg, diastolic blood pressure ≥ 83 mm Hg, waist-hip ratio ≥ 0.94, ratio total cholesterol/HDL ≥ 5.9, glycosilated haemoglobin ≥ 7.1 %, urinary cortisol ≥ 25.7 μg/g creatinine, urinary norepinephrine ≥ 48 μg/g creatinine, urinary epinephrine ≥ 5 μg/g creatinine, HDL cholesterol ≤ 56 μg/dl, dehydroepiandrosterone DHEA ≤ 91 mg/dl). High allostatic load scores in elderly persons with no reported cardiovascular disease, myocardial infarction, stroke, diabetes or high blood pressure at baseline, predicted declining performance 2.5 years later in respect of cognitive function (notably memory decline) and physical performance based on measures of balance, gait, foot taps and manual ability. High allostatic scores 2.5 years earlier also predicted subsequent incidence of cardiovascular disease. Analyses of the data for the MacArthur Successful Aging study indicated that individuals who showed **higher functional performance (functional efficiency)** had **lower allostatic load scores**; but **higher functioning group people** who had the **higher allostatic load scores** had the **highest probability** of cardiovascular disease three years later and also showed the highest rates of decline in measures of cognitive and physical functioning (Seeman et al. 1997).

Parasympathetic functions and allostasis. **McEwen et al. (1999)**: Allostasis is the process of adaptation that helps the body to maintain homeostasis. Allostatic load is the cost of excessive adaptation and reflects overactivity of chemical mediators involved in adaptation. It reflects an imbalance in the activity of mediators, e. g. inflammatory cytokines with inadequate glucocorticoids or excess excitory amino acids in brain after stressor during aging; elevated glucocorticoids, insulin, catecholamines in relation to abdominal obesity and Type 2 diabetes. The parasympathetic and sympathetic components of the autonomous nervous system (ANS) control the involuntary body functions, whereas the enteric nervous system is involved primarily with the internal regulation of the gustatory processes. Blood pressure change patterns. Blood pressure normally falls during the night (the so-called dipper pattern). In some hypertensive patients the blood pressure does not dip at night (non-dippers) and this represents a form of allostatic load that may contribute to the damage caused by chronic hypertension. Non-dippers: this would be consistent with a failure to reduce sympathetic and to increase parasympathetic activity during the night and with the failure to lower blood pressure. Regulation of satiety via vagus and gut.

The two main components of recursion healing involve fever and fasting; with compromised intestinal health, acid-base imbalances and sleep disturbances constituting therapeutic spheres representing both proximate causes and consequences of health impediments.

During rescursion-healing chronic disease states linked to relevant patho-information-engrams (usually the most recent upprermost layer) are being exposed to the reconfrontation with acute immune interactions in pursuit of deletion of the embedded chronic patho-engram information. For the progression of recursion-healing, fever

(Kluger 1979; Heckel 1990; Table 2.1.2c), fasting effects (Fahrner 1985: Table 2.1.2h), intestinal health (Table 2.1.2f: Rauch 1986), acid-base homeostasis (Table 2.1.2e; Jentschura & Lohkämper 2014, Sircus 2014a/b), as well as sleep processes (Walker 2017; Table 2.1.2g) are of central inmportance. Fever- and fasting therapies, intestinal detoxification, as well as regulation of the acid-base system relate to a remarkably broad list of indications, involving physiological, psychological and psychosomatic disorders. This implies that that related functional processes are all involved in self-healing attempts of the body (at the primary or secondary level of causality).

Systemsecological healing basically involves potentiating self-healing processes of the body entity (which is perceived to embrace a cosmic/kharmic information level, a biocybernetic regulatory memory/blueprint and physiological/biochemical processes taking place at the material level: 2.1.2b). Top-down causality of disease across these dimensions (cosmic, biocybernetic, physical) is implicated (Goswami 2004; Mennerich 1979).

Pischinger

Erasure of PIEs from the biocybernetic memory through exposure of associated dysfunctionalities manifesting as symptoms. Exposure via microbes: immune-interactions (inflammation, fever) and fasting (autophagy). Erasing of exposed PIE (chronic blueprint distortions) through acute immne interactions (inflammation, fever) and through targeted functional catalysm (Mennerich 1979).

b) Dimensions of health in systemsecological healing

Following Goswami (2004), physical body forms (cells and organs) are representations of vital body blueprints. This is equivalent to stating that the vital body, termed non-physical morphogenetic fields in modern biology (Sheldrake 2009), provides the blueprint for making physical form. The blueprints of form, being nonphysical and spatiotemporally nonlocal, provide the additional form-making needed for regeneration (*vide* Goswami 2004). Refer also to Laszlo (2014a) on the Akasha paradigm (Table **2.1.2a**: Cosmic-multididimensional information dynamics). Sheldrake (2009) contributed to biology by introducing nonlocal and nonphysical morphogenetic fields in order to explain programs that direct biological morphogenesis.

INVOLVE SHELDRAKE 2009

Stimuli we receive during our lives, especially when repeated, and responses to them produce brain memory (quantum memory of conditioned habit/response patterns of the brain and modifications thereof as we live: Goswami 2004). Here referred to positive or negative quantum memory endograms (negative: patho-information-engrams: 2.1.2a). Inheritance of these modifications of the mind from previous lives (epigenetic engrams), called kharma, has been empirically demonstrated (Goswami 2001, op. cit. Goswami 2004). In the context of systemsecological healing, kharma is not a religion-linked concept, but kharmic law and natural law are both part of cosmic law; applying to non-physical and physical dimensions respectively. **Kharma**: The cosmic law or principle of cause and effect governing the future, involving reward and punishment for the acts performed during succeeding incarnations; causally influencing our destinies (Table 1.1d). It is here conceptualized that, in the cosmic dimension (spatiotemporal concurrency/ubiquity of information) we exist as information entities, whereas in the four-dimensionsional world (three spatial dimensions and time as the fourth dimension) we exist as incarnate beings. As such we are subject to the realization of kharmic and natural laws. In the context of kharma dynamics (interacting cross-dimensional information effects), spatiotemporally unrestricted information availability applies in respect of information entities (*inter alia* genetics, epigenetic engrams, including accumulated patho-information-engram loads, engrams relating to aspirations, social class, character, personality and transgenerational kharmic credits and debt). The realization of kharma dynamics involves construeing optimised conceptual fates on the basis of ubiquitous information availability, as interacting with other information entities and circumstances; subject to cause-effect constraints and possibilities.

TO MASTER LIFE SUBJECT TO BOTH KHARMIC AND NATURAL LAW

As stated by Laszlo (2014a), there is an urgent need to regain contact with the Akashic dimension. The fuller the **conformance with the relevant Akashic blueprint for optimal functioning**, the more robust our health and capacity to resist negative influences will be (Table 2.1.2a).

Positive health is more than the absence of illness (Ryff & Singer 1998). Rather, it should be construed as a multidimensional dynamic process where human well-being is a matter of engagement in living through the expression of a broad range of human intellectual, social, emotional and physical potentialities (Ryff & Singer 1998); having

a sense of purpose towards the realization of one's potential *vide* Aristotle. Positive health centrally involves states of consciousness and understanding allowing for the harmonization of reason, desire and will (Becker 1992, op. cit. Ryff & Singer 1998); that is, brain functional integration of ratio, emotion and instinct (**2.3.1**).

Kharma dynamics is subject to the principle of cause and effect and unless epigenetic patho-information-engrams are erased from the biocybernetic system, associated negative consequences will be experienced during the course of life fulfilling the kharmic pathway of self-realization.

c) Components of systemsecological healing

Consisting of two main components: fever and fasting (autophagy); and acid-base balance, intestinal gealth and sleep quality.

Fever. Fever is a phylogenetically very old phenomenon (Kluger 1979). It occurs in mammals, and also in birds, reptiles, amphibia and fish. Seeking of environments with higher temperature after contact with pyrogens has been established. Kluger (1979) concludes that such million years old energy-expansive reactions (as realized during fever) would not be as widespread today in vertebrates if they did not have an important and useful defensive role in respect of illness conditions. The general ocurrence of fever in vertebrates as immune-function catalyst implicates fever to represent a biological reaction of self-preservation and an adaptive mode supporting survival; thus imparting a selection advantage (Kluger 1979).

Überführung des chronischen Krankheitzustandes in eine Phase akuter Immuninteraktion (siehe unter anderem Scheuerlen 1959, bei nephrotischen Syndrom). Fieber ist ein aktiver Vorgang den der Körper selbst hervorbringt (beinhaltet eine Akutisierung chronischer Krankheitszustände) und sollte nicht mit Hyperthermie gleichgestellt werden (Schmidt 1987). Fieber spielt eine Zentralrolle bei der Löschung von Pathoengramminformation durch fieberhafte Immuninteraktionen mit pathoengrammreflektierenden Mikroben. Ausführliche Erläuterungen zur Fiebertherapie (Heckel 1990: Tabelle 2.1.2a) ist hier nicht gedacht um diese als Allheilmittel darzubieten, sondern um die durchschlaggebende Rolle von Fieber für die Rekursionsheilung offenkundig zu machen. Ansichten und Erkenntnisse über die Rolle

des Fiebers in Gesundheit und Krankheit aus medizingeschichtlicher Sicht (Külken 1985: Tabelle 2.1.2b) und evolutionsbiologischer Betrachtung (Kluger 1979: Tabelle) sind von besonderer Bedeutung. Die Physiologie des 20. Jahrhunderts führte zu einer Renaissance der Sicht von Fieber als Erhaltung- und Wiederherstellungsbestreben des Organismus gegen eingedrungene oder im Organismus selbst entstandene Schädlichkeiten (Külken 1985). Wagner-Jauregg received the Nobel Prize for Medicine in 1927 for his pioneering work on fever therapy (Brown 2000; Karamanou et al. 2013). Göhring (1986) praktizierte pyrogeninduzierte Fiebertherapie mit Erfolg bei Patienten mit malignen und chronisch-entzündlichen Krankheiten. Die konventionelle Medizin blieb jedoch bis heute dem Antipyresegedanken des 19. Jahrhunderts verhaftet (Külken 1985).

DL FEVER-kluger-1998

Tabelle 2.1.2c Heckel (1990) Fiebertherapie: Grundlagen
Ansteigende Körpertemperaturen (bis zu 41°C) im Zusammenhang mit fieberhaften Immunreaktionen gehen einher mit ansteigender Stoffwechselrate, biochemische Abläufe werden induziert bzw. beschleunigt und Reaktionsketten verlaufen eher bis zu den niedrigsten molekularen Endsubstanzen (Heckel 1990). Zellspezifische Funktionsleistungen werden stimuliert, der Verbleib von Stoffwechselzwischenprodukten reduziert und Regenerations- bzw. Reparationstendenzen der Gewebe gesteigert (Heckel 1990).
Schon Von Walter-Jauregg (1927) implizierte die Anregung körpereigene Selbstheilungspotenzen durch Fieber als das wesentliche Element in seinen Heilungserfolgen mit Fiebertherapie.
Durch serielle Abfolge fieberhafter Immunreaktionen (pyrogeninduzierter Fiebertherapie) können langfristig adaptive Reaktionsumstellungen im Organismus eingeleitet werden, das heisst, eine anhaltende Renormalisierung der Reaktionsfähigkeit des Körpers gegen von aussen kommenden Störfaktoren kann erreicht werden. Dauerhafte Heilwirkungen stabilisieren sich bisweilen erst nach 2-3 Monaten (Heckel 1990).
Das Vorkommen von Fieber zeigt eine gute Abwehrlage an. Von Bedeutung in diesem Zusammenhang ist das des öfteren festgestellte Fehlen akuter fieberhafter Infektionskrankheiten in der Vorgeschichte von Krebskranken (Remy et al. 1983). Befragungen bei Patienten mit malignen Tumorerkrankungen ergaben ein statistisch deutlich geringeres Vorkommen von Erkältungskrankheiten, Fieber und infektiöse Organerkrankungen in den vorrausgegangenen 10 Jahren. Berichte über die positive Rolle von hochfieberhaften Infektionserkrankungen für Tumorprävention und Spontanregression/Heilung von Tumoren sollte vermehrte Beachtung finden (op. cit. Heckel 1990). Spontanheilungen von bösartigen Geschwulsten nach interkurrenten fieberhaften Erkrankungen und über ein Drittel histologisch gesicherter Fälle von Spontanremessionen aus der Weltliteratur standen in zeitlichem Zusammenhang mit akuten hochfieberhaften Entzündungen (Selawry 1957 op. cit. Külken 1985).
Anscheinend führt eine erhöhte Stoffwechselumsatzsteigerung dazu dass biochemische Stoffwechselprodukte bis zu den Endprodukten weitergeführt werden und damit einer Anhäufung von metabolischen Zwischenprodukten (Stoffwechselschlacken) entgegenwirkt sowie förderlich ist für eine Herausbeförderung von abgelagerten Stoffwechselschlacken aus bestimmten Geweben (Hecker 1990).
Eine pyrogene Temperaturerhöhung tendiert dazu chronische Entzündungen in ein akuteres Stadium zu überführen. Unter bestimmten Voraussetzungen wird dann das pathophysiologische Ziel der Entzündung (Beseitigung des auslösenden Reizes) vollständiger angesteuert (Heckel 1990).

Chronisch entzündliche Prozesse werden aktiviert und verstärkte Symptomäusserung dadurch induziert (Akutisierung chronischer Krankheitszustände). Klinische Erfahrungen dass im Rahmen einer fieberhaften Zweitkrankheit der Verlauf einer vorbestehenden chronischen Krankheit günstig beeinflusst wird (op. cit. Külken 1985). Heckel (1990) stellt zusammenfassend fest das durch Fiebertherapie stehengebliebene, symptomarme oder symptomlos schwelende Entzündungsprozesse des öfteren einer Ausheilung zugeführt werden können.
Eine immunstimulierende pyrogeninduzierte Fieberreaktion kommt biochemisch durch endogene Pyrogene (Zytokine) zur Wirkung. Die begleitende Temperaturerhöhung (Stoffwechselsteigerung) beim Fieber verstärkt diese immunologische Pyrogeneffekte. Fieber erzeugt eine unmittelbare Stimulierung von Pyrogenen auf das Immunsystem; auch schon bei relativ niedrigen Fiebertemperaturen. (Heckel 1990). Heckel (1990) stellt fest dass Fieber die Immunaktivität auf mehreren Funktionsebenen steigert.
Eine breite Indikationsliste mit positiven Fiebertherapiewirkungen wurde durch Heckel (1990) aus relevanter Literatur zusammengetragen. Diese Auflistung schliesst eine Vielfalt von chronischen und subakuten Krankheitszustände ein in oganspezifischen, infektionsverbundenen, hormondysfunktionellen, gynäkologischen, neurologischen und psychiatrischen Bereichen.
Heckel (1990) stellt zusammenfassend fest: Fieberwirkungen vollziehen sich durch die Aktivierung spontaner Selbstheilungspotenzen und Regulationskräfte in verschiedenen Krankheitsphasen; auch beim Gesunden vor Krankheitseinflüsse schützend.

Tabelle 2.1.2d Külken (1985) Fieberkonzepte in der Geschichte der Medizin

Nach Betrachtung der Geschichte der Fieberlehre identifizierte Külken (1985) vier Grundkonzepte der Fieberanschauung: **Heimsuchung** (Fieber als Tat in den Menschen eingedrungenen Wesens), **Kochung** (Fieber als Erhaltung- und Wiederherstellungsbestreben des Organismus gegen eingedrungene oder im Organismus selbst entstandene Schädlichkeiten), **Entgleisung** (Fieber als bedrohliche Fehlleistung einer gestörten Funktion des Organismus) und **Ertüchtigung** (Fieber als Entwicklungsmittel im Erwerben neuer Fähigkeiten).

1. **Heimsuchung** (Fieber als Tat in den Menschen eingedrungenen Wesens).

Die geschichtlich älteste Grundform der Fieberanschauung. 1. Fieber als Geist und Geissel der Götter (in den Anfängen der Medizin, archaische Medizin) und 2. Fieber als prasitärer Organismus – gezeugt aus der Unvollkommenheit des Menschen (C.G. Carus). Diese viel später entstandene Interpretation beinhaltete bereits die Erkenntnis das relativ gesunde Menschen durch Fieber und Entzündungen befallen werden, derweil bei gesundheitlich Schwächeren Verbildungen (chronische Krankheitszustände) vorherrschen und die ersteren zwei immer weniger ausgeprägt in Erscheinung treten.

2. **Kochung** (Fieber als Erhaltung- und Wiederherstellungsbestreben des Organismus gegen eingedrungene oder im Organismus selbst entstandene Schädlichkeiten).

Fieber als höchste Steigerungsform der Kochung. Fieber wird eine konservative Rolle zugedacht: Wiederherstellung der ursprünglichen Harmonie im Organismus (Anaximander: 611- ca 547 vor Chr.; Hippokrates; Paracelsus: 1495/94-1541; Van Helmont: 1579-1644; E.G. Stahl: 1659-1734; Boerhaave: 1668-1738; Cullen: 1709-1790; Hufeland: 1762-1836; Frank: 1745-1821; Bachhammer; Sydenham: 1626-1689; Hoffmann: 1660-1743; Reil: 1759-1813; Schönlein: 1832; Canstatt: 1854; Heidenhain: 1845; Liebermeister: 1870; Aronsohn 1910; Von Wagner-Jauregg 1927; Selawry 1957; MacPherson 1959; Marat 1979; Banet 1981; Schmidt 1987).

Unter dem Denkansatz der Kochung wurden verschiedene Phasen/Verständnisformen identifiziert (Külken 1985).

- Grundentwicklung des Denkbildes der Kochung im Corpus Hippokraticum.

Ausgehend von der Säftelehre ist der Körper gesund wenn gewisse Körpersäfte sowie Blut, Schleim, gelbe und schwarze Galle im richtigen Mischungsverhältnis zueinander stehen (Eukrasie). Krank ist der Mensch wenn dieses Mischungsverhältnis in Unordnung gerät (Dyskrasie). Die innere Bewältigung dyskrasischer Säfte wird dann durch Kochung angestrebt, mit Fieber als die höchste

Steigerunsform der Kochung. Dem Fieber wurde eine Rolle zugedacht in der Wiederherstellung der ursprünglichen Harmonie im Organismus.

- Der fiebernde Mensch als eine Weltenküche im Kleinen.

Jener Wesensbereich des Menschen der die Lebensfunktionen umfasst wird von Paracelsus als eigenständiges Wesen im Menschen angesehen (Archeus), eine Kraft von oben repräsentierent. Fieber entsteht wenn Archeus eingreft um Schlacken aus dem Organismus zu entfernen.

- Die Kochung als überlegtes Einwirken der Seele auf den Leib durch übernatürliche Kräfte.

Nach van Helmont hat der Mensch den Fluch der Erbsünde auf sich gezogen und damit die Kapazität verloren sich von aussen kommende Krankheitsveranlassern ganz zu verschliessen. Die Ursache von Fieber sah van Helmont als Kampf des Archeus gegen die krankheitsveranlassende Materie. Im Sinne van Helmonts ergibt die Fähigkeit des Leib und Seele verknüpfenden Archeus Fieber zu erzeugen die Möglichkeit die körperlichen Konzequenzen des Abfalls der Menschenseele vom göttlichen Urbild rückgängig zu machen und im Leib den gottgewollten (gesunden Zustand) wieder herzustellen (op. cit. Külken 1985). Fieber wurde gesehen als Kampfwerkzeug eines intelligent waltenden unsichtbaren Prinzips. Nach Hufeland sollte nicht vergessen werden dass bei jedem Fieber die Naturkraft das eigentliche Heilungsprinzip ist und das Fieber selbst der Heilungsprozess. Bachhammer: Fieber als Gesundungsversuch (op.cit. Külken 1985). Canstatt: Das Fieber ist nicht die Krankheit selbst sondern die Reaktion auf die angreifende Noxe. Die Reaktion hemmen zu wollen wäre unsinnig.

- Enthmythologisierung der menschlichen Eigenwärme. Descartes (1596-1650) hielt es nicht für erforderlich zur Erklärung der Lebensvorgänge (Fieber) eine vegetative oder sensitive Seele anzunehmen.
- Kochung als Reaktionsautomatismus in einem rein naturgesetzlich funktionierenden Körper. Reil: Fieber als Reaktionsmechanismus mit Heilwirkungen. Heidenhain: Fieber als naturgesetzlich ablaufende Reaktion auf einen Krankheitsreiz, mit resultierenden Heilwirkungen, die der Arzt nicht stören sollte.
- Veranlassungen und Funktionen des Fiebers in der experimentellen Physiologie des 20. Jahrhunderts. Zunehmende naturwissenschaftliche Forschungsergebnisse (Hensel 1980: op. cit. Külken 1985). Regelmechanismen sorgen für die Erlangung und Konstanthaltung einer erhöhten Sollwert-Körpertemperatur im Fiebergeschehen (MacPherson 1959 op. cit. Külken 1985). Exogene fieberveranlassende Pyrogene (in Bakterien, Pilzen, Viren) veranlassen die Aktivierung endogener Pyrogene. Die Fieberantwort steht damit dem Körper prinzipiell zur Verfügung als eine biologische Selbstbehauptungsreaktion. Differenzierte Ergebnisse wurden erstellt. Die Vermutung das Fieber und Hyperthermie in ihrer Wirkung auf die Abwehrkräfte nicht identisch sind wurde bestätigt und das Fieber unabhängig von thermischen Wirkungen zusätzliche zur Krankheitsabwehr günstige Eigenschaften besitzt (Schmidt 1987). Steigerung von Immunreaktionen bei pyrogeninduziertem Fieber (Marat 1979 op.cit. Külken 1985). Die zur Wärmevermehrung führende Stoffwechselsteigerung bringt im wesentlichen die positiven Fieberwirkungen zustande und nicht unbedingt die erhöhten Körpertemperaturen. Bei experimentell infizierten Ratten war die Überlebensrate positiv korreliert mit der Stoffwechselsteigerung, aber negativ mit der Temperatursteigerung (Banet op.cit. Külken 1985). Positive Effekte parafebriler Reaktionen (mit endogenen Pyrogenen als Mediatoren) bei der Infektabwehr wurden experimentell nachgewiesen. Fieber als ein mit dem Immunsystem integrierter Prozess zur Entfernung externer und interner Pathogenagenzien (Külken 1985).

3. **Entgleisung** (Fieber als bedrohliche Fehlleistung einer gestörten Funktion des Organismus). Fieber als Gleichwichtsstörung/ Fehlleistung (Funktionsstörung/Normabweichung).
    - Fieber als Gleichgewichtsstörung (op.cit. Külken 1985): Galen (129-199 AD); Ali Ibn Rabban (ca 850); Avicenna (980-1037); Sylvius (1478-1555); Brown (1736-1788) und Reich (1800).
    - Fieber als Fehlleistung (op.cit. Külken 1985): Bellini (1643-1704); Clark (1744-1802); Virchow (1821-1902); Liebermeister (1875).

Therapeutische Konsequenzen der Antipyretischen Welle im 19. Jahrhundert. Die Unterdrückung der erhöhten Temperatur (Fieber als Krankheit an sich) rückte in den Mittelpunkt ärztlichen Denkens (*vide* Virchow und Liebermeister) und blieb bis heute das Paradigma der konventionellen Medizin (Külken 1985).

4. **Ertüchtigung** (Fieber als Entwicklungsmittel im Erwerben neuer Fähigkeiten).

Unter dem Denkansatz der Ertüchtigung wurden verschiedene Phasen/Verständnisformen identifiziert (Külken 1985).

- Krankheit als Ferment der Entwicklung (Novalis 1772-1801). Freiherr von Hardenberg (Novalis) vertrat die Anschauung dass die Krankheit das entscheidende Entwicklungsprinzip ist des Schicksals einzelner Menschen sowie aller Evolution (Prinzip: Reifung des Menschen an einer Krankheit).
- Die Wandlungsmacht des Fiebers als Erfahrung (Reil 1759-1813). Reil sah Fieber nicht nur als leiblich bedingter Reaktionsmechanismus mit Heilwirkungen, sondern berichtete auch von Ertüchtigungsphänomenen unter dem Einfluss vom Fieber in körperlichen und geistig-seelischen Bereichen (positive Temperamentsveränderungen; Wachstumförderung, Entwicklungsschübe).
- Fieber als Anstoss zu gewinnbringender Eigentätigkeit des Organismus (Carus 1779-1868). Bei der Entstehung der Krankheit ist die Unvollkommenheit in der Konstitution des Menschen beteiligt. Das Fieber wurde gesehen als Urphänomen im Wechselspiel zwischen der Idee des Organismus und der Krankheit; wobei durch Fiebererkrankungen gesunde Verhältnisse wieder angestrebt werden. Nach überstehen organisch verlaufender fieberhaften Krankeiten wurde regelmässig ein Aufblühen beobachtet. Jede rein verlaufende Krankheit kann zu einer Regeneration führen durch das Ersetzen ausgestossener organischer Substanz mit ätherischer Substanz im Sinne der Idee des normalen Organismus (Carus op.cit. Külken 1985).
- Fieber als ein Erlernen seelischer Fähigkeiten an eigens dafür vom Menschen angestrebte Krankheiten (Steiner 1861-1925).

Krankheit und Selbstheilung in Beziehung zum Karma (Steiner): Nach karmischen Gesetzmässigkeiten wird Fieber als ein Selbstheilungsvorgang verstanden, durch welcher, unter den Bedingungen leiblicher Unzulänglichkeiten, eine Ich-Ertüchtigung des Menschen zu seinem Fortschritt selbst angestrebt wird. Jeder seine Krankheit in diesem Sinne begreifend wird für therapiebedürftige Fieberzustände eine Behandlung suchen die den gewollten Lernprozess nicht ausschliesst (Zusammenfassende Interpretation durch Külken 1985).

REFEREENCE TO THE KHARMIC DYIMENSION Krankheit und Selbstheilung in Beziehung zum Karma (Steiner): Nach karmischen Gesetzmässigkeiten wird Fieber als ein Selbstheilungsvorgang verstanden, durch welcher, unter den Bedingungen leiblicher Unzulänglichkeiten, eine Ich-Ertüchtigung des Menschen zu seinem Fortschritt selbst angestrebt wird. Jeder seine Krankheit in diesem Sinne begreifend wird für therapiebedürftige Fieberzustände eine Behandlung suchen die den gewollten Lernprozess nicht ausschliesst (Zusammenfassende Interpretation durch Külken 1985: Table 2.1.2d).

Säure-Basen-Gleichgewicht.

Acid-base balance. Health benefits of net base-yielding diet: including prevention and treatment of osteroporosis (Sebastian et al. 1994), age-related muscle wasting (Bushinsky 1996 op. cit. Cordain et al. 2005), hypertension and slow progression of age- and disease-related. Alpern & Sakhaee (1997).

chronic renal insufficiency (op. cit. Cordain et al. 2005). Mahajan et al. (2010): ACIDOSIS-ballmer

Chronic metabolic acidosis

DL ACIDOSIS-drochioiu-cachexia

Rekursionsheilung dreht sich um die Löschung von Patho-Engrammablagerungen und impliziert damit auch Schlackenlösung und Ausleitung. Chronische Übersäuerung ist primär das Result von katabolischen Prozessen (beschleunigter Gewebeabbau) im Rahmen von Rekursionsselbstheilungsversuchen des Körpers zum Abbau/Löschung von eingelagerten Pathogramminformationslagen. Fungal parasites prosper under acid conditions (milieu) and the presence thereof in the body is a typical sign of substantial path-information engram-loading (PIE loading). Sekundär spielt die Einnahme von säurelastigen Ernährungsmitteln eine Rolle. Übersäuerung ist demnach ein Symptom der Rekursionsheilung (primary causality), aber auch Ursache gesundheitsschädigender Einwirkungen (secondary causality). Furthermore, ketogenic diets boost catabolic processes, thereby potentially contributing to metabolic acidosis (McCarthy et al. 2015). Die Unterstützung eines funktionstüchtigen Säure-Basen-Haushalts (Tabelle 2.1.2c: Jentschura & Lohkämper 2014) ist infolgedessen von zentraler Bedeutung für erfolgreiche Rekursionsheilung. Zwei (gleichzeitig verlaufende) Phasen können identifiziert werden: 1. Exponierung der Pathogeninformationseinlagerungen durch Gewebe-Abbau (katabolischer Zellverfall/Eiweissabbau: Fasteneffekte). Die überschüssig anfallenden Säuren und Gifte werden neutralisiert zu Salzen (Verbrauch von Mineralreserven) die dann als Schlacken abgelagert werden (Jentschura & Lohkämper 2014). In Phasen aktiver katabolischer Prozesse (Fasteneffekte) werden die Schlacken wieder abgebaut/gelöst. 2. Schlackenausleitung. Gelöste säurelastige
Schlacken werden ausgeleitet im basischen Milieu (Basenfluten). Es ist zu beachten dass Säure- sowie Basenfluten von gleichsamer Wichtigkeit sind für gesundheitsfördernde Körperfunktionen und Entschlackung (Die volle Amplitude von Säure- und Basenschüben muss erhalten bleiben). Eine systemische Alkalose ist demnach genauso schädlich wie eine Azidose die nicht effizient zur Ausleitung kommt.

In order to neutralize acidity in the body the consumption of water with high alkalinity (water with the ability to withstand changes in acidity, i. e. with a high buffering capacity). Such alkaline water has a different viscosity and surfice tension (high alkalinity with a high amount of high active hydrogen, with a negative redox potential) and produces more oxygen in the body; reducing tissue acidity (Redfern 2009). Through the intake of alkaline water, the body increases its ability to absorb water because of its low surface tension. Wastes and toxins are then flushed out easier (Drs Henri Coanda and Patrick Flanagan op. cit. Redfern 2009). Water with a low

surface tension is crucially important; if too high, waste removal is inefficient (*re* Nobel Prize Winner 1912 Alexis Carrel op. cit. Redfern 2009).

Tabelle 2.1.2e Säure-Basen-Gleichgewicht (Jentschura & Lohkämper 2014)

(In dieser Tabelle wird eine Zusammenfassung von Jentschura & Lohkämper 2014 dargeboten. Es wird jedoch empfohlen dieses Buch in seiner Gesamtheid zu studieren. Es ist erhältlich in den folgenden Sprachen: Deutsch, Englisch, Russisch, Französisch, Polnisch, Spanisch, Italienisch, Niederländisch, Ungarisch, Lettisch, Slowenisch und Tschechisch)

Die Funktionstüchtigkeit des Bindegewebes ist nur gewährleistet wenn es in Intervallen mit Säuren und Laugen gefüllt und wechselseitig von diesen entleert wird (Säure- und Basenfluten: Prof. em. Friedrich Sander, op. cit. Jentschura & Lohkämper 2014).

Stoffwechselprozesse funktionieren in einem Fliessgleichgewicht zwischen Säuren und Basen. Ein geregelter Stoffwechsel im Körper erfordert ein annäherndes Gleichgewicht zwischen Säuren und Basen (weder Azidose noch Alkalose: durch z.B. ein fortgesetztes, einseitiges Überangebot von basischen Substanzen wie Natron).

Drei Teilbereiche der Grundregulation:

- Regulation des Säure-Basen-Haushaltes. Der Säure-Basen-Haushalt hat die wichtige Aufgabe des Abfilterns und der Ausscheidung von Stoffwechselschlacken (vor allem durch Eiweissabbau anfallende Stoffwechselschlacken).
- Regulation des Wasse
- rhaushaltes. Wasser wichtig als Lösungsmittel für die Ausscheidung von Stoffwechselschlacken.
- Regulation des Mineralhaushaltes (Elektrolythaushalt). Mineralstoffelektrolyten braucht der Körper zur Neutralisierung von stoffwechselanfallenden Säuren. Bei eimem entschlackungsbedingten Übermass anfallender Säuren werden die Mineralstoffreserven des Körpers verbraucht bzw. entleert. Anfüllung von neutralisierungsfähigen Mineralstoffen ist angezeigt.

Die Neutralisierung übermässig anfallenden Säure verbraucht Mineralstoffe/Elektrolyte (vorzeitiges Altern, Herzinfarkt. Schlaganfall auf der Grundlage einer Azidose: Schlaganfall als Säurekatastrophe im Gehirn).

Schlacken sind neutralisierte und dann abgelagerte Säuren und Gifte. Basenbildende Mineralstoffbestände werden abgebaut zwecks Neutralisierung von Säuren im Blut durch Salzbildung. Selbstheilungsmechanismen des Körpers versuchen einen Säureüberschuss durch Salzbildung (Mineralstoffverzehr) zu neutralisieren. Noch bevor Organschäden erkennbar sind machen sich die verhärteten Schlacken als Gelosen im Bindegewebe bemerkbar (op. cit. Jentschura & Lohkämper 2014; siehe auch Preusser 1987).

Säureträchtige Gewebedeponierungen entleeren sich vornehmlich nachts.

Dreisprung der Entschlackung: 1. Schlackenlösung (Kräutertee, Obstessig). 2. Säureneutralisierung (Mineralstoffe). 3. Säure und Schlackenausleitung (Basische Körperplege, Wasser). Alle drei Schritte sind parallel durchzuführen.

Entschlackung im Dreisprung: Lösung von Schlacken; Neutralisierung und Ausschwemmung/Ausleitung

- Lösung von Schlacken.

Die Auflösung abgelagerter Salze durch die Wiedererweckung bislang neutralisierter Säuren und Gifte im Rahmen von katabolischen Stoffwechselprozessen (zuweilen als Heilkrisen manifestierend ausgelöst durch Fasteneffekte). Heilkrisen, Fastenkrisen oder Erstverschlimmerungen (Homöopathie) reflektieren eine Überschwemmung der Körperflüssigkeiten mit gelösten Säuren und Giften. Schlackenlösung durch Teetrinken (Kräutertee, Obstessig, Apfelessig).

- Neutralisierung.

Neutralisierung der wiedererweckten Säuren und Gifte durch Überversorgung mit energiereichen Mineralstoffen (Nahrunsergänzungsmittel als Lieferant energiereicher Mineralstoffe, Spirulina, Gemüsesäfte). Mineralische Neutralisierungshilfe für die Flüssigkeiten und Sekrete des Organismus.

- Ausschwemmung/Ausleitung.

Basisch unterstützste Ausleitung von Säuren und Giften über die Oberhaut und Schleimhäute. Basische Einläufe. Basentrunk und basische Körperpflege (Entgiftung durch die Haut: basische

Bäder verschiedener Art). Wasser als Transportmedium zur Ausschwemmung gelöster Schadstoffe und erneut neutralisierter Säuren (weiches mineralstoffarmes Wasser).
Stoffwechselprozesse führen zu der Entstehung von hauptsächlich sauren Endprodukten. Mit fortschreitender Übersäurung werden die basenbildenden Mineralstoffbestände abgebaut im Zuge einer Säureneutralisierung via Salzbildung (Säureschlacken). Wenn die Mineralstoffreserven erschöpft sind werden überschüssige nichtausscheidbare säurelastige Schlacken im Binde- und anderen Geweben abgeladen. Auch beim gesunden Stoffwechsel entstehen saure Endprodukte, vornehmlich beim Abbau von Proteinen.
Die neutralisierte Verbindung eines Mineralstoffes mit einer Säure oder einem Gift führt zu chemisch neutralen Salzverbindungen (Schlacken). Solche vom Körper sinnvoll gebildete Neutralsalze werden durch Ablagerung zur Schlacke. Jede Schlackenlösung ist eine Feisetzung von bis dahin gebundener Säuren oder Giften. Diese müssen als ausscheidungsfähige Neutralsalze durch die Nieren oder über die Haut ausgeschieden werden. Eine parallele Schlackenlösung und Neutralisierung gelöster Säuren (Mineralstoffverzehr) ist erforderlich für eine effiziente Entschlackung. Schlackenlösung ist die Auflösung abgelagerter Salze (Wiedererweckung bislang neutralisierter Säuren und Gifte).
Bei Gelegenheit versucht der Körper durch Selbstheilungsversuche mit Heilfieber diese Schlacken zu bereinigen. Das gelingt wenn solche Aufräumungsprozesse nicht durch Medikamente, z. B. Antibiotika, gestört werden.
Zivilisationskrankheit Azidose (Körperübersäuerung): Ablagerung von kristallisierten Säuren in die Blutgefässen, Gelenken, Bindegewebe, Fettgewebe und Lymphgefässen. Selbstheilungsneutralisierung durch Salzbildung = Mineralstoffverzehr (Entmineralisierung von Kniochen, Nägel, Zähne, Haarboden). Verhärtete Schlacken: Gelosen im Bindegewebe, Kristalle an den Gelenken und Wirbeln. Säureablagerungen: Schädigungen der haarfeinen Nervenenden entlang der Wirbelsäure (Muskel und Gliederlähmungen da Impulse von und zum Gehirn gestört werden) und erstarrende Rote Blutkörperchen (hoher Blutdruck). Erhöhte Cholesterienwerte: Säureüberschuss = Mineralraub-Kalziumentnahme aus den Gefässwänden = reichliche Cholesterinproduktion als Ersatz für das verlorene Kalzium zum Schutz der Gefässwände (Erhaltung der Dichtigkeit und Elastizität der Gefässwände).
Natriumfluoriedvergiftung = Gehirngift: Fluoridiertem Trinkwasser, Fluoridierung der Zähne (Zahnpasta). Nach nahmhaften Wissenschaftlern (*vide* Jentschura & Lohkämper 2014) Natriumfluorid schädigt eine bestimmte Region im Gehirn wo der individuelle Behauptungswille angesiedelt ist. Chlor als materielles und energetisches Gift: Chlorierung von Trink- und Badewasser.
Erhöhter Blutdruck. Angesäuertes Kapillarblut → Erythrozytensteife → Durchblutungsstörungen. Mit erhöhtem Blutdruck werden unelastisch gewordene Erythrozyten durch die Kapillargefässe geschoben. Bei weiterer Erythrozytenversteifung sackt der Blutdruck dann scheinbar grundlos ab (Sinnvolle Massnahme um Thrombosen, Embolien, Herzinfarkte und Schlaganfälle zu vermeiden).
Die Frau entschlackt/entsäuert regelmässig während den Monatsblutungen. Sie kann Säuren parken und dann via den Uterus ausscheiden. Die Frau entschlackt via Uterus: Ausscheidungen, Ausflüsse, Monatsblutungen 'Entsorgung' in das Embryo und Fruchtwasser. Der Mann muss anfallende Säuren und Gifte sofort neutralisieren (Androgene transportieren Schlacken in den Haarboden).
Wechseljahre. Hitzewallungen und Schwitzen: Diese repräsentieren fieberartige Prozesse um die, wie in der Kinderzeit, angehäufte Gifte und Säuren abzubrennen. Hormonbehandlung: Bei vielen Frauen kommen die Regelblutungen nicht wieder in Gang. Die Hormontherapie veranlasst aber den Körper anzunehmen das der frühere Weg zur Entschlackung via Uterus und Umgebung wieder zur Verfügung steht. Auf Grund eines so fehlinformierte Stoffwechsels werden Giftstoffe und Stoffwechselschlacken dann so wie früher kanalisiert, oft Unterleibskrebse verursachend in darauffolgenden Jahren. Da zuweilen wieder eintretende Regelblutungen ja nicht unbedingt bis ins hohe Alter durch eine Hormontherapie unterhalten werden sollen wird die Therapie abgebrochen. Ein Verfallen in tiefe Depressionen resultiert dann des öfteren.
Basen und Säurefluten. Basen: 04.00 (stark), 10.00 (mässig), 16.00 (stark) und 22.00 Uhr (mässig). Zu diesen Zeiten sind neutralisierende und ausleitende Basengetränke einzunehmen (nicht kurz vor und nach dem Essen). Säure: 01.00 (mässig), 07.00 (stark), 13.00 (mässig) und 19.00 Uhr (stark). Schlackenlösung mit Essigsäure. Einzunehmen mit den drei Säuretakten des Körpers: 7.00, 13.00 und 19.00 Uhr (Ein Teelöffel auf ein Glass Wasser).

Pilzerkrankungen als Folge von Azidose. Bei Mykosen ist der Basentrunk (Natron: Natriumhydrogenkarbonat) sowie das Trinken von bis zu 1.5 Liter Wasser von besonderer Wichtigkeit.

Darmgesundheit. Darmgesundheit ist die Grundlage effizienter Verdauung und damit von zentraler Bedeutung für alle Heilungsprozesse. Rusch et al. 1985: Immunsystem.

Wright & Lenard (2001): Hydrochloric acid is secreted by special cells in the lining of the stomach in response to a meal. This is a key upstream link precipitating a downstream cascade of digestive events, culminating in the absorption of vital nutrients. When this downstream chain of events is disrupted by insufficiency of stomach acid, proper digestion and health of the gastrointestinal system is compromised; leading to multiple health problems.
Although we have an age-related decline in stomach acid, disorders generally attributed to too much acidity (heartburn, gastroesophageal reflux disease: GERD, with symptoms such as heartburn, belching, upset stomach, bloating/gas, sense of fullness, chronic cough, regurgitation, hoarseness, difficulty swallowing, sore thoat) increase with age, implicating that too high stomach acid levels may not be causally involved in these disorders, but rather too little thereof. Low stomach acid levels are disproportionally involved in indigestion and numerous serious diseases. Correcting digestive malfunction (ongoing acid supplements with meals) often results in pronounced improvements in many diseases. Thus the best way to treat 'acid indigestion' is not with less stomach acid, but almost always with more (Wright & Lenard 2001).

Major roles of stomach acid: Acid promotes the digestion and absorption of many vital nutrients, helps to digest protein by stimulating pepsin production and prevents bacterial and fungal overgrowth.

Acid promotes the digestion and absorption of many vital nutrients.
Stomach acid optimises gastric pH and triggers the action of pepsin for the effective digestion and thus absorption of *inter alia* the peptide and amino acid components of proteins, minerals (such as iron, copper, zinc, calcium, magnesium?), vitamin B_{12} and folic acid. Low stomach acid levels result in incomplete digestion and poor nutrient absorption. Over time the associated selective malnutrion adversely affects vital bodily functions; leading to diseases such as anemia, osteoporosis, cardiovascular diseases, depression and others. Blocking/neutralizing stomach acid disrupts the normal digestive cascade by removing the acid trigger which is required for subsequent digestive events to take place efficiently. Reduced acid also implies less pepsinogen, less pepsin, less secretin, less cholecystokinin, less panchreatic enzymes and less bile. When the digestive system is perfectly tuned, acid, pepsin, gastrin, bicarbonate and other substances are secreted at the right times and in appropriate amounts to regulate the pH environment for optimal food digestion and nutrient absorption. Insufficiency of stomach acid is associated with poor absorption of iron, calcium, zinc, folic acid, vitamin B_{12}, folate, vitamin B_6 and others, essential amino acids tryptophan, phenylalanine, non-essential tyrosine (required for the production of serotonin and norepinephrine) and implicated in the etiology of disorders linked to the relevant nutrient deficiencies. Iron (iron deficiency anemia), calcium (osteoporosis), folic acid (birth defects), vitamin B_{12} (asthma, pernicious anemia), zinc (Some studies have

linked low levels of zinc to macula degeneration due to age and antacids); other nutrients: Vitamins B_6, A, E, B_1, B_2, B_3 and neurotransmitters (depression, neurodegenerative disorders; low stomach acid → reduced absorption of essential amino acids → neurotransmitter: serotonin, norepinephrine deficiency → depression). Absorption of nutrients bound to proteins and protein themselves will be inhibited by gastric acid insufficiency. Reversing B_{12} deficiency: supplementation with HCl, pepsin, intrinsic factor. Injections with vitamin B_{12} and other B vitamins in the elderly. Best absorbed form of supplemental zink is zinc picolinate.

Acid helps to digest protein by stimulating pepsin production.
The secretion of the enzyme pepsin is triggered by the secretion of stomach acid and required for optimum initial digestion of protein. Depressed stomach acid levels and thus low pepsin levels lead to proteins not being broken down into their component amino acids and peptides (two or more linked amino acids). Deficiency of many essential (phenylalanine, tryptophan) and even non-essential (tyrosine) amino acids can result in chronic depression, anxiety, insomnia and other long-term disorders. Incompletely digested proteins ('foreign' proteins) may somehow enter the bloodstream, evoking an immune response and resulting in allergies and autoimmune diseases (such as lupus, rheumatoid arthritis, type 1 diabetes) and others (typically associated with low levels of stomach acid, poor digestion).

Diseases commonly associated with stomach acid deficiency: Acne rosacea, *Addisons disease*, allergic reactions, *celiac disease*, *childhood asthma*, *chronic autoimmune hepatitis*, *diabetes (type 1 juvenile)*, excema, gallbladder disease, *Grave's disease (hyperthyroid)*, *lupus erythematosus*, macular degeneration, multiple sclerosis, *myasthenia gravis*, osteoporosis, *pernicious anemia*, *polymyalgia rheumatica*, Reynaud's syndrome, rheumatoid arthritis, *scleroderma*, *Sjögrens syndrome*, *ulcerative colitis*, *vitiligo*. The listed diseases shown in italics, although being quite different and with diverse symptoms, share common features on the genetic and molecular level. A common thread of these diseases is some dysfunctionality of the upper gastrointestinal tract. Improvements are readily experienced through restoring normal gastric function (with specific reference to asthma: replacement of HCl and pepsin, minimize/eliminate of food allergies, supplementation with magnesium and vitamin B_{12} & B_6).

In infants, an allergy to cow's milk may cause gastroesophageal reflux (Miloco et al., op. cit. Wright & Lenard 2001; Iacono et al., op. cit. Wright & Lenard 2001) and be involved in type 1 diabetes in some infants (Paronen et al. 2000; op cit. Wright & Lenard 2001). Investigators found impaired gastric acid secretion in cow-milk intolerant infants also leading to atrophic gastritis (Kokkonen et al., op. cit. Wright & Lenard 2001).
The gastrointestinal tract forms an extention of the outside world and one of its chief functions is to keep undigested proteins in the bowels, thus 'outside' of the body. Milk or other allergenic proteins undigested or partly digested as a result of hypochlorhydria or achlorhydria trigger inflammatory reactions which damage the intestinal lining, leading to intestinal hyperpermeability (Gardner, op. cit. Wright & Lenard 2001; Walker, op. cit. Wright & Lenard 2001). Foreign proteins crossing the intestinal barriers generally result in allergenic reactions and even autoimmune responses/diseases (including rheumatoid arthritis, lupus erythematosus, multiple sclerosis, ulcerative colitis and others). In this context, an elevated gastric pH

interferes with protein digestion and allows bacterial overgrowth which, in combination, promotes gut leakage. The efficient digestion of protein by pepsin into amino acids requires a gastric p H of < 3. Autoimmune diseases manifest in various forms, including Goodpasture's syndrome (lung and kidney), Hashimotos thyroiditis and Graves' disease (thyroid gland), systemic lupus erythematosus (connective tissue), rheumatoid arthritis (joints), scleroderma (skin and connective tissue), glomerulonephritis (kidneys), type 1 diabetes (pancreas), Sjogren's syndrome (eyes, tear glands, salivary glands, connective tissue, joints), inflammatory bowel disease (gastrointestinal tract), multiple sclerosis (nerve tissue), and others. Shared symptoms of various autoimmune diseases are observed (Reunala & Collins, op. cit. Wright & Lenard 2001). Focusing on symptom suppression through anti-inflammatory drugs, conventional medicine has ignored the research indicating the involvement of stomach acid deficiency in autoimmune diseases (Henriksson et al., op. cit. Wright & Lenard 2001). Connection of low stomach acid and rheumatoid arthritis (Marcolongo & Bayeli, op. cit. Wright & Lenard 2001). The mainstay of treatment of any autoimmune disease program is the identification, elimination, and desensitisation of food and other allergies (Haugen et al. 1999; Wright & Gaby, op. cit. Wright & Lenard 2001); as well as the examination for and treatment/correction of low stomach acid and other digestive malfunction.

Acid promotes prevents bacterial and fungal overgrowth.
Stomach acid kills bacteria ingested (gastric barrier) and counteracts bacterial overgrowth. Bacterial overgrowth as a result of low stomach acid can disrupt absorption pathways resulting in stealing of vitamin B_{12} by bacteria, blocking fat absorption (bacteria breaking down bile salts), carbohydrate malabsorption, water and nutrient loss (bacterial overgrowth causing chronic diarrhea). Acid-suppresssing drugs promote bacterial overgrowth. Human volunteers could increase their risk of cholera infection by first taking a dose of sodium bicarbonate (Cash et al., op. cit. Wright & Lenard 2001). Once established in the stomach *Helicobacter pylori* it becomes a serious health threat: as leading cause of atrophic gastritis, gastric and duodenal ulcers, and a risk factor for gastric adenocarcinoma and lymphoma (op. cit. Wright & Lenard 2001). Elevated pH, as an unnatural associated with disease (e.g. *H.pylori* infection, atrophic gastritis) is an important risk factor for gastric carcinoma (mechanisms: raising gastrin levels, bacterial overgrowth).

(Davis 1972: deficiency in stomach acid hydrochloric acid, pantothenic acid: adrenal exhaustion), MS: REFLUX CH 7	
STOMACH ACID	
Richardson et al. (1976) MS GASTRIC ACID-richardson	

MICROBIOTA-clemente

MICROBIOTA-wang

MICROBIOTA-wang-2017

MICROBIOTA-thorburn

MICROBIOTA-david

MS GUT-kalliomaki-probiotics

MS GUT-moore re stress

MS GUT-blaut-intestinal microbiota

GUT-flora-guarner

GUT-edwards-postnatal

Dethlefsen et al. (2007): Increasing knowledge has been emerging about commensal and mutualistic microorganisms of humans (Eckburg et al. 2005, op. cit. Dethlefsen et al. 2007; Palmer et al. 2007, op. cit. Dethlefsen et al. 2007; Zoetendal et al. 2001, op. cit. Dethlefsen et al. 2007), as well as human pathogens (e.g. Wirth et al. 2006, op. cit. Dethlefsen et al. 2007). Researchers are finding that host-microbe interactions are essential to many aspects of mammalian physiology, ranging from metabolic activity to immune homeeostasis (Bäckhed et al. 2004, op. cit. Dethlefsen et al. 2007; Cash et al. 2006, op. cit. Dethlefsen et al. 2007; Guarner et al. 2006, op. cit. Dethlefsen et al. 2007; Kelly et al. 2004, op. cit. Dethlefsen et al. 2007; Mazmanian et al. 2005, op. cit. Dethlefsen et al. 2007; Rakoff-Nahoum et al. 2004, op. cit. Dethlefsen et al. 2007). A comprehensive review is presented on the ecology and evolution of human-microbe mutualism and disease.

DL GUT-fuller-probiotics

Magensäure (Wright und Lenard 2001)

GUT-wan

PREBIOTICS-raposo

Tabelle 2.1.2f Darmgesundheit (Rauch 1986)	
Die Folgen von Darmträgheit (funktionelle Insuffizienz im Darmtrakt): • **Bildung von Zersetzungsgiften** (Entstehung im trägen Darm von Zersetzungsgiften, Gärprodukte und Fäulnisstoffe: teilweise Rückvergiftigung derselbigen) • **Dysbakterie** (Eine unphysiologische Bakterienbesiedlung des Darmes stört bestimmte Stoffwechselvorgänge und Immunfunktionen. Normale Darmbakterien stärken die Grundgesundheit, vernichten Krankheitskeime und erzeugen nützliche Stoffe wie Vitamine) • **Erkrankungen des Verdauungsapparates** (Darmträgheit geht einher mit verschiedenen Krankheiten im Verdauungstrakt und wird impliziert als Vergiftungsquelle und damit ursächlich beteiligt bei vielerlei Krankheiten im Gesamtorganismus) • **Verschlackung des Körpers** (Wenn der Darm seine Aufgabe das Blut zu reinigen nur unzureichend erfüllt kommt es zu einem Rückstau von Stoffwechselabfällen; was eine Art Selbstvergiftigung zur Folge hat. Die rückgestauten Schlacken werden dann in verschiedenen Körpergeweben abgelagert. Chronische Krankheitsherde)	

• **Verschlechterte Ernährung aller Körperzellen** (Schlecht ernährte Zellen und Körperorgane bedeuten verminderte Funktionseffizienz; zum Beispiel: schlecht ernährte Hirnzellen haben Vergesslichkeit zur Folge) • **Negativauswirkungen auf die höheren Seelenkräfte des Menschen** (Selbstvergiftung durch den Darm erstreckt sich auf den ganzen Körper und damit auch jene Teile des Nervensystems welche als organische Grundlage dienen der Vorgänge des höheren Seelenlebens. Rückvergiftungen können seelische Regungen und Empfindungen stören; mit vielfaltigen Negativfolgen: Seelische Verflachung in allen Lebensbereichen, Ignorierung bisheriger Ideale, seelische Lieblosigkeit, verstärkter Egoismus und Materialismus) • **Darmträgheit macht hässlich** (Abnorme Körperhaltung zum Schutz geschädigter Verdauungsorgane; Darmgifte als Hautschädiger) • **Darmträgheit macht alt** (Arterienverkalkung: der Verkalkungsprozess wird durch Darmträgheit als Hauptursache der Verschlackung gefördert. Die Leistungsfähigkeit der Hormondrüsen: Hirnanhang, Schilddrüsen, Geschlechtsdrüsen, Nebennieren, usw. wird durch den Grad ihrer Vergiftung beeinträchtigt)	
Trudel 1983	
Rusch et al. 1985	

The intestinal-lymphatic system is the central arena of interactive ethiological processes in acute and chronic disease, as well as pre-clinical pathological processes leading up to disease states later on (Weiss 1990). The intestinal-lymphatic system, if overtaxed by being confronted with an overload of metabolic products from overeating and ingested antigens, becomes weakened and its capacity for detoxification is diminished. Even otherwise tolerated food items (grain and milk products) are then received by the body as immunotoxic. The therapeutic protocol to regenerate the intestinal-lymphatic system to its full functional efficiency and detoxification capacity involves several elements (Weiss 1990). General dietary considerations include the avoidance refined carbohydrates, fructose and dairy products. In contrast to current anti-grain considerations (Weiss 1990) considered whole-grains important ingredients of a healthy diet, whereas sugar and cow milk is to be avoided (cow milk clogs the lymphatic system). The inflammatorily compromised stomach-intestinal tract has to be recuperated and its peristaltic vitality recovered. For this Weiss (1990) used with good results, a cooked grain soup of oats, wheat, barley and rye (60-100g whole grain), augmented with some other broths (vegetable broth); three times a day, for three weeks. Some of the health advantages achieved may also be linked to protein fasting effects (Wendt 1985). For four weeks warm water enemas are administered every evening before going to bed and although experienced as rather uncomfortable, have important positive effects towards detoxification and recuperation. Biological medicinals promoting the regeneration of healthy intestinal microbes are also included. Therafter

a three-week period of stepwise change towards the normal recommended diet. This approach is however not suitable when allergies to grain-based allergens (such as gluten) are prevalent. Effective recuperative treatment of the lymphatic system required weekly blood letting (for about three months, case-dependant, 50-200 ml) and improved the well-being of patients in this context (Weiss 1990).

Finally, **oxygen therapy** represented an important element of the recuperation treatment of the intestinal-lymphatic system. Dr Otto Warburg (Nobel Prize winner for Medicine in 1931) discovered that the development of cancer requires a milieu of acidosis and hypoxia (lack of oxygen); the latter two representing two sides of a coin: if you have the one you also have the other. Discoveries in respect of the citric acid cycle (Krebs cycle), involving key sequences of energy-producing metabolic reactions in cells, resulted in Hans A. Krebs receiving the Nobel Prize in Physiology or Medicine in 1953. Through oxygen therapy Weiss (1990) achieved functional catalysm of the citric acid cycle, thereby stimulating and normalising the substance exchange between cells and blood (microcirculation). Repeated application of oxygen therapy is required in chronic disease (Weiss 1990). Sircus (2015)

Schlafprozesse.
Walker EBOOK

SLEEP-simpson Simpson & Dinges (2007)
SLEEP-irwin-2008
SLEEP-irwin-2015
SLEEP-davis-2008
SLEEP-thomas-2011
SLEEP-mullington-2010
SLEEP-irwin-2016
STRESS-nettle
DL SLEEP-herera, MS SLEEP-onge; MS SLEEP-calvin; MS SLEEP-CURTAILMENT-spiegel; MS SLEEP-palmeira; MS SLEEP-copinschi-NB MS DIF-difrancesco-leptin-ghrelin; MS DIF-DR-difrancesco-fat; MS SATIETY-holt
MS CR-parikh; MS CR-speakman-NB DL CR-masoro-NB
SLEEP-jouvet-2 SLEEP-jouvet SLEEP-datta-2-rem SLEEP-datta-NB

Tabelle 2.1.2g	**Schlafprozesse**
Walker (2017) E-BUCH	
SLEEP-chan-2018	
Geist (1978): Activity/alertness is associated with increased metabolism i. e. catabolic activity during which tissue is broken down and burned for energy. When active or alert metabolism is likely to be such that anabolism, that is tissue growth, is likely to be retarded, if not brought to a halt. In particular, tissues of low growth priority such as neural tissue or fat, ought to be most affected by the absence of periods of anabolism. Periods of quiescence would be needed for growth of tissues. In mammals the tonic mechanism supplies a large percentage of the heat for the resting animal. Dispensing with the tonic mechanism and saving the fuel appears to be accomplished in deep sleep in which the body suffers a great loss of tonus. It is also adaptive to enter such a low state of activity in order to permit lipogenesis in order to convert energy in excess of need into fat. I emphasized earlier, that only through lipogenesis could food taken in during the day be converted into a compact form to be used during the following night. Predictions: Sleep will increase during stages of intense ontogenetic growth and after periods of intense catabolism. Sleep deprivation interferes with growth processes.	
Rauch (1986) Während des nächtliche Schlafes wird die Leistungsfähigkeit des Organismus wiederhergestellt. Die Tätigkeit aller Organe wird vermindert oder eingestellt. Die Abendmahlzeit bleibt für längere Zeit halb unverdaut. Durch Vergärungen gelangen dann Gifte in den Blutkreislauf. Von der Abendmahlzeit wird abgeraten (oder möglichst früh und leicht verdauliches. Gründliches Kauen).	
McEwen (2016): Circadian disruption (SLEEP): The SCN (suprachiasmatic nucleus of the hypothalamus) regulates the timing of sleep and activity, so that circadian systems regulate rest-activity cycles and keep organisms in synchrony with the external environment. Disruption of these homeostatic systems are anticipated to contribute to allostatic overload. Sleep restriction to 4 hours per night resulted *inter alia* in increases in blood pressure, increased inflammatory cytokines, decreased parasympathetic tone and promoted increased appetite (McEwen & Karatsoreos 2015, op. cit. McEwen 2016). Sleep deprivation (reduced sleep duration) has been reported to contribute increased body mass, obesity and cognitive impairment (McEwen & Karatsoreos 2015, op. cit. McEwen 2016; Karatsoreos et al.2011, op. cit. McEwen 2016; Cho 2001, op. cit. McEwen 2016).	
Bruni et al. (2004) DL SLEEP-bruni	
Gottesmann (2002) DL ANXIETYDISORDERS-sleep-gottesmann	
Sircus 2014: Magnesium hat eine berühigende Auswirkung auf das Nervensystem; das Anti-Stress Mineral schlechthin. Magnesiumchlorid als schlafqualitätsförderliches Mittel. Insomnia is one of the central/neurotic symptoms of magnesium deficiency (Sircus 2014).	
SLEEP-DIET-everson-1993 Magnesium	

Fasting. Fasting is defined as an induced state were the requirements of the body for macro- and micronutrients are met during a limited time period of shortage or absence of food by nearly exclusively using body reserves (Boschmann & Michalsen 2013). It does not involve a zero calorie diet or starvation, but some intake of vegetable broth or vegetable-fruit juice is indicated; not exceeding 500 kcal/day (Boschmann & Michalsen 2013). Fasting is an age-old method used for the maintenance or recovery of health, often also in in the context of religious practices (Rauch 1986; Geesen 1987; Boschmann & Michalsen 2013). Also at the schools of wisdom in antiquity (e.g.

Pythagoraen, Epicurean, Stoics) fasting was used to improve bodily condition and therewith progress towards the recognition of truth and virtuous self-control (Rauch 1986). Based on intuitive knowledge, Hippokrates himself applied fasting (Rauch 1986). Regular preventive fasting should be part of the lifestyle of anyone who takes the mastering of their lives seriously, also to the advantage of their family lineages and embedding ethnic group (Buchinger 1987). Fasting is the most thorough elimination treatment (a sort of autoprotein therapy under endogenous control), a method for resetting of inter-organ interactive functioning (Umstimmung) and promotion of a deeper sense of awareness (*vide* Dahlke 1990) towards the preparation of psychotherapeutic in-depth resolutions (Buchinger 1987). Fasting crises (elimination crises) indicate acutisation as chronic diseases are processed in reverse order of their development and occurence (Dahlke 1990). Fasting promotes internal digestion (Fahrner 1985) in the context of recursive healing processes. Patho-information engram layers are exposed and therewith subjected to information-erasing immune interactions in the context of autophagic processes. Fasting must be long enough (extended fasting) in order to be effective in the context of recursion healing, since substantial internal digestion (autophagy) has to be achieved. At the same time it is important to realize that any routine day-to-day activity (stress), especially also of a mental nature, needs to be avoided; otherwise partial blockage of fasting effects are to be expected (fasting in winter, with longer nights, provides for ample time for sleep at night and also during the day time).

Autophagy (cellular self digestion) is a crucial mechanism for the clearance of damaged cells (notably oxidatively damaged cells) and otherwise damaged or worn-out macromolecules and organelles (Terman 2006). Cellular degradative processes including lysosomal (autophagic) and proteasomal degradation are responsible to maintain a continuous turnover of damaged biomolecules and organelles. Insufficiency of autophagy and other cellular digestive systems results in the progressive accumulation in long-lived postmitotic cells of waste material (lipofuscin, defective mitochondria, cytoplasmic protein aggregates) which diminishes the proportion of functionally effective structures (Terman 2006). Rubinsztein et al. (2011) AUTOPHAGY-rubinsztein Autophagy is a key homeostatic process where cytosolic components are degraded and recycled through lysosomes (Alirezaei et al. 2010). The physiological importance of autophagy as homeostatic mechanism is reflected in its preservation throughout the eukaryotic phylogenetic tree (yeasts to mammals).

Dysfunction of autophagous processes is linked to the pathogenesis of numerous diseases (Mizushima et al. 2008). Autophagy has been recognized as a crucial defense mechanism against *inter alia* malignancies, infection and neurodegenerative diseases (Alirezaei et al. 2010). Inner self digestion under fasting takes place as a complex interplay between autophagy (self-digestion) and apoptosis (cell death: Mizushima et al. 2008). Ravikumar et al. (2010) provide a comprehensive overview of autophagy in physiology and pathophysiology, relating *inter alia* to the autophagy machinery, pathways, metabolism, autophagic cell death and apoptosis, autophagy and immunity and consequences of autophagous dysfunction in respect of disease. Mizushima & Komatsu (). Fasting and the treatment of geloses (hard, swollen masses of tissue associated with pathology) are mutually supportive (Preusser 1987). Autophagy exposes patho-engram information which can then be erased from the epigenetic information pool.

FASTING-boschmann Boschmann & Michalsen 2013 in ref
FASTING-de Toledo-2013 (paper) not in ref
FASTING-chiappa not in ref
FASTING-stange-leitzman (2010) not in ref

Tabelle 2.1.2h **Fasteneffekte** (Fahrner 1985)
Exponierung und Löschung von Patho-Engramminformation durch Fasten
Fahrner (1985)
Der Organismus im Fasten bezieht seinen Betriebs- und Brennstoffbedarf hauptsächlich aus der Mesemchymentspeicherung. Die Deckung des Funktionsbedarfs wird durch eine sparsame innere Ernährung vollzogen. Die damit intensivierte innere Verdauung ist ein Teil der Regenerationsprozesse die sich in Zellen und Geweben abspielen. Der eigentliche therapeutische innere Verdauungsprozess im Fasten setzt erst ein wenn nicht nur die normalen oder überschüssigen Reserven an Eiweiss und Fett abgebaut sind sondern wenn auch pathogene Ein- und Ablagerungen aus den Gewebs- und Zellsystemen wieder herausgelöst werden können.
Mit der langfrisigen Umkehr der Stoffwechselrichtung im Fasten werden Ablagerungen im mesemchymalen Grossraum dem Abbau durch innere Verdauung bzw. der Ausscheidung zugänglich gemacht.
Fastendauer. Tiefgreifende Selbstreinigung durch fasteninduzierte Anregung der Regeneration durch innere Verdauung ist erst nach drei bis mehrwöchigem Fasten zu erwarten. Regelmässig wiederholtes und richtig dosiertes Fasten ist mit einer positive Beeinflussung der gesamten Immunitätslage verbunden. Eintritt einer Besserung erst vier bis sechs Wochen nach einem Fasten ist bei vielen Krankheitsbildern registriert worden. Fastendauer nach Einschätzung der substantiellen und vitalen Energiereserven. Die Optimaldauer des therapeutischen Fastens liegt für die meisten bei 21 Tagen, derweil eine Ausdehnung bis zu 40 Tagen des öfteren erforderlich ist. Je nach Fastenart und Krankheitszustand kann das Fasten auch auf fünf oder sechs Wochen ausgedehnt werden. Der gesamte Behandlungszeitraum sollte Spielraum lassen für die Einplanung von genügend Nachfastendiätzeit. Es ist wichtig die Regeln für das Fastenbrechen und Nachfastendiät zu beachten. Die beim Buchinger-Fasten hinzugegebenen Obst- und Gemüsesäfte erleichtern das Recycling saurer Zwischenprodukte und Schonung der Alkalireserven. Für optimale Entschlackungserfolge sollte hingegen die volle Regulierung des Säure-Basen-Gleichgewichts nach Jentschura und Lohkämper (2014) fastenbegleitend zur Anwendung kommen. Die Entsäuerung durch

Atmungsaktivität ist ferner von Bedeutung (körperliche Tagesaktivität). Tagesschlafen sollte dabei nicht zu kurz kommen (Tabelle). Ungeachtet der besonderen Fastenart muss eine angemessene Substitution von Mineralien, Vitalstoffen und Vitaminen gegeben sein.
Fasten und Fertilität. Nach dem Fasten kommt es relativ oft zu einer Stabilisierung des Menstruationszyklus und der generativen Funktion (und erlaubt/fördert die Erfüllung eines bisher vergeblich gebliebenen Kinderwunsches).
Gewichtsabnahme. Gewichtsabnahme hängt direkt ab von der Strenge der Nahrungseinschränkung, der Dauer des Fastens und körperlicher Arbeitsleistung. Hormongesteuerte Fettdepots werden langsamer als fettneutrale abgebaut. Geschlechtsspezifische und konstitutionelle Unterschiede bei der Gewichtsabnahme sind in Betracht zu ziehen.
Therapieindikationen. Natürliches Breitbandpsychotherapeutikum. Hypertonie, Herzinsuffizienz, Koronarinsuffizienz, Herzrythmusstörungen, Infarktrisiko, Periphere Durchblutungsstörungen, Diabetes mellitus, Hyperlipidämie, Gicht, Krankheiten aus dem rheumatischen Formenkreis, Polytendomyopathie, degenerative Gelenkerkrankungen, Übergewicht, Fettsucht, Hepathopathien, Obstipation, Dyspepsie, Enteropathie, Kolitis, Asthma bronchiale, chronische asmathoide Bronchitis, Polyallergisierung (allergische Immunkomplexe), Rhinitis, Synobronchitis, Nierenerkrankungen, Hauterkrankungen, Kopfschmerzen, Migräne, Glaukom, reaktive Depressionen. Kontraindikationen: hauptsächlich prekäre katabolische Krankheitsprozesse: aktive Tuberkulosen, konsumierende maligne Prozesse, Hyperthyreose, zerebrovaskuläre Insuffizienz des hohen Alters.
Schlaf (Traumgeschehen).Wie im leiblichen Aufräumungsarbeiten geleistet werden, so auch im Seelisch-Geistigen. Das Fasten erlaubt dem Traumgedanken den Zugang einem erweiterten, intellektuell nicht reflektierten Tiefenbewusstsein unserer Seele. Im Fasten eröffnet sich ein Zugang zu Traumgedanken auch aus anderen transzendenten Bereichen, welche dann einbezogen werden in unentbehrliche Ordnungsprozesse für Leib und Seele (Fasten auch als natürliches Breitbandpsychotherapeutikum).
Vorbeugendes Fasten. Sebst ohne bereits manifeste Krankheitserscheinungen ist Fasten von besonderer Wirksamkeit zur Vorbeugung von solchen und zur Erlangung einer besseren Grundgesundheit. Die periodische Umschaltung auf innere Ernährung und Verdauung bewirkt eine intensive Erneuerung und Regeneration des gesamten Systems. Regelmässig wiederholtes Fasten (alle ein bis zwei Jahre) unterstützt die Lebensqualität und kann zu einer erhöhten Lebenserwartung beitragen.
Fahrner (1985) zitiert Gandhi: > Das Fasten mit dem Ziel, einen vollkommeneren Ausdruck seiner Selbst zu erreichen, die Kraft, zu geistiger Dominanz und Führung leiblicher Bedürfnisse zu gelangen, ist eine der wirkungsvollsten Massnahmen für den Fortschritt unserer Menschlichen Entwicklung <
Jentschura & Lohkämper (2014): Beim Fasten werden Schlacken gelöst und die vormals neutralisierten Säuren und Gifte reaktiviert (Säurefluten). Starke Muskeltätigkeit (Fastenmärsche) bewirken einen weitern Milchsäureschub. Trinken von schlackenlösenden Kräutertees. Zur Neutralisierung ist energiereiche Mineralstoffzufuhr (Gemüsesäfte: mineralisches Neutralisierungsangebot) angesagt und zur Ausschwemmung ausreichend Wasser, sowie konsequente Schlackenausleitung mit Basentrunk und durch basische Körperpflege (basisches Ableitungsangebot: basische Bäder zur Entgiftung über die Haut: Unterstützung der Leber mit basischen Wickeln; Basische Fuss- und Vollbäder mit möglichst langer Dauer (1-3 Stunden).

A clear distinction needs to be made in respect of fasting applications/protocols, depending on the goals to be pursued and the circumstances under which they can be undertaken: (I) Support, achievement and maintenance of a healthy metabolism through daily intermittent fasting and alternating fast/non-fasting states, such as intermittent protein fasting according to Wendt (1985). Such types of fasting do not require the suspension of daily work routines. In fact, daily intermittent fasting is intended for life-long implementation as an integral part of ones dietary lifestyle (Table 2.5.1.5e: Integrative PALEO diet) and (II) In pursuit

of effective recursion healing more extended fasting schedules (usually for 3-4 weeks) are required in order to expose and eliminate deeper-layer patho-information-engrams through autophagous processes and other healing stimuli (Extended fasting: Table 2.1.2h; Schrothkur-fasting: Table 2.1.2i). For these types of fasting, fasting individuals must be free from the stresses of daily work routine and its associated environment; and specialized procedures and services need to be provided to patients. Such conditions are only available in professional fasting institutions.

Note: Chronic low carbohydrate/low calorie diets, mainly used for the purposes of weight loss, should not be considered appropriate means to achieve health-promoting fasting effects (2.5.1.5c; Table 2.5.1.5e).

Four forms of fasting are of particular relevance in the context of recursive healing: daily intermittent fasting, intermittent protein fasting, extended full fasting (Table **2.1.2h**: above) and Schrothkur-fasting (Table **2.1.2i**). Daily intermittent fasting involves the integration of fasting effects into the daily lifestyle thereby realizing the full benefits of both animal proteins (performance based on raised basal metabolic rates) and vegetable carbohydrate-rich and nutrient-rich carbohydrates for optimal performance and maintenance of body condition; and the prevention of patho-information-engram load accumulation (Sections **2.1.2** and **2.1.3**; Table **2.5.1.5f: Daily intermittent fasting**). It is practised by traditionally healthy living populations (**2.5.1.2**). However, as thoroughly outlined by Wendt (1985), the efficiency of the protein metabolism is compromised to variable degrees in individuals living under conditions of sustained (transgenerational) affluence (substantial patho-information-engram loading). In order to address this situation of an insufficiency of the protein metabolism therapeutically, (intermittent) protein fasting or Schrotkur-fasting is strongly indicated/required.

Intermittent protein fasting.

Wendt (1985) realized that not only does the body provide for storage of carbohydrates and fat, but also for proteins (in basal membranes). Overconsumption of protein, and/or when the protein is not fully processed, results in pathological thickening of capillary basal membranes and their permeability is reduced due to insufficiency of protein degradation processes (hypoporopathies: reduced capillary-membrane permeability of basal membranes). This results in disease conditions such as elevated blood pressure,

raised blood sugar levels, elevated erythrocyte and haemoglobin values and kidney damage with albuminurea (**2.5.1.3b**). Following Wendt (1985) protein fasting involves the exclusion of all sources of proteins in the diet to the extent that the body remains in a continuous state of being below the minimum protein demand. Only under such conditions is the body induced to break down and eliminate protein deposits on the basal membranes. Thus, protein fasting entails the strict exclusion of all forms of meat and eggs, also baked products with eggs as ingredients; no milk products of any kind (cheese, yoghurt, cream cheese); that is, any ingredient from animal sources. Peas, lentils, beans and soya have high levels of plant proteins and should also be avoided. If artherosclerosis is evident dietary cholesterin-carriers should be replaced with poly-unsaturated fatty acids. Protein fasting is usually to be continued for a few weeks at a time, but can be implemented without breaking the daily work life routine, unlike extended full fasting. Protein fasting can be undertaken when therapeutically indicated; it can also be incorporated as an intermittent dietary life style feature (e.g. every third months). Blood-letting at the start of protein fasting induces protein elimination from the basal membranes to start immediately, thereby increasing the efficiency of the therapy. In general, efficient protein digestion should be supported (Table **2.5.1.3a**); as assised by the daily consumption of bone broth (Table **2.5.1.5e**).

Schrothkur-fasting (Table **2.1.2i**) represents an effective form of protein fasting, with benefits resembling those of full fasting (Wendt 1985). This type of fasting regime was developed by Dr Johann Schroth (1798-1856; Austria); which included alternating dry and drink days, cold body wraps and a specific carbohydrate-based, reduced calorie diet (Rhode 2012).

Table 2.1.2i Schrothkur-fasting (Rhode 2012; Brosig 2011)
Schrothkur-fasting involves four components: daily cold body wraps (Schwitzpackungen), alternating dry and drinking days, a reduced calorie diet of mainly vegetable/fruit/whole grain composition (absence of animal protein) and a balanced rest-activity rhythm.
Schrothkur-fasting normally should last for three or four weeks; and should be repeated in the case of particularly chronic disease states. A weekly schedule, as outlined by Rhode (2012): Cold wraps daily; first and second day: moderate drinking days; third day: dry day (rest day); fourth day: drinking day (day of physical activity); fifth day: dry day and day of rest; sixth day: moderate drinking day; and seventh day: drinking day. Resting associated with dry days and physical activity with drinking days (Brosig 2011).
Whole or three-quarter body cold wraps are applied daily in the morning and are intended to induce thermogenesis and sweating. Application for at least two hours and longer as long as the patient feels comfortable. Artificial induction of fever, mobilizing immunological and detoxification processes (Brosig 2011). In order to be functional, body wraps need to be applied in a specific, professional manner (Brosig 2011). Before applying the cold body wrap, the body must be warm in the bed (facilitated by providing hot herbal teas) in order to ensure an adequate cold response towards increased thermogenesis (Brosig 2011).

Schrothkur-fasting diet: calorie reduced (500-600 kcal), carbohydrate-rich (minimal protein, fat and salt content); pastries and whole grain bread, gruel, vegetable soups and salads; also soaked dry fruit, potatoes, semolina, rice and herbs (ensuring adequate availability levels of vitamin and minerals: Brosig 2011). Beverages include wine, fruit juices, teas and mineral water. Depending on the amount offered, dry (restricted fluid intake: one glass of fresh orange juice per day) and drinking days (abundant fluid intake: 0.5-1 liter per day) are differentiated. On drinking days wine, water, teas or juices are offered. Alternating dry and drinking days are intended to facilitate tissue drainage with detoxification effects and stimulation retuning of systemic processes (Umstimmung: Brosig 2011). Activation of self-healing processes through reactivation/exposure of chronic inflammatory conditions and resorption thereof by induced fever during a state of fasting (Brosig 2011).
Cold-wrap body responses (Hesseln 1980, op. cit. Rohde 2012) in three phases. First phase: Sympathicotony (c. 10-20 min); cold stimulus, vasoconstriction, blood pressure rising and invigorization. Second phase (warming phase): Vagotonic (c. 0.5-1 hour); thermogenesis, vasodilation, declining blood pressure, nerve calming and muscle relaxation. Third phase: Sympathicotony (c. 0.15-1 hour); increasing blood pressure, increased blood circulation, increasing body temperature, increased metabolic rate and sweating. During the body wrap application an increase in body temperature of about 1-2 °C (Brosig 2011); which can be interpreted as an induced fever reaction, accompanied by enhanced immunological activity. Hentschel (1998, op. cit. Rohde 2012) summarized the current state of knowledge then available in respect of body wrap effects.
Schothkur-fasting effects are described by *inter alia* (op. cit. Rohde 2012): Hentschel 1960, Krauss 1960, Krauss & Hartmann 1964, Hesseln 1977, Wenzel et al. 1984, Steiniger et al. 2003.
Wenzel et al. 1984 (op. cit. Rohde 2012): Over three weeks an average weight loss of 11.2 kg was achieved and a nitrogen loss of 143.8 g (loss of body protein of 688.3 g); resulting in a negative nitrogen balance. With a body weight reduction of about 10 %, parallel reductions of indices of biological age are found (Steiniger et al. 2003).
Main indications for fasting: metabolic syndrome (including obesity, type 2 diabetes), hypertension, hyperlipidemia, hyperuricemia (Rhode 2012); also, as listed by Brosig (2011): migraine, psoriasis, acne, chronic infammation of the mucus membranes (forehead- and paranasal sinuses, eyes, ears, nose, thoat), heart and circulatory disorders, prevention of heart attacks, arterial calcification and hypertonia; fatty liver, disorders of the gastrointestinal tract, disorders of menstruation, menopause, glandular dysfunction; gout, circulation disorders of the brain, hypothyroidea, diseases of the respiratory tract (chronic bronchitis, bronchial asthma); skin disorders, excema,furunculosis, allergic skin disorders; wear and tear of the spinal column, kidney and bladder disorders, soft tissue rheumatism, varicose vains, lower leg ulcerations and tendencies of oedematous accumulations in the body; wearing of joints.
Contra-indications (Rohde 2012; Brosig 2011): cachexia, anorexia nervosa, advanced cerebrovascular insufficiency (e.g. dementia) and advanced liver and renal insufficiencies. Also counterindicated during acute infections, tuberculosis, cancerous growth, hyperthyroidea, neurological disorders (endogenous depression, psychosis, schizophrenia), acute liver diseases and liver cirrhosis. Contraindicated during pregnancy and infancy.

Within the context of systemsecological healing, thus recursive healing, Schrothkur-fasting can play a vital role, particularly also for individuals with pre-clinical and clinical disorders associated with an impaired protein metabolism (**2.1.3.2**: *inter alia* on the basis of epigenetic patho-information-engram loadings resulting in impaired protein metabolism: IPM). Schrothkur-fasting represents *inter alia* a particularly efficient form of protein fasting (*vide* Wendt 1985). Self-healing fasting effects are potentiated through various stimuli, but most importantly by fever effects and an associated elevated metabolic rate (Table **2.1.2c**). The minimum duration of Schrothkur-fasting is three weeks, but four weeks is optimal; in both cases followed by an appropriate fast-breaking protocol (Brosig 2011). For recursive healing, an annual

repetition over some years is/may be indicated. Presently this type of fasting is professionally offered mainly in Oberstaufen (Germany).

d) Autophagic catalysis of healing processes

These processes of immune interaction are cornerstones of recursion healing. Exposure to active immune interaction is prominently functionalised by fever and .autophagy during fasting (2.1.2c/d). p 49 2/1.2a

Healing requires elimination of essence-compromizing HMT healing processes via catalysis of these to overcome PIE loads. Chronic to acute exposure
PIE chronic inflammation to acute reconfrontation/exposure; overcoming the need/basis for chronic inflammation via central metabolic catalysis (methionine-homocysteine etc) mechanism.

Refer also to CISD syndrome 2.2.2i. **HYPERHOMOCYSTEINEMIA as marker of chronic inflammation ex PIE**

Catalysis of immune interactions at the exposure interface
Methyl catalysts
Imtermittancy reaching the epigenetic level repeated confrontation
In a recursion-friendly environment – diet lifestyle
Sympathetic parasympathetic state IgA up also meditation
Transcriptional and epigenetic control of autophagy (Füllgrabe et al. 2014)
Catalytic synergy, clear exposure of successive layers, time, repetition
B6-B9-B12 (Zn, Mg); basic autophagic catalytic energy-boosting self-healing system contra EPIES
Methionine-homocysteine system; raised homocysteine product or marker of a compromised h-m system and/or associated pathology

Seisenberger et al. (2012) Reprogramming DNA methylation

MS HYPERHOMOCYSTEINEMIA-ibrahimagic-parkinson
MS HYPERHOMOCYSTEINEMIA-vandenberg-vitaminB6-plus
MS HYPERHOMOCYSTEINEMIA-modaghegh-folicacid
DL HYPERHOMOCYSTEINEMIA-douaud-vitB-alzheimer

MS HOMOCYSTEINE-fenech-chromosome-
MS HOMOCYSTEINE-ganzi-factors
MS HOMOCYSTEINE-rasmussen
MS HOMOCYSTEINE-nurk
MS HOMOCYSTEINE-refsum
DIET-HOMOCYSTEINE-arija

Füllgrabe et al. (2014): A whole-cell-view of autophagy is presented that encompasses both cytoplasmic and nuclear events. Recent studies have unveiled a transcriptional and epigenetic network that regulates autophagy. Macroautophagy (referred to as autophagy) has been implicated in several physiological processes that are important for human health and disease. It is a catabolic process that results in the autophagosome-dependent lysosomal degradation of bulk cytoplasmic contents, abnormal protein aggregates and excess or damaged organelles (Mizushima et al. 2008). Compelling evidence has revealed that the nucleus is actually a major regulator of autophagy. Although autophagosome formation itself may not rquire the nucleus, knockdown of TPR (translocated promotor region), a component of the nuclear pore complex, facilitates autophagy (Funasaka et al. 2012, op. cit. Füllgrabe et al. 2014). It has been proposed that the depletion of TPR promotes autophagy by inhibiting the nuclear export of factors that are known to regulate autophagy, such as heat shock protein 70 (HSP 70) and heat shock factor 1 (HSF 1), and p53. P53 activation has ben shown to inhibit mTOR activity and to promote autophagy via transcriptional events (Feng et al. 2005, op. cit. Füllgrabe et al. 2014; Crighton et al. 2006, op. cit. Füllgrabe et al. 2014). Depletion of the nuclear pore component TPR which results in the nuclear accumulation of p53, also facilitates autophagy (Funasaka et al. 2012, op. cit. Füllgrabe et al. 2014).

Discovery of an epigenetic programme that controls autophagy (Füllgrabe et al. 2013, op. cit. Füllgrabe et al. 2014). The adaptive autophagic stress response has been referred to as being biphasic (Pietrocola et al. 2013, op. cit. Füllgrabe et al. 2014). In light of the discovery of autophagy-regulated histone modifications, the presence of a triphasic effect is implicated. After a rapid autophagic response involving the post-translational modification of cytosolic proteins (phase 1), a collection of transcription factors upregulate the expression of genes encoding proteins that sustain and regulate, generally increasing, autophagic flux (phase 2). After prolonged exposure to autophagic stimuli, a global change in histone modifications acts as a negative regulatory feed back loop (phase 3: Pietrocola et al. 2013, op. cit. Füllgrabe et al. 2014). The same enzymes that are involved in the first two phases of autophagy (for example, Esa 1 and SIRT1) are also likely to have a role during the third phase.
The global downregulation of active histone marks could serve three purposes. I) As over-stimulating or prolonging autophagy can be lethal for cells (Levine 2005, op. cit. Füllgrabe et al. 2014), loss of active chromatin marks can inhibit the transactivation of autophagy genes by several transcription factors, thus acting as a feedback loop to protect cells against a lethal level of autophagy. II) A second role of global chromatin silencingmight be to save energy during times of prolonged starvation. III) The third role of global chromatin silencing could be the establishment of an autophagy 'memory'. Histone modifications have the potential to induce stable changes in the chromatin landscape, potentially even affecting subsequent generations (Greer et al. 2011, op. cit. Füllgrabe et al. 2014). Thus, a prolonged starvation response might prepare an organism for a future starvation event.

Altogether, a nuclear autophagic network has emerged in which a plethora of transcription factors have a role in the upregulation of autophagy relared genes.

Betaine anhydrous

Link to chronic inflammation 2.2.2i

2.2.2i) Chronic immune system dysregulation syndrome

Ruiz-Núñez et al. (2013) presented a review of lifestyle and nutritional factors underpinning a state of chronic systemic low-grade inflammation (below). Following on such considerations, the ***chronic immune system dysregulation*** (**CISD**) syndrome, in the context of patho-information-engram load accumulation and life history modes, is defined and developed. MORE P 174/5

2.5.1.4c Sirtuins p

Guarente (2013): New data show a systematic redirection by sirtuins of mammalian physiology in response to dietary sirtuins. Data similarly suggest that sirtuins are conserved mediators of longevity. SIRT1-activating compounds (STACs), such as the polyphenol resveratrol found in red wine, were reported to activate the enzyme *in vitro* by lowering its Km for substrate (Howitz et al. 2003, op. cit. Guarente 2013: ***Lowering of the Michaelis constant of SIRT1 for both the acetylated substrate and NAD$^+$ and increasing cell survival by stimulating SIRT1-dependent deacetylation of p53). The lower Km the higher is the catalytic efficiency***.

Lamming et al. (2004): Caloric restriction (CR) works in most species, implying a conserved mechanism. It extends lifespan because it is a mild biological stressor activating Sir2, a key components of yeast longevity and the founding member of the sirtuin family of deacetylases. Sirtuins are found in plants, yeast and animals and seem to underly the remarkable health benefits of CR.
Research in ageing has identified important genes and pathways involved in longevity. These include the family of nicotinamide adenine dinucleotide (NAD)-dependent protein deacetylases, known as sirtuins. They represent a unique class of proteins linking protein acetylation to metabolism; thereby having important effects on mammalian physiology and diseases of ageing (Guarente 2011).

Mennerich (1979) catalysis of healing processes autophagic catalysis SIRTUIN Michaelis constant

1) Potency (stressed environments, fresh and together with other compounds in same plant tissue)

2) Synergy (multiple substances)

3) Time

Brunet, A., Sweeney, L. B., Sturgill, J. F., et al. (2004). Stress-dependent regulation of FOXO transcription factors by the SIRT1 deacetylase. *Science* 303: 2011-2015.

Wu et al. (2009): Culturing autophagy deficient cells in the presence of the antioxidant N-acetylcysteine (NAC) resulted in a reduction of ROS levels (Wu et al. 2009).
Data suggests that antioxidant treatment of autophagy-impaired cells is beneficial in preventing the glucose intolerant phenotype within pancreatic β cells. It is known that pancreatic secretion of insulin is sensitive to changes in the cellular redox state and mitochondrial functionality. In the context of impaired autophagy, the in vivo use of antioxidants interrupted the vicious cycle of mitochondrial generated ROS inducing further mitochondrial damage. Such observations suggest that antioxidant targeted therapy might be of benefit for conditions where deficiency or impairment autophagy is involved (Wu et al. 2009).

Durlach et al. (2002): MS MAG-durlach-2002 Magnesium enhances melatonin secretion by the pineal gland through stimulation of serotonin N-acetyl transferase activity, the key enzyme in serotonin synthesis.

Vitamin B12 (cobalamin) is particularly important for normal nerve activity and brain function. In combination with folate and vitamin B6, homocysteine levels are kept under control.

Folic acid. Wright & Lenard (2001): Folic acid (folate) is a B vitamin which is required to control the amino acid homocysteine towards reduced levels for i.a. healthy functioning of the cardiovascular system and preventing certain birth defects. With advancing age, folate levels tend to decline which is then associated with rising homocysteine levels. Adequate folic acid intake (400-800 micrograms/day) through the diet is often not achieved and its absorption compromised due to stomach acid insufficiency.
Vitamin B12 deficiency (Dr Edward Group; Global Healing Center)
1. **Cognitive impairment**. In the elderly, B_{12} (cobalamin) deficiency cognitive impairment and dementia. This deficiency has also been linked to other neurodegenative disorders such as multiple sclerosis and Parkinson's disease (McCaddon 2013). MS VITB12-mccaddon- 2. **Psychosis**. Depressed mood, hallucinations, seizures and hypertension have been found in subjects who tested positive only for low vitamin B_{12} levels. Administration of vitamin B_{12}

has been found to result in recovery within a week (Dogan et al. 2012). MS VITB12-dogan-

3. **Melancholic depression**. Individuals suffering from melancholic depression (caused by physical rather than psychological factors) have consistently displayed an inverse relationship between vitamin B_{12} levels and depression (Seppälä et al. 2013). MS VITB12-seppala
4. **Stroke**.
5. **Alzheimers disease**. A recently published study demonsrated a treatment of folic acid, B_6 and B_{12} as a significant improvement in the reduction of cerebral atrophy (Douaud et al. 2013). DL HYPERHOMOCYSTEINEMA-douaud-vitB-alzheimer
6. **Cardiovascular disease**. Without vitamin B_{12} the body cannot convert homocysteine. This leads to a build-up of homocysteine levels which have been associated with atherosclerosis and increased risk of cardiovascular mortality (Refsum et al. 2006). MS HOMOCYSTEINE-refsum

Vitamin B12 (cobalamin) is particularly important for normal nerve activity and brain function. In combination with folate and vitamin B6, homocysteine levels are kept under control.

MS DEPRESSION-vancampfort-metaboilicsyndrome
MS VITB12-stanger-B6-folicacid
MS VITB12-king
MS HYPERHOMOCYSTEINEMIA-ibrahimagic-parkinson
MS HYPERHOMOCYSTEINEMIA-vandenberg-vitaminB6-plus
MS HYPERHOMOCYSTEINEMIA-modaghegh-folicacid
MS HYPERHOMOCYSTEINEMIA-clarke-folate-B12
DL HYPERHOMOCYSTEINEMIA-douaud-vitB-alzheimer
MS HOMOCYSTEINE-fenech-chromosome-
MS HOMOCYSTEINE-ganzi-factors
MS HOMOCYSTEINE-rasmussen
MS HOMOCYSTEINE-nurk
MS HOMOCYSTEINE-refsum
DIET-HOMOCYSTEINE-arija

Homocysteine metabolism

Table 2.1.2j Methionine-homocysteine-cysteine metabolism

Braverman et al. (2003):
Methionine. Methionine is a crucial amino acid that brings methyl groups and sulfur into the body, and as such is the first amino acid incorporated into proteins. It is a code breaker, initiating translation of the genetic blueprint sent by DNA via the messenger ribonucleic acid (RNA) which carries instructions making new body protein. It is equired for the formation of body tissues and for antioxidant and detoxification processes. Methionine has a critical role as catalyst for important

metabolic processes. Methionine performs three major roles in the body – it is a sulfur donor, a mrthyl donor and an essential precursor of the important sulfur amino acids cysteine, glutathione and taurine. Methionine as abundant sulfur amino acid enables the initiatiation of translation of the DNA instructions for the proteins of the body. From methionine, cysteine, glutathione and taurine, the most powerful antioxidants and detoxifiers, are created. Methionine, like all other sulfur amino acids, requires adequate amounts pyridoxine (vitamin B_6), cyanocobalamin (vitamin B_{12}) and folic acid (vitamin B_9) in order to be properly metabolized. Methionine metabolism results in the production of important sulfur-containing nutrients that are necessary to provide adequate and optimal functioning of cardiovascular, skeletal and nervous systems, such as coenzyme A. Methionine also helps to boost serotonin metabolism in the brain.

Homocysteine. Homocysteine is an amino acid metabolite that is created nzaturally in the body from the essential amino acid methionine. This sulfur-containing amino acid occurs only transiently during methionine metabolism before being converted to the amino acid cysteine. The conversion of dietary methionine to homocysteine is controlled by enzyme systems that require pyridoxine (vitamin B_6), cyanocobalamin (vitamin B_{12}) and folic acid (vitamin B_9). Homocysteine is needed to make cysteine and glutathione (two most powerful antioxidants) from methionine. Adequate intakes of folic acid, cyanocobalamin and particularly pyridoxine prevent a toxic build-up of homocysteine. There is a known stimulatory effect of pyridoxine on other pyridoxine-linked enzymes involved in sulfur amino acid metabolism, specifically the enzyme cystathionine synthase.

Homocysteine, a naturally-occurring sulfur containing amino acid, is produced only after ingestion of methionine, which is most common in animal protein. The metabolic breakdown of homocysteine occurs either through remethylation, which regenerates methionine, or trans-sulfuration which degrades homocysteine into cysteine and then taurine. When excessive methionine has been consumed, and only inadequate amounts of pyridoxine, cyanocobalamin and folic acid are available to convert homocysteine into cysteine or taurine, then homocysteine remains circulating and becomes toxic. This toxicity is expressed by promoting damage to epithelial cells that line the circulatory system, encouraging the formation of fibrous plaques that sequester circulating fatty deposits and cellular debris, narrowing the available flow space for blood (increasing the risk for coronary artery disease and arteriosclerosis).

Elevated homocysteine accelerates growth of the intimal and median cells and tissues of arteries, triggering the many processes that lead to loss of elasticity, narrowing, hardening and calcification, and formation of blood clots within arteries.

Cysteine. Cysteine is a non-essential amino acid. It consists of the basic chemical amino structure – nitrogen, carbon, oxygen and hydrogen – plus a sulfur-containing thiol group. Cysteine is active in many different situations in the body because of the special properties of its thiol grouping. Thiol compounds help to prevent oxidation of sensitive tissues and they also help the body processes rendering harmless toxic chemicals and carcinogens. It is what makes cysteine and its derivatives N-acetylcysteine and glutathione, extremely powerful compounds.

From cysteine, the body makes N-acetylcysteine (NAC), one of the most well-documented and effective nutritional agents in medicine today.This slightly modified form of cysteine is thought to be an intermediary in cysteine detoxification systems. As cysteine goes about clearing the cells of toxins, it may be converted temporarily to N-acetylcysteine. It performs as a detoxifying agent. It also implicated to increase

glutathione production. An important role of cysteine takes place in the liver where it helps glutathione to detoxify carcinogens and other dangerous pollutants. In all cells of the body it serves as a major scavenger of oxidants. In addition to the detoxifying function that results from the conversion of cysteine N-acetylcysteine and glutathione, cysteine plays an important role in energy metabolism. Like some other amino acids, it can be used as fuel if necessary. Another important energy system of which cysteine is an active part is fatty acid synthase. Cysteine sulfinic acid and glutathione have been identified as neurotransmitters. Cysteine is made by the body only from the essengtial amino acid methionine. Cysteine, like all the sulfur amino acids, require ample adequate amounts of pyridoxine (vitamin B_6), cyanocobalamin (vitamin B_{12}) and folic acid in order for the conversion from one amino acid to another can take place. High doses of pyridoxine are of special value when kidney tumors, thyroid therapy galactosemia, or pyridoxine deficiency itself can cause the appearance of an error in the conversion of mdethionine to cysteine, known as cystathionin-uria.
Methionine food sources: eggs, fish, milk, cheese and meat; sunflower seeds. Folate food sources: dark green leafy vegetables and whole-grain products. Marginal deficiencies of pyridoxine may result in accumulations of homocysteine even in healthy people. Cysteine is best obtained from eggs, meat, dairy products, grains and beans.
Contra homocysteine: daily combination of 400 mcg of folic acid, and 100 mg of pyridoxine along with a one time injection of 9 mg of cobalamin. Increasing dietary fruit and vegetables, which typically have high pyridoxine and folic acid content, in stead of taking supplements, may be enough to maintain acceptable levels of these compounds. Supplementation with cysteine, N-acetylcysteine and methionine, without inclusion of pyridoxine may result in the accumulation of excess homocysteine.
Finkelstein & Martin (2000): Homocysteine does not occur in the diet, but is an essential intermediate in normal mammalian metabolism of methionine. Each compound, methionine or homocysteine, is the precursor of the other. Similarly, the synthesis of the one is the mechanism for the detoxification of the other. The ubiquitous methionine cycle is the metabolic basis for this relationship. In some tissues the transsulfuration pathway diverts homocysteine from the cycle and provides a means for the synthesis of cysteine and its derivatives. Methionine (or homocysteine) metabolism is regulated by the disposition of homocysteine between the competing sequences. Both pathways require vitamin-derived co-factors, pyridoxine (vitamin B_6) for transsulfuration and both folate (vitamin B_9) and cobalamin (vitamin B_{12}) in the methionine cycle. Hyperhomocysteinemia, a metabolic impairment that may result from genetic variations, acquired pathology, toxicity and nutritional inadequacy (increased levels of homocysteine: causative agent or marker for the pathology). **Finkelstein (1998):** Two pathways, the methionine cycle and transsulfuration, account for virtually all methionine metabolism in mammals. Every tissue possesses the methionine cycle. Therefore each can synthesize AdoMet (S-adenosylmethionine), employ it for transmethylation, hydrolyze AdoHcy (S-adenosylhomocysteine), and remethylate homocysteine. Transsulfuration which occurs only in liver, kidney small intestine and pancreas, is the means for catabolizing homocysteine. The liver has a unique isoenzyme of MAT that allows

for the utilization of excess methionine for the continued synthesis of AdoMet. Metabolic regulation is based on the distribution of available homocysteine between remethylation and conversion to cystathionine. The tissue content of the enzymes and their kinetic properties provide the basis for the regulatory mechanism.
Methionine is an essential nutrient. This amino acid and its and its metabolic products are involved inmultiple fundamental biological processes. These imclude protein synthesis, the synthesis of AdoMet which is utilized both by multiple transmethylation reactions and in the formation of the polyamines spermidine and spermine, and the synthesis of homocysteine. The latter compound is a key substrate in three additional essential reactions or sequences: I) the recycling of intracellular folates; II) the catabolism of choline and betaine; and III) the transsulfuration pathway that leads to the formation of cystathionine, cysteine, glutathione, and other metabolically important metabolites.
Finkelstein et al. (1983): Betaine-homocysteine methyltransferase catalyses a reaction which is essenetial for the catabolism of choline in the mammalian liver. The reaction is significant in the regulation of methionine metabolism both as a means for the maintenance of hepatic concentrations of methionine during periods of inadequate intake of this amino acid and for removal of excessive homocysteine following excessive intake of methionine (Finkelstein et al. 1982, op. cit. Finkelstein et al. 1983; Finkelstein 1978, op. cit. Finkelstein et al. 1983).

Atkuri et al. (2007): Loss of balance between the antioxidant defence and oxidant production in cells, which commonly occurs as a secondary feature of many human diseases, is loosely termed oxidative stress. This balance is important because the intracellular redox environment must be motre reducing than oxidative to maintain optimal cell function. Four major interdependent redox couples – GSH/GSSG, NADHP/$NADP^+$, NADH/NAD^+ and thioredoxin – interact to regulate this redox environment (Schafer et al. 2001, op. cit. Atkuri et al. 2007). N-acetylcysteine (NAC), a cysteine prodrug, replenishes intracellular GSH (glutathione) levels. Loss of antioxidant capacity in an oxidatively stressed cell is mainly due to a decrease in GSH and/or increase in GSSG, because glutathione (GSH) is the most abundant intracellular free thiol. Oxidative stress thus translates to deficiency of GSH and/or its precursor, cysteine.
The primary function of NAC is to cysteine necessary for GSH synthesis and replenishment. Orally delivered NAC is readily taken up in the stomach and gut and sent to the liver where it is converted to cysteine (Cotgreave 1997, op. cit. Atkuri et al. 2007). The liver converts much of the cysteine into GSH, which is then largely secreted into circulation (Griffith & Meister 1979, op. cit. Atkuri et al. 2007).

Table 2.1.2k

New Biology, Metaphysics and Medicine

(citations from Mennerich 1979)

Die Entropie, die physikalisch als Verlust gedeutet wird, muss aber dynamisch-biologisch anders gesehen werden, und zwar als notwendiger Energierückstand, den jedes funktionelle Energiesystem bewahren muss, um im Rahmen eines Funktionsystem wirksam zu sein; denn dieser Energierückstand ist der Ausgangspunkt für den Aufbau der autonomen Tonusspannung, auf die die Leistungen aller organischen Funktionssysteme bezogen sind. Unter biologisch-dynamischem Aspekt geht also keine Energie im Sinne der Energie *verloren*,

sondern es wird bei den Energieumwandlungen im Organismus als Ausdruck autonomkosmischen Geschehens ein Energierest zurückbehalten, um *durch den ständigen Wechsel von Energieabgabe und Energierückspannung im Sinne der reversiblen Redox-Prozesse das Leben zu gestalten*.

In Hinblick auf das Entropie-Problem sind beim Organismus zwei Wesenheiten grundlegend zu trennen:
Der Organismus ist eine kreisförmig energiekonstante Grösse, in der durch ständige Bewegungen Energieumwandlungen als *Wechselwirkung* stattfinden und damit Gegenstand des 1. Energiesatzes;
der Organismus ist linienhaft eine autonome Einheit, deren in sich geschlossene Funktions-Systeme durch entropie-charakterisierte Energiebindungen in Wechselbeziehungen stehen und somit Gegenstand des 2. Energiesatzes. Kein tiefgreifendes dynamisch-biologisches Problem ist ohne diese differenzierung der kreisförmigen Wechselwirkung und der linienhaften Wechselbeziehung, die bis jetzt nicht erkannt wurde, zu verstehen.
Im Gegensatz zum physikalischen Bereich gibt es im lebenden Organismus irreversible und reversible Prozesse. Die reversiblen Abläufe sind zu gliedern in redox-potentielle Umwertungen und autonom-dynamisch charakerisierte Funktionen, die als spezifisch tonusgebundene Funktionen anzusprechen sind.
Die reversiblen Systeme, *Redoxpotentiale* genannt, bewirken als Vitamin der anaeroben und Hämine der aerobe Phase aus Energiekomponenten der Nahrung über die Kettenreaktionen der Wasserstoffoxidation neben Wasser eine *Einheit*, und zwar *Wärme*, die die Basis der *Energiequelle* des Organismus darstellt – 1. Funktionsebenen. Im Bereich dieser 1. Funktionsebene wird durch ein Fermentsystem oxydativ-reduktiver Art die Mannigfaltigkeit der Nahrungsenergien freigelegt und in eine Einheitsenergieform – Wärme - gebracht. Hier kann - an sich – also ohne autonomdynamische Insuffizienz - eine Vermehrung der Entropie nicht eintreten, wodurch der gesetzmässige Ablauf redoxpotentieller Umwertungen garantiert wird. Mit Beginn der 2. Funktionsebene tritt ein spezifisch biologisches Geschehen in Erscheinung, das, von nur körpereigenen Katalysatoren als treversibles System bewirkt, die Umwandlung der Wärmekalorien in spezifische Organenergien vollzieht und dadurch im Ablauf formgerecht dem Begriff des 1. Energiesatzes entspricht. Damit wird *jene Funktionsebene berührt und entropisch analysiert, die mit der Einheitskalorienquelle beginnt und mit der Organfunktionsbasis endet*. Es ergibt sich, dass diese organ-energetisch-biokatalytische Einheit ein Funktionssystem darstellt, das *an sich* – also ohne pathologische Zustände im Organismus – *ohne* Entopiezunahme das funktionelle Geschehen sichert und die Voraussetzung für die reaktive Funktionsdynamik bildet. Auch hier tritt durch das reversible System – an sich – eine physikalisch Entropie nicht ein.
Im Gegensatz zu diesen beiden redoxpotentiell gebundenen Funktionsebenen unterliegt die 3. Funktionsebene des autonom-funktionelle Systems, die im Sinne einer funktionelle Bindung ebenfalls reversibel ist, *der Entropie als Verlust, weil sie die Sicherung der Funktion, der Harmonie und der Gestalt vollzieht*.
Während es sich bei den ersten beiden Funktionsebenen im Krankheitsfall *um partielle Funktionsanomalien handelt, die, an sich an ein reversibles System gebunden, an sich nicht nicht verlust-entropisch sind, ist die 3. – spezifisch autonome – Funktionsebene, weil kosmisch-metaphysisch charakterisiert, den Gesetzen der Enropie im Sinne des Todes unterworfen.*

Die Energieumwandlung im Organismus lässt bei diesen *Prozessen zwei gleichgerichtete entropische Erscheinungen darin erkennen, dass erstens nicht die gesamte Energiemenge freigegeben wird und zweitens, dass an sich das Bestreben besteht, in den energieärmeren, spannungsgeringeren oxydativen Zustand überzugehen, um einem ruhebedingten, tonusgebundenen Zustand zum Zwecke einer Arbeits-, bzw. Funktionsleistung zuzustreben.* Sind beide Prozesse gekoppelt, so nimmt die Entropie auch im Reich der Nichtumkehrbarkeit, der 3. spezifisch autonomen Funktionsebene *an sich nicht zu*, weil das zweite, parallel geschaltete reversible System eine Entropie-Zunahme der irrevesiblen Prozesse durch Rückspannung eines reduktiv oder oxydativ stärkeren Systems pendelartig ausgleichend, verhindert. Durch das Moment der möglichen Rückspannung im Bereich der reversiblen Systeme und der dadurch gegebenen Beeinflussung der irreversiblen Prozesse erhält die Entropie biologisch ein anderes Gesicht wie in der Physik, *weil die Entropie der biologisch reversiblen Prozesse offenbar eine sinngerechte Energiesicherung zwecks möglicher Aufnahme neuer Energie darstellt, wodurch das Leben erst möglich wird*.
Daraus ergibt sich, dass dieser – autonom bedingte – Energierückstand bei einem Wechsel der Energieform da sein muss, um im Bereich des Werdens die lebende Funktion zu garantieren. Deshalb is die Entropie nicht a priori als Verlust anzusprechen, sondern könnte erst *dann* in physikalischer Übereinstimmung so benannt werden, wenn die autonom gegebene Energiesicherung – physikalisch Entropie genannt – sich durch autonomisch dynamische Insuffizienz vermehrt. Da unter Krankheitsbedingungen im Organismus eine Vermehrung der Entropie - eine positive Entropie – eintritt, wird der Entropiebegriff für die Autonom-dynamische Biologie ein Feld entscheidender Problemstellungen.

In genauer Übereinstimmung der biologisch-dynamischen Erfahrungen mit dem physikalischen Grundgesetz (Wirkung = Energie.Zeit) lässt die Funktionsleistung im Organismus nach, wenn im Krankheitsfall entweder die Substanzenergie oder die katalytische Geschwindigkeit, bzw. beides geringer wird. Da sich die Masse der Energie mit der Geschwindigkeit der Elektronen ändert, besteht hier eine gesetzmässige Beziehung, die für die ärztlichbiologische Therapeutik von entscheidender Bedeutung ist; denn ohne normale Geschwindigkeit der Reaktionen, d. h. der Elektronenbewegungen, tritt eine Verringerung der Masse als Wirkung ein und demzufolge eine Vermehrung der Entropie, bzw. eine Zunahme entropiecharakterisierter Anomalien auf den verschiedenen Funktionsebenen des Organismus.
Der zum 1. Energiesatz in Beziehung gebrachte 2. Energiesatz kann als Idee nur Sinn und Inhalt bekommen durch die dynamisch-autonome Auffassung, *dass bei einer Energieumwandlung ein Energierückstand des Systems eintreten muss, um durch ein reversibles System das Leben zu bedingen*. Damit wird in dynamischen Systemen des Organismus kausales und akausales Geschehen derart gebunden, dass das akausale Moment dynamisches Prinzip der funktionellen Kausalität ist, und die Aktivierung und Dynamisierung der autonomen Funktion die Überwindung der primär möglichen Vermehrung der Entropie des Organismus bedeutet.

Die dynamisch-biologische Konzeption ruht demnach auf der hier erstmalig sinngerecht zusammengefassten Formulierung des 1. und 2. Energiesatzes: Bei dem Vollzug der in jedem dynamisch-physikalischen und dynamisch-biologischen System möglichen Energieumwandlung bleibt – autonom bedingt –

ein bestimmtes Energiequantum als ›Entropie‹ gebunden. Bei der an sich möglichen Vermehrung der Entropie wird die Konstanz der Entropie und Sicherung der raumenergetischen Ordnung dadurch garantiert, das die Konstanz der Entropie, die die Voraussetzung der gesetzmässigen Energieumwandlung darstellt, im lebenden Organismus durch ein zweites reversibles System als Ausdruck autonom-dynamischer Funktionsleistung vollzogen wird und im Kosmos durch Eruptionen von Energie-Systemen.

Eine Therapie, für die die Mittel nicht Medikamante, sondern energiegebundene Symbole funktionell-dynamischer Struktur sind, ist infolge ohne eine *neue* gestaltende Sinngebung des Entropiesatzes nicht denkbar. Zu versuchen vom Mittel auszugehen, wie es jede andere therapeutische Form der Medizin tut, würde Autonom-dynamische Biologie zu einem Nichts im leeren Raum machen. Diese neue Konzeption, festgefügt nach allen Seiten, dynamisch-biologisch und nicht mechanisch-medizinisch fundiert, ist vor allem auf die Redoxpotentiale – Ferment-Systeme mit wasserstoffaktivierender-anaerober – sauerstoffaktivierender-aerober – Komponente – reversible, also anders charakterisiert.
Vitamine und Hormone sind trotz reichlicher Zuführung wirkungslos, wenn die katalytische Dynamik, die der Organismus durch Oxydationssteigerung bewirkt, verringert ist. Dazu tritt ein zweites Moment hinsichtlich der Energiemasse. Beim Einbruch einer toxischen Krankheit wird Substanzenergie hinsichtlich Masse und Geschwindigkeit herabgesetzt. Da Wechselbeziehungen betehen und eine verringerte Ablaufgeschwindigkeit die Wiekunsenergie vermindert, hat das dynamische Feld zu wenig *Wirkung*. Es *muss* sich also – im Sinnne der anorganischen Natur – die an sich konstante, aber, aber entropisch vermehrte Tonus-Energie umwandeln, um notwendigerweise durch Atomzerfall die Entropie zu vermindern, d. h. das autonome Feld wird in der Leistung negativ. (autonome Funktions-Insuffizienz infolge energetischer Wirkungsverminderung). Der Organismus gerät also energetisch-dynamisch nach zwei Seiten in ›Verlust‹ und ist also hinsichtlich der Substanzenergie und der Geschwindigkeit zu sichern, die wiederum nach zwei Seiten entsprechende Substrate gesetzmässig fordern. Man kann schon hieraus ermessen, wie sinnlos es ist, dass dieser oder jene Pflanzenextrakt ›als Mittel‹ eine Krankheit ›heilen‹ soll, die eine *Summation* von tiefgreifenden dynamischen, sich wechselseitig bedingenden Fehlleistungen darstellt.

Die schulmedizinische und landläufig biologische Form begnügt sich der ›Substitutionstherapie‹, d. h. mit der Zuführung des ›äusseren‹ Faktors. Die dynamische Form unternimmt es, den ›inneren‹ *dynamischen* Faktor zu normalisieren, d. h. das Kraftaufgebot der konstitutionellen Energie, die im Vegetativen wurzelt, und die erforderlich ist, um die notwendige Simplexverbindung zwischen Kolloid und Wirkstoff (Vitamin, Ferment, Hormon) zu ermöglichen, wieder herzustellen.
Aufgrund der Kenntnis der Probleme der Hormon-Vitamin-Ferment-Einheitswirkung in ihren Voraussetzungen und gesetzmässigen Bindungen (Agon-Pheron) liegt in der Unspezifität des Handelns die Spezifität des Zieles. Ob man dabei wissenschaftlich das Grundphänomen der oxidativ-reduktiven Abläufe überprüft und das Problem von der Seite der Reduktionsfähigkeit als Mass für die Grösse der freien Energie sieht oder die Empfindlichkeit der der Wirkstoffe gegenüber der Oxidation unter Einschaltung, dass in Gegenwart von

Farbstoffsensibilisatoren der Sauerstoffverbrauch besonders bei biologischer Strahlung gesteigert wird – berücksichtigt, immer bleibt grundsetzliche Forderung der Therapie, die konstruktiven Gesetzmässigkeiten des komplizierten biologischen Geschehens als *Gesetz* von der vegetativen Funktionserhöhung als Gesetz zu wandeln und zu formen.
Die Therapie der biologischen Dynamik unterscheidet sich in drei Punkten von sonstigen Behandlungsformen:

1. Sie berücksichtigt grundsätzlich die letzteren Ursächlichkeiten der Störung im bereits dargelegten Sinne.
2. Sie berücksichtigt diese letzte Ursächlichkeit nicht als individuelle Einzelerscheinung, sondern als funktionelle Störung eines gesetzmässigen Krankheitsbegriffs.
3. Sie berücksichtigt folgerichtig nicht nur ein einzelnes ›Mittel‹ sondern in grundsätzlicher chemisch-physikalischer Verbindung einen therapeutischen Begriff in bestimmter Abstufung und Verteilung, der dem Krankheitsbegriff gerecht wird.

Die von mir entwickelte Behandlung, die nach umfassender klinischer Untersuchung der Organe, des Blutsystems und der Stoffwechselfunktionen in Form einer Kur durchgeführt wird, ist die Verbindung von dynamischer Biologie und dynamischer Homöopathie. Durch die Bindung dieser beiden Behandlungsformen wird eine besonders erfolgreiche Wirkung auf die verschiedenen Krankheitsbegriffe und eine *Potenzierung* hinsichtlich des Gesamtorganismus erreicht. Der Grundgedanke bei dieser Kombination liegt in dem Prinzip begründet, *biologische Funktionen* dynamisch zu beeinflussen, um vom *Nervensystem* her eine *Heilung* der akuten und chronischen Organerkrankungen zu vollziehen. Die übliche ärztliche Auffassung, dass man eine Krankheit mit einem Mittel heilen könne, ist irrig. Im Gegensatz dazu wird hier ein System *verschiedener*, *aufeinander* bezogener ›Mittel‹ angewandt, um gegebenenfalls auch *mehrere* Krankheiten *zugleich* zu heilen bei gleichzeitiger hochwertiger Beeinflussing des Gesamtorganismus. Die eigentliche Idee dieser neuen Therapie, die eine *allgemeine* Behandlung fordert, liegt darin, dass die bei den einzenen Krankheiten gestörten *Funktionen*, also das eigentliche Wesen einer Krankheit behandelt wird.
Die dynamische Therapie, die dem *neuen* physikalischem Denken (Quanten-Physik) verbunden ist, wird ergänzt und verstärkt durch Lichtbiologie, Ultrakurzwellendurchflutungen und Kontaktbestrahlungen des Eigenblutes. Eingeschaltet wird – in geeigneten Fällen – die Ultra-Schall-Therapie – nachweislich völlig ungefährlich – und die Tiefenpunktmassage. Es kommt aber *nicht* auf die *technischen* Anwendungsformen an, d. h. *was* gemacht wird, sondern auf die gedanklichen Auswertungen wissenschaftlich gebundener Konzeptionen, d. h. auf die Problemlösung wie eine so komplizierte Erscheinung, wie sie eine Krankheit darstellt, restlos beseitigt werden kann.
Den Kernpunkt der Therapie bildet das Beziehungssystem biologischer und homöopatischer Energiesubsrate, die in ständig kombiniertem Wechsel auf breiter Beziehungsbasis gegeben, das Neuartige und Wirkungsvolle darstellen. Sie werden als Injektionen oder in Form von Einreibungen in die Haut verabreicht, sie erhalten aber erst die volle Resonanz und die entscheidende Wirkungskonsequenz im Zusammenklang mit den anderen Anwendungen.

Die Behandlungen (lt Erfahrung bei chronischen Leiden im Durchschnitt 40-50 Behandlungen, bei akuten Erkrankungen wesentlich weniger) wird bestimmt durch die *Dauer* und *Schwere* sowie die *Zahl* der festgestellten Erkrankungen. Es ist wenig verständnisvoll, auf eine Verkürzung der Behandlung zu drängen, da der *Abbau* der stets vorhandenen ver*dickten* Gewebspartien eine biologisch gegebene Zeit erfordert. Diese Gewebsverdickungen sind die eigentliche Voraussetzungen für eine mögliche bösartige Entartung.

Torkler

1. Biologisch-therapeutische Form der körpereigenen Organsubstrate die aber – nicht as Medikament – sondern als Potential-Energien verwertet werden.
2. Sympathicus/Parasymphaticus: Gleichgewicht und Arzneimittelwirkung
3. Homöopathische Mineralenergien (neu entwickelt)
4. Heilung geschieht nur unter der gesetzmässigen Voraussetzung der Dynamisierung der autonomen Funktion.
5. Dynamisch-biologische Schmerzbekämpfung: Hier wird nicht das Nervensystem betäubt, sondern es wird der *Tonus* des Gewebes durch Entspannung normalisiert.
6. Mit der ›Entropie‹ als Funktionsvoraussetzung, wird die Energiekonstanz als Totalitätspotenz durch redox-potentielle Katalisoren in Form von pflanzlichen und tierisch-menschlichen Energiesubstraten vollzogen. Wir vollziehen eine Dynamisierung der Funktion, die vor allem eine Normalisierung des Gewebstonus einschliesst.
7. Schmerztherapie. Da die dynamisch-therapeutischen Wirkungen von Dauer sind, wird erwiesen dass Substanzenergien über ein autonomes Feld auf alle Funktionen dynamisierend und damit normalisierend wirksam sind.
8. Als dynamisch-biologisches Grundgesetz gilt, dass alle dem autonomen Nervensystem verbundenen organischen Zellkomplexe, auf akut wirkende oder chronisch wiederkehrende Schädigungen, in ihrer energetischen Funktionsleistung vermindert werden. Dadurch nimmt die Präzision der autonomen Lenkung ab, und pathologische Erscheinungen sind die Folge, deren therapeutische Beseitigung nur durch Intensität, Summation und Zusammenwirkung von Energien möglich ist, die entweder dem lebenden Organismus oder der Pflanzen- und Mineralwelt entstammen.
9. Nicht dass ich körpereigene Organ-Substrate als funktionsfördernde Energien gebe, nicht, dass ich direkte Bestrahlung, bzw. Durchflutung des Blutes anwende, nicht, dass ich katalytisch, bio-katalytisch oder elektrobiologisch behandle, ist entscheidend; auch nicht dass ich in sinngerechter Kombination mit diesen Behandlungsfaktoren nicht die klassische, sondern die dynamische Homöopathie verwerte. Das allein Bestimmende bei Anwendung dieser Behandlungsfaktoren ist die gedankliche Ausrichtung auf die entscheidenden, soeben entwickelten dynamischen Grundprobleme der neuen Physik und der neuen autonomen Biologie.
10. Reaktivierung/Aktivierung des Biokatalysorensystems in Form einer direkten Beeinflussung des vegetativen Systems.

2.1.3 Transgenerational accumulation of Patho-Information-Engram loadings

2.1.3.1 Epigenetics

a) Evolutionary dimensions

Genes communicate with the environment and gene expression may be altered in response to external information from the environment. Genes appear to have at their disposal alternative strategies of development which they switch or suppress in accordance with environmental dictates. Such dynamically changing information is inherited from generation to generation by epigenetic mechanisms (Geist 1978). It is here termed epigenetic information. The incorporation of information from the environment buffers against selection at the genetic level, but involves positive as well as negative environmental information (Patho-Information-Engramm-Einlagerung). Paleolithic people thus began taking advantage of the hidden epigenetic mechanisms through which our genes can express themselves in order to maximise undividual adaptability to the highly diverse demanding periglacial and cold zones they colonized.

Jablonka & Lamb (2014):

Pigliucci (2007): Increasingly compelling indications of heritable epigenetic effects (Rap & Wendel 2005, op. cit. Pigliucci 2007; Richards 2006, op. cit. Pigliucci 2007). Understanding evolutionary processes furthermore requires the inclusion of impacts of the phenomena of phenotypic plasticity, the possibility of evolutionary capacitance and epigenetic inheritance (Pigliucci 2001, op. cit. Pigliucci 2007; West-Eberhard 2003, op. cit. Pigliucci 2007). The interplay between plasticity and selection is complex, as plasticity in itself is an evolvable property of the genetic-developmental system of living organisms (can be selected for and become adaptive). At other times it may buffer the action of selection, leading to the build-up of genetic redundancy (Lenski et al. 2006, op. cit. Pigliucci 2007). Plasticity and its related opposite, developmental canalization (Waddington 1942, op. cit. Pigliucci 2007; Flatt 2005, op. cit. Pigliucci 2007), involve the possibility of evolutionary capacitance (storage and release of variation; Rutherford & Lindqist 1998, op. cit. Pigliucci 2007; Masel 2005, op. cit. Pigliucci 2007), i.e. the accumulation of hidden genetic variation becoming relevant under conditions of stress; thereby possibly presenting alternative pathways for the origin of new phenotypes. Finally, much evidence has emerged for the existence of inheritance at the epigenetic level (Jablonka & Lamb 2005); with genotype and epigenotype interaction manifesting in a compex array of short- and long-term heritable combinations.

b) Epigenetic mechanisms

Jablonka & Lamb (2007):

Jablonka et al. (1995): Studied the adaptive value of carry-over effects, the persistence of induced phenotypes representing particular phenotypic memories, persisting over several generations despite the change in conditions that first induced these phenotypes. Three different organismal strategies were compared: non-inducible (genetic), completely inducible (plastic) and intermediate (carry-over: the lingering of a particular phenotype over one or more generations) were compared in terms of fitness. Model analyses showed that under certain circumstances phenotypic memory (transgenerational carry-over of phenotypic memory) has adaptive advantage and is selected. Memory is advantageous in random and temporally fine-grained environments; whereas the plasticity strategy is superior in periodically changing coarse-grained environments (the plastic organism is then adapted to the prevalent environmental conditions most of the time). Evolutionary success involves a spectrum of adaptations, from short-term individual adaptations, through medium-term adaptations lasting only a few generations, to long-term stable adaptations.

GXE-keller 2014
EVOLUTION-FITNESS-bouchard

Jablonka, E. & Raz, G. (2009). Transgenerational epigenetic inheritance: Prevalence, mechanisms, and implications for the study of heredity and evolution. *The Quarterly Review of Biology*, 84 (2): 131-176.

c) Medical implications

McEwen (2016): Epigenetics refers to the regulation of the expression of genetic information without altering the DNA sequence. Various mechanisms are involved: CpG methylation, histone modifications that repress or activate chromatin unfolding (Allfrey 1970, op. cit. McEwen 2016), actions of noncoding RNAs (Mehler 2008, op. cit. McEwen 2016), the actions of transposons and retrotransposons (Griffiths & Hunter 2014, op. cit. McEwen 2016 op. cit. McEwen 2016) and RNA editing (Mehler & Mattick 2007, op. cit. McEwen 2016). In this context a major challenge throughout the life course is to find ways of redirecting future behaviour and physiology in more positive and healthy directions (Halfon et al. 2014). Gene expression in the brain changes continually with experience through into adulthood (Grey et al. 2014, op. cit. McEwen 2016). The loss of resilience of neural architecture with ageing (Bloss et al. 2010, op. cit. McEwen 2016) can be redirected with exercise (Erickson et al. 2011, op. cit. McEwen 2016). Chronic anxiety, possibly resulting from adverse childhood experiences, can respond to behavioural intervention in adulthood (Holzel et al. 2010, op. cit. McEwen 2016). Gard, Holzel & Lazar (2014, op. cit. McEwen 2016) and Gard et al. 2014 (op. cit. McEwen 2016) outlined the potential effects of meditation on age-related cognitive decline. A sense of meaning and purpose in life has been shown to benefit overall health and cognitive function (Fredrickson et al. 2013, op. cit. McEwen 2016). Resilience can be viewed as an active process involving ongoing adaptive plasticity without external intervention (Russo et al. 2012, op. cit. McEwen 2016). However, resilience is decreased and vulnerability increased by adverse childhood experiences which can result in the biological embedding of trajectories of the response

to stressful life events (Shonkoff et al. 2009, op. cit. McEwen 2016) throughout the life course (Halfon et al. 2014). This contributes disproportionately to allostatic overload in the form of physical and mental disorders over the life span (Felitti et al. 1998, op. cit. McEwen 2016; McGowan et al. 2009, op. cit. McEwen 2016).

Skinner et al. (2010): Transgenerational inheritance arises from the ability of environmental factors to promote a phenotype or disease state not only in the individual exposed but also in subsequent progeny for successive generations. The majority of environmental factors such as nutrition or toxicants such as endocrine disruptors do not promote genetic mutations or alterations in DNA sequence. However, these factors do have the capacity to alter the epigenome. Epimutations in the germline that become permanently programmed can allow transmission of epigenetic transgenerational phenotypes. Epigenetics is defined as 'molecular factors and processes around DNA that are mitotically stable and regulate genome activityindependent of DNA sequence'. Thus, environmental factors regulate genome activity independent of DNA sequence manipulation (e.g. epigenetics). An additional consideration for environmental influences on disease etiology is the developmental stage of exposure. Exposures during a crucial time of development can alter genome activity associated with the differentiation programming of cells or organ systems. This altered program and gene expression profile can then promote an abnormal physiology and disease at the later adult stage of development.
Although numerous environmental factors influence and promote adult-onset disease (such as nutrition and stress), this review focuses on endocrine disruptors, as this group of environmental compounds is one of the largest people are exposed to in society. Endocrine disruptors are environmental chemicals that affect the function of the endocrine system by mimicking or blocking the actions of hormones, altering hormone signalling or disrupting hormone production (Crisp et al. 1998, op. cit. Skinner et al. 2010). Accordingly, a large number of environmental compounds have endocrine disruptor activity; and the early life exposure to endocrine disruption can promote adult-onset diseases.

Epigenetic influences have been observed with environmental compounds, nutritional factors (Bertram et al. 2008, op. cit. Skinner et al. 2010; Heijmans et al. 2008, op. cit. Skinner et al. 2010) such as methyl donors (e.g. folate: Cooney et al. 2002, op. cit. Skinner et al. 2010; Cropley et al. 2006, op. cit. Skinner et al. 2010), inorganic contaminants such as arsenic (Singh & Du Mond 2007, op. cit. Skinner et al. 2010; Waalkes et al. 2004, op. cit. Skinner et al. 2010), airborne polycyclic aromatic hydrocarbons (Perera et al. 2009, op. cit. Skinner et al. 2010), drugs such as cocaine (Novikova et al. 2008, op. cit. Skinner et al. 2010), endocrine disruptors such as BPA (Dolinoy et al. 2007, op. cit. Skinner et al. 2010; Yaoi et al. 2008, op. cit. Skinner et al. 2010), phytoestrogens (Dolinoy et al. 2006, op. cit. Skinner et al. 2010; Guerrero et al. 2008, op. cit. Skinner et al. 2010), and chemicals used as fungicides (Anway et al. 2005, op. cit. Skinner et al. 2010) or pesticides (Andersen et al. 2008, op. cit. Skinner et al. 2010). Some studies have also demonstrated behavioural effects on DNA methylation, including maternal effects on nursing behaviour (Champagne et al. 2006, op. cit. Skinner et al. 2010) or depression (Oberlander et al. 2008, op. cit. Skinner et al. 2010). Exposures to environmentally relevant doses of BPA during the neonatal developmental period in rats produced DNA methylation changes associated with carcinogenic processes (Ho et al. 2006, op. cit. Skinner et al. 2010). Maternal exposure to BPA has been shown to alter methylation in the fetal mouse forebrain (Yaoi et al. 2008, op. cit. Skinner et al. 2010) and to roduce changes in behaviour responses in the

offspring (Palanza et al. 2008, op. cit. Skinner et al. 2010). These findings correlate with other studies showing epigenetic changes resulting from endocrine disruptor exposure, which affected aspects of neuronendocrine systems (Gore 2008, op. cit. Skinner et al. 2010) and behavioural neurorendocrinology (Crews 2008, op. cit. Skinner et al. 2010; Crews et al. 2007, op. cit. Skinner et al. 2010; Skinner et al. 2008, op. cit. Skinner et al. 2010).

Epigenetic transgenerational phenomena. A special category of genes called imprinted genes are subject to epigenetic programming and can be influenced by environmental exposures. From an epigenetic perspective, imprinted genes are a special class of genes because they have relatively unchanged DNA methylation patterns over generations and are not affected by the overall reset in methylation patterns that occur early in development (Constancia et al. 1998, op. cit. Skinner et al. 2010).
The germline is required for transmitting genetic information beyween generations and a permanent epigenetic modification in it can result in transgenerational phenomena (Jirtle & Skinner 2007). Epigenetic programming of the germline occurs during the migration of the primodial germ cells in the embrio. The migrating primordial sperm cells in the genital ridge undergo an erasure of methylation of the DNA during migration and colonize the early bipotential gonad before gonadal sex determination (Allegrucci et al. 2005, op. cit. Skinner et al. 2010). Once gonadal sex determination is initiated, the primordial germ cells develop female or male germ cell lineage and remethylate the DNA in a male- or female-specific manner. Therefore, the germ cell epigenetic programming during gonadal sex determination is a period sensitive to environmental factors (Allegrucci et al. 2005, op. cit. Skinner et al. 2010). The female germline then enters meiosis in the developing embryonic ovary, wheras male germ cells continue to proliferate until immediately before birth and then resume proliferation after birth until puberty (Durcova-Hills et al. 2006, op. cit. Skinner et al. 2010; Trasler 1998, op. cit. Skinner et al. 2010). The crucial period for epigenetic regulation and modification of the germline is during the embryonic period of primordial germ cell migration and gonadal sex determination. Multiple generation phenotypes (direct exposure of a gestating female F0 generation, the F1 generation embrio and the germline that will generate the F2 generation: Skinner 2008) must be differentiated from the transgenerational phenotype. The permanent alteration in the epigenetic programming of the germline appears to be the mechanism involved in the transgenerational phenotype (Jirtle & Skinner 2007).
Definition of transgenerational phenotype. Transgenerational phenotypes, by definition, exludes direct exposure and must be transmitted through several generations (Jirtle & Skinner 2007; Skinner 2008). The ability of a direct exposure to influence several generations is defined as a multiple generational phenotype, contrasting a transgenerational phenotype which requires the absence of a direct exposure to at least the F3 generation (Skinner 2008).

DOC EPI-REPROGRAMMING-morgan
DOC EPI-EARLY NUTRITION-waterland
Interestingly, transgenerational exposure of $A^{vy/a}$ mice to an ad libitum diet produces amplification of obesity, an effect that is suppressed when the diet is methyl-supplemented with extra folate (Waterland et al. 2008, op. cit. Skinner et al. 2010).

DOC EPI-METHYL-waterland

DOC EPI-

DOC EPI-skinner
DOC EPI-skinner-2008 108
DOC METHYL-jirtle 1

DOC EPI-TRANSGENRRATIONAL-matthews
DOC EPI-early life adversity-roth
DOC EPI-TRANSGENERATIONAL RESCUE-arai

Javierre et al. (2011): Autoimmune disorders comprise a wide range of genetically complex diseases, including systemic lupus erythematosus, rheumatoid arthritis, type 1 diabetes and multiple sclerosis. Epigenic mechanisms control gene expression and are influenced by external stimuli, linking environment and gene function. There is considerable evidence of epigenetic changes, particularly DNA methylation alterations, in diseases like systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis. Autoimmune disorders constitute a group of more than 80 different diseases characterized by immune attack of components a person's own body, mediated by autoantibodies and autoreactive T cells. The common feature that defines autoimmune diseases is the breakdown of immune tolerance and the subsequent malfunction of the immune system, resulting in inflammation and tissue destruction (Cho & Gregersen 2011). More people in in developed countries are affected by autoimmune diseases. Genetic susceptibility has a major role in autoimmunity development (Cho & Gregersen 2011). However, genetics cannot fully explain the hereditary patterns of autoimmune disorders. Genome-wide association studies have shown that genetic polymorphisms account for only 20 % or less of the phenotypic variance (Wallace 2010; Ballestar 2010). Environmental factors can directly or indirectly induce epigenetic changes, which modulate gene expression and thereby associating with changes in immune cell functioning. Epigenetics provides a source of molecular mechanisms which can explain environmental effects of the development of autoimmune disorders. DNA methylation alterations induced by a special maternal diet in descendent mice demonstrated the close relationship between environmental factors and epigenetic status (*inter alia* Waterland et al. 2010). Evidence for epigenetic changes induced by the environment also documented for humans (Waterland & Jirtle 2004; Heijmans et al. 2008; Katari et al. 2009; Waterland et al. 2010). Epigenetics focuses on the study of mechanisms and chemical marks that influence gene activity and ultimately cell function. There are two main epigenetic modifications: DNA methylation and histone modifications, both of which are associated with transcriptual regulation and determination of the cellular transcriptome, thereby contributing to cell identity and function (Portela & Esteller 2010). The breakdown of epigenetic regulation is now known to play a key role in the development of diseases. Exploiting the reversibility of epigenetic marks opens up the possibility of developing novel targets for therapeutic treatment. The importance of epigenetics in autoimmunity was first evidenced by the observation that DNA demethylating agents results in drug-induced autoimmunity (op. cit. Javierre et al. (2011). Although MZ twins are genetically identical, they are often discordant for autoimmune disorders. Thi discordance is the result of environmental influences, frequently operating through epigenetic mechanisms. A recent study showed that MZ discordant for SLE display differences in DNA methylation and expression in a number of genes associated with immune

function (Javierre et al. 2010). The global deregulation of the DNA methylation content is affected in many cell types in a range of autoimmune disorders. SLE (Lei et al. 2009); RA (Neidhart et al. 2000); progressive systemic necrosis (Lei et al. 2009); ulcerative colitis (Gloria et al. 1996); psoriasis (Zhang et al. 2010). Global changes in the DNA methylation content can have different effects, including gene expression alterations, imprinting signature modification, and reactivation of endoparasitic sequences, all of which contribute to the breakdown of immune tolerance checkpoints. Symptomatology is directly associated with the reduction in the level of this epigenetic mark (Richardson et al. 1990). CHECK

The global decrease of DNA methylation is also supported by autoreactivity in lupus-like disease as a consequence of hydralazine treatment, a drug that decreases DNA methylation levels (Mazari et al. 2007). Furthermore, global DNA hypomethylation has been detected in blood cells and synovial tissue of RA patients (Neidhart et al. 2000). Conversely, peripheral blood mononuclear cells from psoriasis patients are characterized by an increase of DNA methylation characterized by DNMT1 upregulation (Zhang et al. 2010). On the other hand, chromatin is chemically modified by apoptosis, generating new epitopes that may be recognized by the immune system (Boix-Chornet et al. 2006). Interestingly, this type of cell death is a typical feature of autoimmunity due to the increased rate of this event as well as the insufficient clearance of apoptotic debris noted in many autoimmune disorders. Moreover, cell death causes these new intra-cellular autoantigens to be released into the extracellular medium, explaining why the majority of autoantibodies react mainly react against intracellular components. A recognized apoptosis-induced change in the chromatin is the generalized loss of methylation (Emlen et al. 1994; Kaplan et al. 2002). The injection of apoptotic DNA into healthy mice generates a lupus-like disorder, but this autoimmune response is not obtained by methylated DNA (Wen et al. 2007). Non-methylated DNA is more antigenic than the methylated form, so the immune system can interpret the apoptotic DNA as microbial material, and so react against it (Krieg 1995; Yung et al. 1995). Genes important for immune homeostasis and cellular biology are affected by this this epigenetic deregulation mechanism. Specifically, many gene promotors are hypomethylated in autoimmune disorders (SLE: Javierre et al. 2010; Kaplan et al. 2004; psoriasis: Chen et al. 2008; Zhang et al. 2010; 2007).On the other hand, other gene promotors are hypermethylated (RA: Takami et al. 2006; scleroderma: Wang et al. 2006; ulcerative colitis: Tahara et al. 2009; 2009).

The enzymatic addition or elimination of chemical groups, including acetyl, methyl, or phosphate groups, among others, to the histone tails, determines the interaction of chromatin with different nuclear factors, regulating nuclear organization, gene expression, and genomic stability (Kouzarides 2007). The alteration of the histone modification profile can generate alterations in cellular phenotype and genomic stability, collaborating to produce the loss of immune tolerance in immune cells. The most widely accepted environmental conditions that trigger autoimmunity through epigenetic mechanisms are drugs, pollutants, viruses and other pathogens, sex hormones, radiation, heavy metals and stress.

Progressive Abnahme der Kinderzahl über Folgegenerationen, vor allem in begabten, erfolgreichen Familien in Europa. Gloria-Bottini et al. (2005) Is delayed childbearing

EPIGENETIK

DTB-EPI-auger-NB

XEPI-gluckman

XEPI-godfrey-

XAgrawal (2001) DL EPIagrawal

XFeinberg (2007)NB

Kegel (2015)

Riggs & Xiong (2004)

Jablonka und Lamb (1995)

Weaver et al. (2004)

Jablonka et al. (1995).

Jablonka & Raz (2009)

Sapolsky (2004)

Bonduriansky & Day (2009)

Richards et al. (2010)

Simmons (2009) PREGNANCY

Aguilera et al. (2010) EPI-aguilera

Pál (1998) PLASTICITYpal (DL)

Vaiserman (2011) NB

Skinner et al. (2010)

Godfrey et al. (2007).

Waterland & Jirtle (2004).

Mcmillen & Robinson (2005)gestationfetalprogramming MS

Mill & Petronis (2008)

Weaver et al. (2004) DL ADHDweaver

Meaney (2001)

Petronis (2004) MS: EPIpetronis

Phillips (2007) MS: EPIphillips2007NB

Phillips et al. (2006): MS: EPIphillips2006

Godfrey et al. (2007) EPI-godfrey

Jablonka and Lamb (1995): The genome can be described as an active response system as well as a passive information carrier. There are epigenetic inheritance systems, which enable cells with identical genotypes to acquire and transmit different phenotypes. Epigenetic variations are transmitted in somatic cell lineages. The chromatin-marking inheritance system, in which chromatin marks, such as patterns of

DNA methylation, are transmitted between cell generations and may determine cell phenotypes. The same DNA sequence may carry different marks; although the DNA sequence dertermines which marks are possible, the particular variant that is actually present and inherited does not depend on the DNA base sequence alone, but also on the environmental and developmental history of the lineage. Genomic imprinting: in which the parental origin of chromosomes influences gene expression in the progeny. The reversible imprints established during oogenesis and spermatogenesis are a special case of transmission of epigenetic variations. Epigenetic inheritance systems have both direct (because epigenetic variations can be selected) and indirect effects on evolutionary changes (because the existence of cellular memory imposes constraints on various developmental strategies).

There is evidence suggesting that there are mechanisms that enable the genome to sense environmental change, respond to it, and transmit the response to descendants (thus two inheritance systems: genetic and epigenetic). Chromatin restructuring that goes on during gametogenesis resets the genome and ensures that most previous epigenetic information is erased. In spite of this some epigenetic information persists.

Present evidence that epigenetic variations are transmitted through the germ line, occasionally for many generations. Parental age effects in which the age of the parents influences the phenotype of the offspring and Lansing effects. Lansing (op. cit. Jablonka and Lamb 1995) drew attention to the way in which parental age affected the longevity of the next generation. The progeny of old parents do not live as long as those of young parents. This effect is cumulative, but also reversible.

Wallace (2010): The availability of and demand for energy is central and the flow of energy through the cell is primarily mediated by the mitochondria which oxidize reduducing equivalents to generate ATP through oxidative phosphorylation (OXPHOS). The mitochondrial encompasses hundreds of nuclear DNA (nDNA)-encoded genes and 37 mitochondrial DNA (mtDNA)-encoded genes. Milder, potentially adaptive mutations are introduced into the population through female oocytes. The expression of mutations in nDNA-encoded bioenergetic genes is modulated by histone phosphorylation and acetylation (using mitochondrially generated ATP and acetyl-CoA). This permits increased gene expression, growth and reproduction when calories are abundant. Accordingly, mtDNA mutations provide heritable and stable adaptation to regional differences, whereas mitochondrially-mediated changes in the epigenome permit reversible modulation of gene expression in response to fluctuations in the energy environment. Common genomic changes that interface with the environment and cause complex diseases are therefore considered to be of mitochondrial and epigenomic origin.

Hanson (2013): According to studies the estimated heritability of life expectancy is about 25 %, but epigenetic mechanisms result in individuals with the same genotype to have increasingly divergent phenotypes with age. Gene expression is influenced by the environment through epigenetic modifications (op. cit. Montesanto et al. 2012). There may also be epigenetic changes in response to individual social experiences thoughout life (Champagne 2010).
Champagne (2010) EPI-champagne Affluence, urbanization effects, patho-information-engram loading (accumulation in epigenome): earlier transgenerational impacting on upper class, wealthy through life mastering competence (middle class) Relevant studies have provided evidence for profound effects of social interactions on the developing brain. Mother-infant attachment studies where secure attachments favour long-term resilience to physical and psychological distress and insecure relationships resulting in increased risk of anxiety and depression (Sroufe 2005). Effects of variation in parental care can persist into adulthood with high parental bonding being associated with elevated self-esteem, reduced trait anxiety decreased salivery cortisol and reduced activation within the ventral striatum (op. cit. Champagne 2010). The quality of the social environment beyond infancy is capable of shifting patterns of gene expression with consequences for the functioning of the the individual within the social context. These epigenetic effects may play a critical role in developmental plasticity and in mediating adaptive responses to environmental conditions within and across generations. Epigenetic regulation of gene expression is particularly important during the early stages of development. Maternally and paternally imprinted genes exhibit parent-of-origin expression patterns that are maintained through epigenetic mechanisms such as DNA methylation, These genes have a variety of functions and the appropriate silencing of either the maternal or paternal allele is essential for the establishment of normal patterns of growth and development.There is increasing evidence for the epigenetic influence of maternal nutrition, physiology and psychological state on the developing fetus that are relevant to our understanding of how the social and environmental experiences of the mother can lead to divergent developmental pathways of offspring (Curley et al. 2008). The notion that the quality of the social environment can have a transgenerational impact is gaining considerable empirical support The biological embedding of the quality of the social environment may have adaptive versus maladaptive consequences depending on the context of the individual (Miller et al. 2009). The induction of a defensive phenotype, based on a low socio-economic status early in life, characterized by heightened immune and HPA reactivity which may prepare an organism for conditions of threat, but long-term exposure to these defensive responses may increase the likelihood of physical and psychiatric illness.

Laszlo (2014a): 56:

Citro (2011): 214

Geist (1978): Although the sequence of genes in the DNA is fixed, the way
that sequence affects the body is flexible; it is governed by the epigenetic system; which is adaptive. Not only would this produce inquisitive, vigorous and intellectually

competent individuals, but also people that could control themselves. Dispersal phenotypes ought to be able to suppress and control appetites, forego temptations and aversions; to do something in spite of their emotions and internal monitoring systems. Individuals respond to the dictates of reason far more than under maintenance phenotype conditions. Humans who are born to perpetual conflicts between internal drives are born with and the dictates of reason. The closer individuals develop ontogenetically to a dispersal phenotype, the less difficult self-control and self-disciplin ought to be for them because the threshold for pain and pleasure ought to be higher.

Hohe Kampf-Flucht Reaktionsschwelle.

2.1.3.2 Epigenetic PIE syndromes

a) EPIE-impaired protein metabolism (IPM)

(according to homeopathic terminology this would include the tubercular miasm; Traditional Chinese Medicine: spleen and kidney yin/yang deficiency, probably on the basis of essence deficiency) also Wendt

b) Cognitive performance and emotional harmony: EPIE-anxiety disorders syndrome (ADS) MS DIET-dyslexia

Anxiety Disorder Syndrome

ADHD (ADHS: Aufmerksamkeits-Defizit-Hyperaktivitäts-Störung) is part of the *Information Processing Response Dysregulation Syndrome* (IPRDS). Der Zusammenhang zwischen Allergien und Hyperaktivität ist seit langem bekannt und bestätigt (Rochlitz 1989). Damit lässt sich die Hyperaktivität bei Kinder als eine Reaktion auf Allergene im Alarm- und Anpassungsstadium (*vide* Selye 1978) erklären (Rochlitz 1989). Solcherart Anfälligkeit ist bei einer niedrigen Kampf-Flucht Reaktionsschwelle zu erwarten (2.3.2); als eine Art von psychoallergischer Reaktion auf Reizüberflutung. This syndrome also includes other/related clinical disorders such as adult ADHD (this condition is maintained in more than 50% of adults with ADHD in childhood and generally occurs in patients with dyslexia/dyscalculia). ADHD in adults is associated with impairments in many life activities, increasing the risk of chronic stress in every-day life activities (Hirvikoski et al. 2009). ADHD is the most common neurobehavioral disorder presenting in children and such children represent a group at risk in respect of their further emotional and social development (Mousain et al. 2011). ADHD is considered a neurodevelopmental disorder; associated with a variety of comorbidities (including psychiatric and behavioural disorders such as

conduct problems, alcohol misuse, mood disorders, social cognitive impairments). Symptoms of this disorder in adults include hyperactivity, aggressiveness, emotional lability, stress-proneness, impulsivity, sleeping disorders, anxiety, loss of selfrespect and self-trust, easily upset, panic attacks and recurrent nervous breakdowns (Mousain et al. 2011). Adults with ADHD suffer from increased vulnerability to daily life stressors, experiencing significantly greater subjective stress (Lackschewitz et al. 2008). These symptoms are typically as expected in compromised individuals with low fight-flight reaction thresholds, spontaneously responding in states of alarm or exhaustion (Selye 1978). A dysfunction of the dopaminergic system appears to be involved in ADHD (Warton et al., op. cit. Papadopol & Nechifor, in Vink & Nechifor 2011). Dopaminergic and serotonergic neurotransmitter imbalances are implicated in ADHD (Del Campo et al. 2011; Wu et al. 2012).

Pyroluria (a condition widely accepted in orthomolecular medicine) is commonly associated with other disorders, such as depression, anxiety spectrum disorders, mood disorders, immune problems and alcoholism (Scott 2011; Gedgaudas 2011). Pyroluria patients are generally stress intolerant and share many symptoms often also typical of adult ADHD, such as morning nausea, pale skin or poor tanning, hypersensitivity to load noises, dyslexia, poor ability to cope with stress, mood swings or temper outbirsts, argumentative, new situations or changes in routine are experienced as stressful, anxiety, easily upset by criticism, carry a lifelong inner tension and bouts of depression or nervous exhaustion (Scott 2011; Gedgaudas 2011). Testing for pyroluria (cryptopyrrole levels) is thus indicated in cases of ADHD and comorbid disorders, such as anxiety disorders. In pyroluria cryptopyrroles are not adequately excreted, binding to zinc and vitamin B6, with negative implications for neurotransmitter production, immune functioning, cognitive functioning, digestion and many more other functions (Gedgaudas 2011). Following Niederhofer & Pittschieler (2006), celiac disease, a destructive inflammatory disease of the mucosa of the upper small intestine, is treated by permanently excluding gluten from the diet (avoiding gluten as allergen). Patients affected by CD showed ADHD-like symptomatology (and CD-associated forms of neurological dysfunction: depression, mental and behavioural disorders) before initiation of treatment. An assessment after at least 6 months of a gluten-free diet, showed a significant decrease in the prevalence of ADHD-like symptoms. Such improvements of symptoms with a gluten-free diet is implicated to be associated with concomitant elevations in plasma concentrations of tryptophan (a

precursor of serotonin). Insufficiency of tryptophan in the central nervous system predisposes to disturbances in the central serotonergic system, with depressive disorders and aggression dysregulation (op. cit. Niederhofer & Pittschieler 2006).

Findings from a literature review indicate that both inherited and noninherited factors contribute and their effects are interdependent (Thapar et al. 2013). Environmental factors can influence how genes express themselves (Mill & Petronis 2008; Weaver et al. 2004). Heritability of ADS-IPRDS-type conditions apparently involves epigenetic patho-information-engram loading induced or sustained by fetal programming (refer also to Kudielka et al. 2009). Repeated reporting suggests that prenatal stress/stress during neuro-ontogeny may lead to abnormalities in brain development; particularly involving insults to the hippocampus during early development (op. cit. Huizink et al. 2004). Regarding altered HPA axis regulation in prenatally stressed offspring, the generally held hypothesis involves a) prenatal stress leads to enhanced release of maternal stress hormones, b) placental and maternal stress hormones enter the fetal circulation, and c) affect fetal hippocampal ontogeny by down-regulating glucocorticoid receptors, altering receptor sensitivity and exerting neurotoxic effects on the hippocampus (op. cit. Huizink et al. 2004). **These findings underpin the links between the anxiety disorder syndrome (ADS), neurological disorders, central nervous hyperexcitability, allergies, low fight-flight reaction thresholds; ultimately linked to metabolic functional inefficiencies as a result of accumulated (epigenetic) patho-information-engram loading.**

Deficiencies of zinc, iron, magnesium and vitamin B6 are implicated in ADHD (Vink & Nechifor 2011; refer also to Table 2.5.1.3b: The Magnesium Factor). Zinc, magnesium and polyunsaturated fatty acid insufficiencies do not appear to have causal healing effects; but supplementation has been found to ameliorate symptoms (Scott 2011; refer also to Bloch & Qawasmi 2011: omega-3 fatty acids). Central nervous system hyperexcitability (refer also to Durlach et al. 2000; Table 2.5.1.3b: The Magnesium Factor) is a characteristic magnesium deficit disorder and associated symptoms respond favourably to oral administration of magnesium (Papadopol & Nechifor, in Vink & Nechifor 2011). The results of the study by Bardgett et al. (2005) contributed to our understanding relating to changes in Mg^{2+} levels to brain function and behaviour. In congruence with other studies showing that Mg^{2+} supplementation improves memory after traumatic brain injury (Smith et al., op.cit. Bardgett et al. 2005), reductions in dietary Mg^{2+}, even in normal animals, resulted in memory deficits.

Intracellular magnesium deficiency affects neural transmission, and parents having provided high doses of pyridoxine (vitamin B6) and magnesium to their ADHD children have observed decreased aggressiveness and improved social responsiveness (Mousain-Bosc et al., in Vink & Nechivor 2011; Nogovitsina & Levitina, op. cit Mousain-Bosc et al. 2011). From the findings of their study on migraine patients, Lodi et al. (2001) conclude that the reduction in free Mg^{2+} in tissues with mitochondrial dysfunction (low brain cytosolic magnesium) is secondary to the associated bioenergetics deficit. This is in agreement with Barbiroli et al. (1999) who found that treatment with coenzyme Q_{10} increased the efficiency of oxidative phosphorylation and was accompanied by an increased cytosolic free Mg^{2+}, consistent with the hypothesis that brain cells regulate their cytosolic free Mg^{2+} as a function of the energy charge of the cell. This implies that supplementation with both Mg^{2+}-Vit B6 and coenzyme Q_{10} in combination is indicated.

Anxiety disorder syndrome. Head & Kelly (2009): Chronic exposure to psychological stress results in the chronic engagement of the fight-flight mechanism. Associated overreactions of the sympathetic nervous system induce increased secretion of stress hormones, such as cortisol and epinephrine; with numerous negative health consequences. Blood is also shunted away from the digestive system, thereby compromising its functional efficiency. Adrenal fatigue is often embedded within the syndrome of anxiety disorders (Scott 2011); associated with anxiety, neurotransmitter imbalances and restless sleep (Head & Kelly 2009).
Stress significantly affects the balance of intestinal microflora (Moore et al, op. cit. Head & Kelly 2009; Lizko et al., op. cit. Head & Kelly 2009).
Head & Kelly (2009) list a number of adrenal/central nervous system **adaptogens** (Adaptogens increase the resistance to physical, chemical or biological stressors and act as general stabilizers/normalizers: Davydov & Krikorian 2000); substances with relevance to the treatment of adrenal fatigue: *Panax ginseng*, *Eleutherococcus senticosus*, *Glycyrrhisa glabra/uralensis*, *Withania somnifera* (Ashwagandha) and *Rhodiola rosea*. DL ADAPTOGENS-OBESITY-herbal weight loss Withania administered to animals counteracted many biological changes accompanying extreme stress (Archana & Namasivayam, op. cit. Head & Kelly 2009). Chronic stress effects (hyperglycemia, glucose intolerance, raised plasma corticosteroid levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression, depression) were attenuated by Withania. Although having similar therapeutic effects, Withania does not present ginseng-abuse symptoms, such as high blood pressure, water retention, muscle tension and insomnia when consumed in excess (Bhattacharya & Muruganandam 2003). **Cortisol modulators** include phosphatidylserine (Some researchers implicated that oral administration of phosphatidylserine counteracted stress-induced activation of the HPA axis, op. cit. Head & Kelly 2009), fish oil (Delarue et al. 2003), plant sterols/sterolins and alpha-lipoic acid (op. cit. Head & Kelly 2009). Concerning fish oil, analyses by Delarue et al. (2003) support the interpretation that supplementation of such oil (rich in n-3 fatty

acids) inhibits sympatho-adrenal activation induced by mental stressors. Mental stress significantly increased heart rate, mean blood pressure and energy expenditure. It also increased plasma epinephrine, plasma cortisol and plasma non-esterified fatty acids. After three weeks of of dietary supplementation with n-3 fatty acids, the stimulation by mental stress of epinephrine, cortisol and non-esterified fatty acid concentrations were all significantly blunted (Delarue et al. (2003). Sympatho-adrenal activation is implicated in the pathogenesis of insulin resistance and the effects of fish oil may be involved in the prevention of insulin resistance (Björntorp & Rosmond 2000). DL STRESS-bjorntorp-obesity DL OMEGA3-hamazaki **Anxiolitic botanicals** (n=12) are also listed by (Head & Kelly 2009). These are involved in modulating neurotransmitter activity and dopaminergic/serotonergic pathways; generally with stress-attenuating, calming and sleep-promoting effects. One of these is L-theanine (from *Camellia sinensis*), also found in black and green tea: increases alpha brain wave activity, increases dopamine, serotonin and glycine (an inhibitory neurotransmitter). Increased alpha wave production in the brain after intake of only 50 mg of theanine; enhancing a mental state of relaxed alertness (Nobre et al. 2008). Oral L-theanine administration of 200 mg resulted in increased alpha brain waves, subjective sense of relaxation and an alert state of mind 40 minutes oral intake (Ito et al., op. cit. Head & Kelly 2009). An acute stress response induced by a test in mathematics was attenuated by 200 mg of theanine (Kimura et al. 2007). **Neurotransmitters** Gamma-aminobutyric acid (GABA), L-tryptophan/5-hydroxytriptophan, melatonin, L-tyrosine. **GABA** is the most important inhibitory neurotransmitter in the CNS. Persistent excitation (sympathetic nervous system overarousal) can result in a variety of anxiety disorders (including insomnia) and must be balanced by inhibitory modulation. Low GABA levels are linked to several psychiatric and neurological disorders, such as anxiety, depression and insomnia (Nemeroff 2003; Gottesmann 2002). GABA fo r sleep enhancement (Gottesmann 2002). Natural-source GABA, but not synthetic GABA, was shown to produce relaxation, as indicated by *inter alia* changes in brain wave patterns (increased alpha to beta wave activity) and a reduction of stress markers such as salivary cortisol (op. cit. Head & Kelly 2009). GABA-albers The anti-stress activity of GABA was also demonstrated in a study by Abdou et al. (2006), reporting the increase of alpha (indicative of relaxed alertness) to beta waves (prominent in stressful situations). **L-tryptophan** is the metabolic precursor to serotonin (neurotransmitter), melatonin (neurohormone) and niacin (vitamin B_3). The sedative and sleep-promoting effect of L-tryptophan does not limit cognitive performance or inhibit awakening (Lieberman et al. 1985). Brain serotonin activity is implicated to be involved in sleep promotion and cognitive processes. Markus et al. (2005): Brain uptake of the serotonin precursor tryptophan is considered to be dependent on nutrients that facilitate the availability of tryptophan by changing the ratio of plasma tryptophan relative to other neutral amino acids. α-Lactalbumin protein has a substantial tryptophan content, particularly so when enriched for experimental purposes (tryptophan content: 4.8 g/100 g). Increased plasma tryptophan availability for uptake into the brain in the evening enhanced sustained alertness in the following morning, an outcome attributed improved sleep quality. EXPAND MS TRYPTOPHAN-markus and Silber & Schmitt (2010) DL Tryptophan-silber **Hydroxytryptophan** The enzyme tryptophan hydroxylase is rate limiting for serotonin production. It involves the conversion of tryptophan to 5-HTP (hydroxytryptophan). Availabilty of this enzyme is reduced by stress, insulin resistance, magnesium deficiency, vitamin B6 deficiency or increasing age (op. cit. Head & Kelly 2009). Decarboxilation of 5-HTP to serotonin requires the presence of

the active form of vitamin B6, pyridoxal-5-phosphate (P5P). Further conversion to melatonin reqires S-adenosyl-L-methionine (Head & Kelly 2009).
5-Hydroxyptryptophan primarily acts by increasing CNS levels of serotonin and oral administration has also been shown to increase levels of melatonin, dopamine, norepinephrine and beta endorphin (op. cit. Head & Kelly 2009). The enhancement of serotonin and melatonin levels by 5-HTP is beneficial in cases of sleep disorders (Bruni et al. 2004). **Melatonin** Sleep onset time was significantly earlier during melatonin treatment. Melatonin appears to act as a phase setter for sleep-wake cycles in subjects with a delayed sleep phase syndrome (Dahlitz et al. 1991). During the biosynthesis of melatonin, tryptophan is converted by tryptophan hydroxylase to 5-hydroxytryptophan which is then decarboxylated to serotonin. The synthesis of melatonin from serotonin is catalized by two enzymes largely confined to the pineal gland (Brzezinski 1997). Melatonin is apparently involved in various biological functions (Brzezinski 1997): sleep regulation (hypnotic effect), control of circadian rhythms, immune response enhancement and may be involved in cyclic mood disorders (depression), antiproliferate effects in cancer and cell protective effects during aging. **L-Tyrosine** Stress-induced (psychosocial and physical stress) performance decline is associated with depleted brain reserves of the catecholamine neurotransmitters norepinephrine and dopamine. Tyrosine (an amino acid precursor of catecholamines) supplementation counteracts stress-induced depletion of brain catecholamines (nervous system norepinephrine); thereby enhancing performance under a variety of stressfull circumstances such as sleep deprivation, combat training, cold exposure and irritating background noise (Salter 1989 op cit. Head & Kelly 2009). Tyrosine improved cognitive performance under exposure to stress-inducing background noise (Deijen & Orlebeke 1994, op. cit. Head & Kelly 2009). **Vitamins** (Bs and C) as co-factors in stress modulating processes. Head & Kelly (2009) summerized the roles of the B vitamins in relation to stress: B_1 Thiamine (protective nutrient for adrenals, decreases stress-induced cortisol response), B_3 Niacinamide (involves sleep quantity and quality, shunts tryptophan to serotonin), B_5 Pantothenic acid (protective nutrient for adrenals, decreases stress-induced cortisol response), B_6 Pyridoxal 5' phosphate, P5P (cofactor for synthesis of GABA, serotonin and dopamine), B_{12} Methylcobalamin (resetting of circadian rhythms for improved sleep and normalizing cortisol peak), Folate, 5-Methyltetrahydrofolate (involved in neurotransmitter formation regarding serotonin, dopamine, norepinephrine, epinephrine). DL BRAIN-mattson, DL FOLATE-EPI-mattson MS-NEURONAL DEGENERATION-mattson DL INTELLIGENCE-NUTRIENTS-benton-306
Vitamin C (ascorbic acid) as cofactor in rate-limiting hydroxylase enzymes involved in monoamine neurotransmitter synthesis.
ADS: Positive effect of adjunctive nutraceuticals (review) such as omega-3 fatty acids for depression (Sarris et al. 2016). MS Tryptophan-sarris (in ref list);
SCOTT-1

Permanently subclinical

Information Processing Response Dysregulation Syndrome (IPRDS)

Clinically manifested ADS

Scott Hyman

Psychological well-being: central role of the serotonergic system

E-BOOK

Manuck et al. (2004) investigated the effect of socioeconomic status on adult central serotonergic responsivity. Consistent with findings summarized by Belsky and Pluess (2009) relating to depression, anxiety and persistent ADHD, individuals manifested the most and least serotonergic responsivity depending on whether they were of low or high socioeconomic status. CHECK
Muldoon et al. (2006) CHECK

Bracht 2018

c) EPIE-obesity disorder syndrome (ODS)

This syndrome relates to pathogenic obesity or overweight and should not be confused with fattines/bulkiness related to constitutional body types.

2.1.3.3 Recursion-healing

Vitalitätsstatus Link: Patho-Information-Engrammbelastung-reduzierter Vitalitätsstatus (Körperfunktionsenergetische Effizienz)-wenig evolutionskompetente Führungskapazität Abnahme von evolutionskompetentem Verhalten generell
Epigenetische Entrümpelung: Rekursionsheilung (Ernährung, Stressminimisierung, speziell: Schwangerschaft und Stillzeit; Ausheilung akutfieberhafter Erkrankungen: speziell: im Kindesalter; Naturheilweisen, Darmgesundheit, Fasten)
GS metabolic mode (Europe), adaptability, epigenetic load. Dispersal mode genetically fixed, importance of epigenetic adaptability, Nachteil: Patho-Engrammanhäufung (epigenetic load: adaptation to low nutrient, high stress: maintenance conditions and K-reproductive strategy).
Kafiren/Hunza: Vorbild von Vitalitätsnachhaltigkeit. Rekursion: create dispersal type conditions (nutrients/energy, absence of stress, fasting, exercise)
Constant influx of procursive impacts: stress, medications, environmental toxins
Rekursionsheilung ist ein generationsübergreifendes Projekt. Es durchläuft verschiedene Phasen, jede mit ihren phasenspezifischen Erwägungen (Vorreproduktive Erwachsenenphase: **2.3.3**; Schwangerschaft, Stillzeit, Frühkindheit und Kindheit: **2.3.2**).

Prokursionsimpakte = wenn nicht überwunden, werden als Pathoinformations-Engramme eingelagert (Überlebenswichtig zur Zeiten der Impakte) um dann zur späteren Verarbeitung im Zuge einer akuten Rekonfrontation wieder gelöscht zu werden (Rekursionheilung). Als epigenetische Information vererbt zur Vorbereitung der Nachkommen für eine Umwelt mit relevanten Prokursionsimpakten. Eine Löschung der (epigenetischen) Pathoengramme durch Rekursionsheilungsprozesse in der Form akuter Erkrankungen.

LASZLO 2008: 152 +

Dahlke 1987

Four forms of fasting are of particular relevance in the context of recursive healing: daily intermittent fasting, intermittent protein fasting, Schrothkur-fasting (Table **2.1.2i**) and extended full fasting (Table **2.1.2h**: above). Daily intermittent fasting involves the integration of fasting effects into the daily lifestyle thereby realising the full benefits of strongly indicated/required carbohydrate-rich and nutrient-rich carbohydrates for optimal performance and the prevention of patho-information-engram accumulation (Sections **2.1.2** and **2.1.3**; Table **2.5.1.5f**: **Daily intermittent fasting**). It is practised by traditionally healthy living populations (**2.5.1.2**). However, as thoroughly outlined by Wendt (1985), the efficiency of the protein metabolism is compromised to variable degrees in individuals living under conditions of sustained (transgenerational) affluence (AS: substantial patho-information-engram loading). In order to address this situation of an insufficiency of the protein metabolism therapeutically, (intermittent) protein fasting is required. Finally, recursive healing of epigenetic disorder syndromes (such as Impaired Protein Metabolism, Anxiety Disorder Syndrome and Obesity Disorder Syndrome) generally requires full extended fasting (Table **2.1.2h**).

IPM

The ultimate goal of recursive healing is to erase accumulated patho-information-engrams from the biokybernetic system of the body (**2.1.2**).

For the treatment of hypo-poropathies, protein fasting is indicated (refer to Section **2.1.2: Fasting**), but during full extended fasting (Table **2.1.2h**) more protein deposits are broken down and more effective treatment of more severe diseases (e.g. diabetic microangiopathy, nephrosclerosis, coronary heart disease) is achieved (Wendt 1985).

Blood-letting, in conjunction with protein fasting, is very effective in order to clear pathological protein deposits in the body. Any disease conditions which result in protein depositions should be addressed and followed up with protein fasting; starting off with blood-letting. It is important to ensure a functional carbohydrate-energy metabolism (sufficiency of carbohydrate supply; replacement of cholesterin with poly-unsaturated fatty acids). When additionally required, plasmapheresis can also be considered to further enhance/complete this therapy (Wendt 1985). (Blood-letting and plasmapheresis to be undertaken under the supervision of a medical professional).

ADS

ODS 440-442 wendt

For obesity/overweight, one fasting day per week is considered useful, but for more severe cases a series of fasting weekends (e.g starting Friday afternoon to Monday morning) would be required. Calorie-free fluids *ad libitum* (Wendt 1985).

2.2 Life history trade-off relationships as context for health and disease

2.2.1 Evolutionary medicine: origins of disease vulnerability

a) Trade-off-constraints in health and disease

Understanding the evolutionary origins of disease vulnerability (ultimate causality), together with an understanding of the more proximate causes of disease, synergistically promote a fuller understanding of cause-effect relationships of diseases (Nesse 2011). Most diseases are not shaped directly by natural selection or other evolutionary forces and are not in themselves appropriate for evolutionary explanation. Rather, evolutionary explanations require focussing on aspects of the body that make it vulnerable to disease. Predictive adaptive responses are therefore important areas of evolutionary medicine (Gluckman et al. 2005). DL EVOLUTION-gluckman The

trade-off between the capacity for enhanced competence at the cost of increased vulnerability to illness is manifesting, for example, in uric acid metabolism (2.2.1c). Most vertebrates have the enzyme uricase, whereas the hominid line lost the relevant gene in the Miocene (uricase mutations), resulting in high levels of gout and vulnerability to diverse disease states; most notably gout (Johnson et al. 2010; Choi et al. 2005). Uric acid is actively reabsorbed in the kidney suggesting some adaptive function (fitness advantages). Genes which give an advantage in terms of reproductive fitness can become fixed, even when they involve some disease vulnerabilities (Nesse 2011). Competitive competence in males (based on high metabolic turnover underpinned by elevated uric acid levels) increases their fitness more so than in females, whereas in females their reproductive body condition promotes fitness (based on lower metabolic turnover favouring storage: Table 2.3.2b). Men thus, on average would live seven years longer if their metabolism and behaviour were like that of women (Kruger & Nesse 2006).

Cordain et al. (1999): Neel (1962, op. cit. Cordain et al. 1999) originally presented the thrifty genotype hypothesis according to which genes, which conferred exceptionally efficient storage of food energy (associated with insulin resistance), were selected for during periods of starvation; and that this capacity resulted in diabetes and obesity under conditions of prolonged overabundance of food resources. Thrifty gene hypotheses were based on the assumption that pre-agricultural people must have gone through regular, periodic episodes of starvation that had a negative impact on reproductive potential and hence resulted in the selection of a gene or genes which would have survival value during the fluctuations between 'feast and famine'. This concept is frequently invoked to explain the high incidence of the diseases of insulin resistance (type II diabetes, hypertension, obesity and coronary artery disease) in affluent/Westernized societies. However, Brand, Miller and Colagiuri (1994, op. cit. Cordain et al. 1999) suggested that the high protein intake and low carbohydrate intake would have represented a more likely environmental pressure responsible for selecting for multiple genes originally hypothesized by Neel to be 'thrifty genes'. Their hypothesis proposes that an insulin-resistent genotype evolved to provide survival and reproductive advantages to populations adapted to a high meat, low plant food (low carbohydrate) nutritional environment. Insulin resistence would have conveyed a selective advantage for populations consuming high protein and low carbohydrate diets long-term because it would have maximized gluconeogenesis and thereby redirected glucose away from muscles, facilitating the preferential use of glucose by the brain, fetus and mammary gland (Brand, Miller and Colagiuri (1994, op. cit. Cordain et al. 1999). (**AS: Irrespective of whether the evolutionary pressure leading to the emergence of insulin resistence was related to periods of inadequate nutrition or with the consumption of a high protein/low carbohydrate diet, there is consensus that insulin resistence once had survival value (evolutionary useful); but is linked to negative health outcomes under current conditions of nutritional affluence**).

Plasticity mechanisms provide the basis for high performance capacity realization, but they inevidably involve susceptibility to both positive and negative contextual circumstances, either resulting in enhanced performance or increased vulnerability to disease conditions respectively (Belsky & Pluess 2009; Ellis et al. 2011a).

Belsky & Pluess (2009) outlined the central thesis that, those individuals most adversely affected by stressors are also those who benefit most from environmental support and enrichment (including absence of adversity), and that such individual differences are reflecting (developmental) plasticity to environmental conditions, with some individuals being far more affected than others by both negative and positive contextual conditions (as stipulated by the differential susceptibility hypothesis: e.g. Belsky 2005, op. cit. Belsky & Pluess 2009; Belsky & Pluess 2009, op. cit. Belsky & Pluess 2009; and the biological-sensitivity-to-context thesis: Boyce & Ellis 2005, op. cit. Belsky & Pluess 2009). Such variability in susceptibility in response to environmental conditions (notably in children during developmental phases) is indicative of plasticity (which may apply to variable extents for different individuals) and congruent with an evolutionary logic according to which dispersion of genes to future generations is the ultimate biological imperative (goal of all organisms). Plasticity as heritable character is subject to natural selection (Pigliucci 2007). From the perspective of modern evolutionary biology, natural selection pertains to organisms in respect of both survival and reproduction. Such reproduction can be direct by producing immedidiate descendants (children, grandchildren), but also indirect when one's kin (such as brother, sister, niece, nephew) reproduce, passing on genes which they share in varying proportions. Reproductive fitness refers to the dispersion of the genes of an individual in future generations, and inclusive fitness relates to the fact that genetic material of individuals is distributed both directly and indirectly (This is not evoking group selection but regards the individual as the unit of selection). This evolutionary-biological foundation forms the basis for the concepts of differential sensitivity and biological-sensitivity-to-context according to which the very individual attributes that make some individuals disproportionately susceptible to adversity simultaneous make them disproportionately likely to benefit from supportive ones (Belsky & Pluess 2009; Ellis et al. 2011a).

As the future is and always has been uncertain parents cannot know (have known) what child-rearing practices would prove most effective in promoting the reproductive fitness of their offspring and their own inclusive fitness. As a result, natural selection

would have shaped parents to bear children varying in development plasticity (Belsky & Pluess 2009). For adaptive reasons, children in both supportive and unsupportive developmental contexts are therefore expected to develop and maintain high levels of physiological stress reactivity as part of the plasticity mechanism (Boyce & Ellis 2005). Particularly in the case of children growing up in supportive contexts the physical, behavioural and psychological embodiment of a favourable resource base, as provided by the family and broader ecology, is expected to enhance social competiveness and other competencies; increasing their eventual reproductive fitness (Belsky & Pluess 2009). Congruent conceptual models and supporting evidence are presented in Ellis et al. (2011a).

Ellis et al. (2011a): Advance an evolutionary-neurodevelopmental conceptual model of the role of neurobiological susceptibility to the environmenting regulating environmental effects on adaptation, development and health. It is highlighted that characteristics of individuals that make them disproportionately vulnerable to adversity often make them disproportionately likely to benefit from contextual support (e.g. Bakermans-Kranenburg & van IJzendorn 2007, op. cit. Ellis et al. 2011a; Belsky 2005, op. cit. Ellis et al. 2011a; Boyce & Ellis 2006, op. cit. Ellis et al. 2011a). Accorduing to this conceptional model, as empirically confirmed, individual differences in susceptibility to the environment have several defining characteristics: I) Individuals with heightened environmental susceptibility display enhanced sensitivity to both negative (risk-promoting conditions) and positive (development-enhancing conditions) environmental conditions; II) Enhanced sensitivity increases developmental receptivity to the environment; implying that more susceptible individuals are more likely to experience sustained developmental change in response to environmental exposures; III) Susceptibility to the environment involves neurobiological susceptibility. Genetic susceptibility factors operate through neurobiological processes. IV) Both developmental experience and heritable polygenic variation is involved in determing individual differences in neurobiological susceptibility; V) Variation in neurobiological susceptibility accordingly constitudes a central mechanism in the regulation of alternative patterns of human development; and VI) Individual differences in neurobiological susceptibility are adaptive in the evolutionary sense and have been conserved by fluctuating selective pressures generating different fitness payoffs. Both stressful and supportive environments have been part of human experience throughout evolutionary history as developmental systems responded adaptively to both types of contexts. Accordingly, when people encounter stressfull environmental conditions, rather than primarily disturbing their development, their developmental pathways are directed or regulated toward strategies that are adaptive under stressful conditions. Developmental adaptations to high-stress environments enable individuals to make the best of a bad situation (mitigation of associated fitness costs); even though the best may still represent a high risk strategy jeoperdizing health and survival of the persons concerned (e.g. Shonkoff et al. 2009, op. cit. Ellis et al. 2011a).

Individuals most likely to to be adversely affected by negative environmental conditions are also those most likely to benefit from supportive ones. The typical pattern which emerged was that highly biologically reactive children exposed to high

adversity child care settings or home environments had substantially higher illness incidences than all other groups of children; whereas highly reactive children living in more supportive childcare or family settings (low adversity) had the lowest rates; even lower than low reactivity childrenin comparable settings (Boyce et al. 1995, op. cit. Ellis et al. 2011a). (**AS: link between high performance realization and increased vulnerability to disease: 2.2.2j**). As part of the functionality of stress response systems, biological reactivity to stressors comprised an integrated system of central neural and peripheral neuroendocrine responses designed to prepare the organism for challenge or threat. Stess reactivity was thus conceptualized more broadly as biological sensitivity to context; defined as neurobiological susceptibility to both cost-inflicting and benefit-conferring features of the environment and operationalized as an endophenotypic property indexed by heightened reactivity in one or more of the stress response systems (Boyce & Ellis 2005, op. cit. Ellis et al. 2011a). Individuals thus differ in neurobiological susceptibility to environmental contexts that are both positive in character (i.e. afford resources and support potentially enhancing fitness) and negative in character (i.e. embody stressors and adversities that potentially undermine fitness). (**AS: relating to the benefits and costs of functional plasticity**).

Ex Belsky and Pluess (2009)
Caspi et al. (2003) in their GxE research were able to show that individuals carrying short alleles (marking plasticity) responded to developmental or concurrent experiences in a for-better-and-for-worse manner depending on the nature of the relevant experience. They were able to show that individuals carrying the ss allele were most adversely affected in terms of depressive symptoms, suicide ideation/attempts and major depression episodes at age 26 years CHECK CASPI Caspi & Moffitt (2006)

Worthman and Kuzara

GXE-oberlander-2008

DEVELOPMENTAL PROGRAMMING-gluckman-hanson-2014 act 2008
DEVELOPMENTAL PROGRAMMING-gluckman-2006 2005
EARLY LIFE EVENTS gluckman-2007
DEVELOPMENTAL PROGRAMMING-gluckman-2011
DEVELOPMENTAL PROGRAMMING-EPI-vaiserman
DEVELOPMENTAL PROGRAMMING-EPI-vaiserman-2015-NB
Gluckman-2 2005
GLUCKMAN-HANSON IN PRINT

GXE-belsky-2013
PLASTICITY-belsky-pluess 2013 NB
PLASTICITY-pluess-belsky-2013- vantage sensitivity NB

Pluess & Belsky (2011): Individuals vary not only in the degree to which they are vulnerable to the negative effects of adversity experienced, but generally in their developmental plasticity. (**AS: Refer also to Worthman & Kuzara (2005) who placed this into the context of life history strategy differentiation; 2.2.2a**). Accordingly, higher plasticity individuals are more susceptible than others to

environmental influences for better or for worse; i.e. both to adverse developmental outcomes associated with negative environments and positive developmental consequences of supportive environmental conditions. Evidence for the involvement of three sets of susceptibility factors (genetic, physiological, behavioral) in prenatal programming of postnatal plasticity is presented and discussed. Since the future is inherently uncertain, fitness optimization strategies involving the hedging of bets, natural selection shaped parents to bear children varying in developmental plasticity (Belsky 2005, op. cit. Pluess & Belsky 2011).
Pluess & Belsky (2011) provide evidence for their view that individuals do not only vary in the degrees to which they are vulnerable to *negative* effects of *adverse* experiences, but they also vary more generally in their *developmental plasticity*. Less susceptible individuals (less plasticity/greater resilience) are less affected by rearing conditions (whether supportive or undermining of well-being). While some research indicates that susceptibility to positive and negative experiences is related to certain gene variants (Belsky et al. 2009, op. cit. Pluess & Belsky 2011) and thus a function of *nature*; physiological stress reactivity moderating environmental effects in a better or for worse manner is at least partially a function of *nurture* (Boyce & Ellis 2005; Ellis et al. 2011b; Pluess & Belsky 2009; Belsky 2005, op. cit. Pluess & Belsky 2011; Belsky & Pluess 2009), including the effects of prenatal experience (prenatal programming of postnatal plasicity). The fetal programming hypothesis, according to Gluckman & Hanson (2005), involves the fetus adjusting its phenotype (e.g. metabolism and stress reactivity) in utero on the basis of transferred maternal nutritional and hormonal cues about the outside world as a means of optimally adapting to the conditions of the postnatal environment.

PLASTICITY-CHILDCARE
EPI-skinner-2010
Miller et al.
PREGNANCY-dl giudice-fetal programming
CHILDCARE-pluess-belsky-2009

Bateson et al. (2004)

Korte et al. (2005) in ref

DL EPI-NUTRITION-jimenez-chillaron-NB EPI DIET EVOLUTIONARY MEDICINE
EPI-TELEGONY-crean NB RE EPI

Korte et al. (2005): Allostasis is generally defined as as an adaptive process for actively maintaining stability through change (**AS: through flexibility based on plasticity**). It is important during both unpredictable events as well as predictably fluctuating conditions (e.g. triggering seasonal events). Costs arising to the body (allostatic loads) result if mediators of allostasis (adrenal hormones, neurotransmitters, immune-cytokines, etc.) are released too often or if they are insufficiently managed. The balance between allostasis and and allostatic load was shaped during evolution by trade-offs on the basis of benefits (**AS: arising from flexibility in coping with arising situations**) and costs (**AS: plasticity costs**) which occur at different stages of the life cycle or are affected by season, social status, sex or environmental change. The benefits of of allostasis and the costs of adaptation (allostatic load) lead to different trade-offs in health and disease. According to the

conceptual framework of Hawks (aggressive; proactive stress coping style; territoriality = interference competition; high energy consumption) and Doves (cooperative; reactive stress coping style; danger/stress avoidance; energy conservation), the former are more likely to be violent, develop impulse control disorders, hypertension, cardiac arrhythmias, atypical depression, chronic fatigue states and inflammation (due to inefficient management of mediators of allostasis. (**AS: lowered reaction response thresholds**). The latter were found to be more susceptible to anxiety disorders, metabolic syndromes, melancholic depression, psychotic states and infection (due to the greater release of mediators of allostasis. (**AS: lowered reaction response thresholds**). Neuroendocrine responses: Hawks – high HPG (hypothalamic-pituitary-gonadal) output (testosterone), low HPA (hypothalamic-pituitary-gonadal) output, sympathetic reactivity/dominance; Doves – low HPG output, high HPA output, parasympathetic reactivity/dominance. Hawk allostasis is advantageous/induced by stable and abundant food availability and high population densities, whereas Dove allostasis is of advantage under conditions of food scarcity and sustained under low population density stress. The existence of both bevavioural strategies is widespread, not only between males and females, but also within the same gender. From the perspective of controlling resources both strategies may be successful.

Mediators of allostasis (such as adrenal hormones, neurotransmitters, immunocytokines) act on receptors in various tissues to produce effects that are adaptive in the short term, but can produce an allostatic state which may be damaging if the mediators are not shut off. Allostatic state implies a state of chronic deviation of the regulatory system from its normal mean operating level. Four types of allostatic states leading to allostatic load have been identified (Mcewen & Wingfield 2003): I) repeated challenges; II) failure to habituate with repeated challenges; III) failure to shut off the response after the challenge is over; and IV) failure to mount an adequate response.
Sympathetic system hyperactivity also affects the immune system. Allostatic load can result from a hyperactive sympathetic system and a hyporeactive HPA axis (potentially leading to inflammatory and autoimmune disturbances and 'lower than needed cortisol disorders', including fibromyalgia (Crofford et al. 1994, op. cit. Korte et al. 2005), asthma (Elenkov & Chrousos 1999, op. cit. Korte et al. 2005), and chronic fatigue syndrome (Poteliakhoff 1981, op. cit. Korte et al. 2005). (Hawks) High sympathetic reactivity and relatively low parasympathetic counteraction supports redistribution of blood to the muscles, speed ups heart rate, dilates bronchi, block the digestive process and activates adrenal glands in preparation of the body for vigorous emergency action in the face of acutechallenges (fight-flight). The associated hyperimmune state together with a blunted HPA axis activity incurs costs of increased risk of inflammation and autoimmune disease; disease states due to a shift of autonomic balance toward sympathetic dominance (Hawks). Parasympatheic functionalty supports energy storage in in the form of fat depositions which are beneficial during times of food shortages (AS: and for female reproductive condition asbased on a positive energy balance). However, parasympatheic dominance, in association with HPA axis reactivity (Doves) may result in a stress sensitization cascade and increased risk of developing syndrome-X (metabolic syndrome leading to diabetes type II, hypertension and cardiovascular disease).

INTERACT WITH SECTION ON OXIDATIVE STRESS Wallace (2005):
Mitochondria use oxidative phosphorylation (OXPHOS) to convert dietary calories into usable energy, generating reactive oxygen species (ROS) as a toxic byproduct. It is implicated that the delayed onset and progressive course of age-related diseases result from the accumulation of somatic mutations in the mtDNA of post-mitotic tissues. Variations in individual and regional predisposition to degenerative diseases may result from the interaction of modern dietary caloric intake and ancient mitochondrial genetic polymorphisms. In accordance, mitochondria provide a link between our environment and our genes and mtDNA variants which permitted our ancestors to energetically adapt to their ancestral environments and are influencing our health today.
In recent decades individuals can live their entire lives free from hunger. It has however been known for over 70 years that laboratory rodents maintained on restricted calorie diets are healthier, more active, more intelligent, live longer and have fewer cancers (e.g. Sohal et al. 1994, op. cit. Wallace 2005). The mitochondrial genetic system is known to be present in thousands of copies per cell, to exhibit striking regional genetic variation and to be directly involved in calorie utilization. The mtDNA is maternally inherited and shows pronounced regional genetic variation which was a major factor in permitting humans to adapt to different global environments they encountered and mastered. The mitochondria are also the only human genetic system containing the features necessary to explain the observed characteristics of the common age-related diseases (Wallace 1999).
Wallace (2005) makes the case that mitochondrial decline and mtDNA damage are central to the etiology of age-related and degenerative diseases, ageing and cancer. The rate of mitochondria and mtDNA damage and thus mitochondrial decline is modulated by the extent of mitochondrial oxidative stress. Mitochondrial ROS (reactive oxygen species) production is increased by the availability of excess calories, modulated by regional mtDNA genetic variation, and regulated by alterations in nDNA expression of stress response genes.

DL GENDER-kruger
EVOLUTION-gluckman
EVOLUTION-gluckman-2
EVOLUTION-gluckman-3
Hales & Barker (2001)

DEVELOPMENTAL PROGRAMMING-2006
DEVELOPMENTAL PROGRAMMING-hanson-gluckman
DEVELOPMENTAL PROGRAMMING-gluckman-2011-EPI
DEVELOPMENTAL PROGRAMMING-gluckman-hanson-2014
DEVELOPMENTAL PROGRAMMING-gluckman-2008
DEVELOPMENTAL PROGRAMMING-gluckman-2006
PREGNANCY-del giudice
EPI-Skinner
PREGNANCY-developmental programming-pluess-belsky-2011
PLASTICITY-belsky-pluess-2009
PLASTICITY-belsky
PLASTICITY-pluess-belsky-2012
EVOLUTION-gluckman-2

EVOLUTION-gluckman-3
EVOLUTION-gluckman
EARLY LIFE EVENTS-gluckman-NB
EPI-gluckman-fetal-neonatal
LHS-PLASTICITY-nettle-bateson
PREGNANCY-rassmussen

b) Developmental origins of health and disease

Observations that early life influenes can alter later disease risk resulted in the 'developmental origins of health and disease' (DOHaD) paradigm (Gluckman et al. (2007). For Gluckman et al. (2007) the DOHaD phenomenon was taken to represent a subset of broader processes of developmental plasticity according to which organisms adapt to their environment during their life courses. In this context it is contended that developmental programming entails a forecast of environmental conditions (nutritional and otherwise) the baby will encounter after birth, inducing changes in its physiology and metabolism in accordance with those forecasted by maternal condition (Table 2.2.1a). Prevailing thinking presumes that fetal programming involves prenatal stressors compromising later development (Table 2.2.1a). However, Pluess & Belsky (2011) contend that these prenatal experiences promote plasticity and thereby the openness of the organism for both positive and negative future experiential input; i.e. prenatal programming of postnatal plasticity in the context of gene/environment (GxE) interaction. There is substantial evidence that the fetal programming process is characterized by GxE interaction (Gluckman & Hanson 2005); as mediated by epigenetic processes. Findings related to epigenetic mediation by Oberlander et al. (2008), for example, showed that maternal suppressed mood in pregnancy predicted increased methylation of the human glucocorticoid receptor gene *NR3C1*, which itself forecasts elevated cortisol stress reactivity at age 10 months; thereby identifying one of the biological mechanisms that may be central to fetal programming of postnatal plasticity (consistent with the biological-sensitivity-to-context thesis of Boyce & Ellis 2005). Accordingly, on the basis of fetal programming research, plasticity is a function of experience as much as a function of genetics.

AS notion of increased plasticity (physiological reactivity amplitude) negative experiences programming vulnerability → plasticity → opening scope for positive physiological reactivity to positive expeiences, inter alia, healing processes facilitated

Gluckman et al. (2007): Observations that early life influenes can alter later disease risk resulted in 'the developmental origins of health and disease' (DOHaD) paradigm. The authors consider the DOHaD phenomenon a subset of broader processes of developmental plasticity according to which organisms adapt to their environment during their life courses.

Ex Belsky and Pluess (2009)
Caspi et al. (2003) in their GxE research were able to show that individuals carrying short alleles (marking plasticity) responded to developmental or concurrent experiences in a for-better-and-for-worse manner depending on the nature of the relevant experience. They were able to show that individuals carrying the ss allele were most adversely affected in terms of depressive symptoms, suicide ideation/attempts and major depression episodes at age 26 years CHECK CASPI
Caspi & Moffitt (2006)
PLASTICITY-belsky-pluess 2013 NB
PLASTICITY-pluess-belsky-2013- vantage sensitivity NB
PLASTICITY-pluess-belsky-2012 actually 2011
PLASTICITY-CHILDCARE
PLASTICITY-belsky-pluess-2009

Table 2.2.1a Developmental origins of health and disease
MS FETAL PROGRAMMING-hypertension-alexander; DL GESTATION-mcmillen; DL DEVELOPMENTAL PROGRAMMING-joseph-kramer-1996; DL DEVELOPMENTAL PROGRAMMING-victora; DL DEVELOPMENTAL PROGRAMMING-smith; Godfrey et al. 1996; Godfrey 1998; Godfrey & Barker 2000) and early-life programming of ageing and longevity has been emerging (Gluckman et al. 2007; DL DEVELOPMENTAL PROGRAMMING-langley-evans-NB; DT-enthringer; DT-entringer-2015) MS FETAL PROGRAMMING-hypertension-alexander; DL GESTATION-mcmillen; DL DEVELOPMENTAL PROGRAMMING-joseph-kramer-1996; DL DEVELOPMENTAL PROGRAMMING-victora; DL DEVELOPMENTAL; EPI-gluckman PROGRAMMING-smith; Godfrey et al. 1996; Godfrey 1998; Godfrey & Barker 2000) (Gluckman et al. 2007; DL DEVELOPMENTAL PROGRAMMING-langley-evans-NB; DT-enthringer; DT-entringer-2015)
DL DEVELOPMENTAL PROGRAMMING-gluckman-2008 DL DEVELOPMENTAL PROGRAMMING-langley-evans-2015-nutrition DL DEVELOPMENTAL PROGRAMMING-gluckman-2011-EPI DL DEVELOPMENTAL PROGRAMMING-LONGEVITY-EPI-vaiserman-2014 DL DEVELOPMENTAL PROGRAMMING-EPI-vaiserman-NB MS DEVELOPMENTAL PROGRAMMING-epi-vaiserman-2015-NB MS DEVELOPMENTAL PROGRAMMING-reynolds-glucocorticoids MS DEVELOPMENTAL PROGRAMMING-reynolds-2013 MS DEVEOLPMENTAL PROGRAMMING-todd-2017 MS DEVEOLPMENTAL PROGRAMMING-garfield-father-role GESTATION-mcmillen MS DEVEOLPMENTAL PROGRAMMING-langley-evans

MS DEVEOLPMENTAL PROGRAMMING-langley-evans-2008-nutritional
MS DEVEOLPMENTAL PROGRAMMING-heindel
EARLY-LIFE EVENTS-gluckman-NB
DL EARLY-LIFE-ADULT MORTALITY-hayward-2004
PregnancyADULT DISEASE (3 items):
Early-life-origins-of-adult disease (Vaiserman 2011)
Fetal origins of adult disease (Calkins et al. 2011)
Unravelling the fetal origins
PREGNANCYADULT DISEASEEPI-simmons
MS DEVEOLPMENTAL PROGRAMMING-burdge-nutrition
MS DEVEOLPMENTAL PROGRAMMING-EPI-burdge-2010-nutrition
MS DEVEOLPMENTAL PROGRAMMING-EPI-li
MS DEVEOLPMENTAL PROGRAMMING-MATERNAL CARE-korosi-NB
DL DEVEOLPMENTAL PROGRAMMING-CHILDHOOD-moore
MS DEVEOLPMENTAL PROGRAMMING-MATERNAL-walker-NB
DL DEVEOLPMENTAL PROGRAMMING-FAMINE-de rooij
DEVELOPMENTAL PROGRAMMING
Gavrilova et al. (2009) Early life predictors
Miller et al. (2009) Low early life

Barker (2001a): Due to plasicity in early life, growth and development are moulded by environmental conditions then experienced. Fetal growth is guided by the generative programme contained in its genome but also limited by nutrients supplied by the mother. In evolutionary terms this plasticity (of structure and function of the body) is advantageous and accordingly a general phenomenon of early development. Adaptive responses of the human baby to available nutrients involves altering its production of hormones, and the sensitivity to these, changes in metabolism and the redistribution of its cardiac output to protect key organs (especially the brain). The associated slowing of growth is adaptive since it reduces requirements for substrate. These physiological changes made during development result in life-long changes in the structure and function of the body (developmental programming).
Evidence emerged suggesting that the etiology of important chronic diseases of adult life, including coronary heart disease, stroke and type 2 diabetes, was linked to fetal malnourishment (inadequate maternal food intake around the time of conception and during pregnancy).

Hales & Barker (2001): The thrifty phenotype hypothesis suggests that type 2 diabetes originates due to poor nutrition during fetal life and infancy; leading to insulin resistance accompanying changes in glucose and lipid metabolism. The thrifty baby thereby has become adapted to poor nutritional conditions. Such adaptations are beneficial as long as conditions of poor nutrition persist. However, they are no longer beneficial with increased food intake, decreased enery expenditure and as obesity developes. Accelerated weight gain during infancy or adolescence (catch-up growth) is connected to an increased risk of type 2 diabetes, especially of those individuals who weighed 3000 g or less. Pronounced insulin resistance, as combined with reduced capacity to secrete insulin as a result of impared pancreatic β-cell development leading to impaired glucose tolerance; and ultimately to the insulin resistance syndrome and type 2 diabetes. Mechanisms of fetal nutritional thrift altered the growth of different organs; selectively protecting brain growth. Such altered growth results in permanent

changes of the structure and function of the body. The variety of changes associated with the metabolic syndrome might be accounted for by various combinations and timing of nutritional deficiencies during fetal life and infancy.

Barker (2001b): The diet of the mother during pregnancy seems to have relatively little effect on size at birth of the baby; but significant programming nevertheless takes place in that the fetus adapts to undernutrition by changing its metabolism, altering its production of hormones and the sensitivity of tissues to them, redistributing its blood flow and slowing its growth rate. Such adaptations permanently alter the structure and function of the body. Maternal supply of nutrients to the fetus, regulating its growth, depends on the body composition and size of the mother, her diet during pregnancy and the transport of nutrients to the placenta and transfer across it. Any weakness in this fetal supply line results in fetal undernutrition when demand for nutrients exceeds its supply. Fetal ability to sustain growth during periods of undernutrition depends on their pevious growth rate; with faster growing fetuses with a high demand for nutrients being less able to sustain growth (Woods & Bruton 1989, op. cit. Barker 2001b; Harding et al. 1992, op. cit. Barker 2001b). Since male fetuses grow faster than those of females they are less able to withstand undernutrition. Different types of fetal adaptations apply to early, mid- and late pregnancy, as fully outlined by Barker (2001b). Undernutrition in late gestation can *inter alia* result in reduced growth of the kidney which is then developing rapidly. This effect is seemingly permanent since there is no capacity for renal cell division to catch up (Widdowson et al. 1974, op. cit. Barker 2001b; Hinchcliffe et al. 1992, op. cit. Barker 2001b).
Genes allowing to the fetus to adapt successfully to undernutrition are likely to be favoured by natural selection even if such adaptations result in disease and premature death in post-reproductive life. Intergenerational constraints on fetal growth: Apart from the effects on birth weight of maternal body composition and diet, the birth weights of mothers are related to those of their children and grandchildren (Klebanoff et al. 1984, op. cit. Barker 2001b; Klebanoff et al. 1989, op. cit. Barker 2001b; Carr-Hillet al. 1987, op. cit. Barker 2001b Emanuel et al. 1992, op. cit. Barker 2001b). Mothers who were small for gestational age at birth have twice the risk of having a small for gestational age baby and their babies are more likely to die during the perinatal period (Skjaerven et al. 1997, op. cit. Barker 2001b). The weight of the father affects the placental weight. It can be concluded that mothers constrain fetal growth and that the degree of such maternal constraint is set when they are themselves are *in utero* (Ounsted et al. 1986, op. cit. Barker 2001b), as mediated in the limited capacity of the mother to deliver nutrients to the fetus (Gluckman et al, 1992, op. cit. Barker 2001b). Thus, the fetus adapts its rate of growth and life-long structure and function of its body not only to its mother, but also to the environment its grandmother provided for its mother (underpinning adaptive plasticity for conditions of transient famine).

c) Uric acid: metabolic performance and disease

Uricase mutation.

Among mammals, significant levels of seum uric acid are only found in higher apes and man; other mammals possessing the enzyme uricase which oxydises uric acid to allantoin. It has been suggested that uric acid, like other purines, can stimulate the

cerebral cortex, and that the superior intellectual powers of the higher primates may be to some extent a consequence of high uric acid levels through mutations causing loss of uricase activity (Orowan, op. cit. Sofaer & Emery 1981).

Orowan (op. cit. Johnson et al. 2009) proposed that the emergence of intelligence in the primate line arose from a single evolutionary event, the loss of the enzyme uricase, with the result that uric acid became the end product of purine metabolism. Uric acid is produced from purines by the enzyme xanthine oxidase via the purine metabolic pathway. During the Miocene mutations occurred resulting in a non-functioning uricase gene. Uric acid levels are accordingly relatively higher in humans; in men usually higher than in women (Kutzing & Firestein (2008). De Giorgi et al. (2015): The presence of hyperuricemia in hominids has allowed an evolutionary advantage in several aspects such as high blood pressure, even under conditions of low salt intake (Watanabe et al., op. cit. De Giorgi et al. 2015), greater stimulation of the cerebral cortex (Sofaer & Emery 1981) and and protection by antioxidant effects with progressively longer life spans of hominids. These conditions represent mechanisms in the maintenance of upright position and intellectual supremacy on other primates, crucial steps towards evolutionary development and human dominance (De Giorgi et al. 2015).

Purine metabolism and uricemia.

Relative to other mammals, humans have relatively high uric acid levels due to the loss of uricase (uricase mutation). Of significance here is that urate is actively reabsorbed in the kidneys (despite its high energy costs); suggesting that elevated uric acid levels (uricemia) have some fitness value. The associated positive effects of elevated uric acid include *inter alia* a non-specific activation role, notably the enhancement of cognitive functions and motivations (*vide* Tovchiga & Shtrygol' 2014). Tovchiga & Shtrygol' (2014) summarize the biochemical basis of these effects as the potential of uric acid to synthesise uric acid in the CNS and the penetration of the blood-brain barrier by its precursors, the interrelations between uric acid metabolism in the CNS and the metabolism of catecholamines and dopamine, and neuroprotective and antioxidant activity of uric acid.

Tovchiga & Shtrygol' (2014): Uricemia increases in starvation during the protein-breakdown phase, after exhaustion of lipid reserves; being associated with accelerated body weight loss. Concentrations of uric acid increase simultaneously with cortisol

levels; but tend to be negatively correlated with lipid reserves (Tovchiga & Shtrygol' 2014). As pointed out by De Giorgi et al. (2015), uric acid is produced only in tissues that contain xanthine oxidase (liver and small intestine). The production of uric acid is due to the degradation of proteins or degrading of purines (So & Thorens 2010). Plasma uric acid levels change over age and sex, being lower in childhood (3-4 mg/dl) and increasing in the male during puberty and in women after menopause. Pathological serum uric acid concentrations are > 7mg/dl in men and > 5.7 mg/dl in women (De Giorgi et al. 2015).

Uric acid as metabolic performance catalyst.

According to references cited by Tovchiga & Shtrygol' (2014) uric acid is a marker of catabolic processes but also an activation factor. Like other biologically active metabolites, uric acid has an optimum concentration range in blood. The relationship between uricemia and intellectual human activity is linear only between certain limits (hypouricemia – uricemia – hyperuricemia) and can be expressed by a curve line in the form of an inverted letter U (Tovchiga & Shtrygol' 2014). Uric acid is a metabolic product of purine metabolism generated from the breakdown of DNA, RNA and ATP (Johnson et al. (2008). The immediate precursor enzyme is xanthine oxireductase which converts xanthine to uric acid with the generation of oxidants. Its action as a neurostimulant suggests it may have a role in increasing reaction time, locomotor activity and mental performance (Johnson et al. 2008). Uric acid acts as a neurostimulant (Johnson et al. 2009). There is a positive relationship of uric acid levels with IQ (Sofaer & Emery 1981), achievement-oriented behaviour (Kasl et al. 1970; Lorenzi et al. 2010), school performance and increased locomotor activity (Barrera et al., op. cit. Johnson et al. 2009). Uric acid levels are increased with emotional and physical stress (Rahe et al., op. cit. Johnson et al. 2009).

Kasl et al. (1970) found that students attending college or planning to do so, had higher uric acid levels, above and beyond the association with high school grades; and that there was a positive association between uric acid and activities of an extracurricular, social nature or dating behaviour. (Positive relationship to college attendance, extracurricular and social activities, and vocational aspirations). Regarding 113 professors at the University of Michigan, Brooks & Mueller (1966) found highly significant positive correlations between uricemia and intensity of activity, professional

productivity, organizational skills, placing demands on oneself, breadths and mulifacetted nature of activities.

Inouye et al. (1984) reported that heritability of plasma uric acid levels, corrected for age and sex and standardized, was estimated at 0.8 in twin families (consisting of twin parents, spouses and children). Significant correlation was detected of IQ on corrected and standardized uric acid levels in twin children. The results indicate a genetic basis of blood uric acid levels, which may have resulted from polymorphisms in purine metabolism pathway, the end product of which is uric acid in man. The significant correlation between plasma uric acid level and IQ suggests a contribution of partly common gene loci to the two quantitative traits (Inouye et al. 1984).

Uricemia activity promoting health.

Uricemia has beneficial effects as powerful antioxidant (Ames et al. 1981; Becker 1993) and by its neuroprotective effects (Scott & Hooper 2001; Squadrito et al. 2000). De Giorgi et al. (2015) reviewed available knowledge of the positive effects of uric acid in terms of antioxidant effects, neuroprotection, cognitive function, and intellectual performance. Uric acid has a stimulating effect on the cerebral cortex and this could have allowed humans to develop higher brain mass volume and better intellectual performances than other animals. Serum uric acid levels below normal concentrations are associarted with a variety of disease states e.g. multiple sclerosis, Alzheimers and Parkinson's diseases. In this context, peroxynitrite is considered to have pronounced negative effects on cell function and survival (Pacher et al. 2007). Peroxynitrite is a strong oxidant causing oxidative damage when reacting directly with certain biological molecules, resulting in damaging a number of processes that are crucial for normal cellular functioning (Pacher et al. 2007). Peroxynitrite has ben shown to exert negative impacts in a number of disease states: cardiac diseases, vascular diseases, cancer, stroke, neurodegenerative disorders and diabetes (Pacher et al. 2007). Uric acid scavenges superoxides which also helps to prevent the formation of peroxynitrites. High uricemia (hyperuricemia), after controlling for cardiovascular risk facors, was associated with a decreasing risk of dementia and better cognitive performance in adulthood; attributed to a protective role of uric acid as an antioxidant against oxidative stress (Euser et al. 2009). Li et al. (2010) detected an inverse correlation between the risk of cognitive impairment and serum uric acid in men; i.e.

in male nonagenarians and centenarians higher serum uric acid levels were related to lower risk of cognitive impairment.

Sufficiently high concentrations of uric acid (but still within the uricemia range) substantially contribute to the total antioxidant activity in human blood (Ames et al. 1981; Johnson et al. 2009). Urate may serve as a primary antioxidant in human blood since it can remove singlet oxygen and radicals as effectively as vitamin C (Ames et al. 1981). During primate evolution, a major factor improving in lengthening life-span and decreasing age-specific cancer rates may have been improved protective mechanisms against oxygen radicals. Ames et al. (1981) proposed that one of these protective systems is plasma uric acid, scavaging singlet oxygen and radicals (acting as powerful antioxidant). Plasma urate levels in humans are considerably higher than ascorbic acid levels, making it the one of the major antioxidants in humans (Ames et al. 1981). Urate prevents inactivation of endothelial enzymes and preserves the ability of the endothelium to mediate vascular dilatation in the face of oxidative stress, suggesting a particular relationship between the site of urate formation and the need for a potent antioxidant (Becker 1993).

De Giorgi et al. (2015): Hyperuricemia is associated with many pathological conditions (including cardiovascular disorders) due to its effect on endothelial function and metabolic homeostasis. ***Glutamate, a toxic metabolite for the brain reaches high extracellular concentrations when uric acid concentrations are low*** (Rothman & Olney 1986, op. cit. Giorgi et al. 2015). Uric acid considered an important antioxidant in humans (Ames et. al. 1981). ***Uric acid represents a neuroprotective metabolite acting through suppression of oxyradical accumulation, stabilisation of calcium homeostasis and preservation of mitochondrial function***. Squadrito et al. (2000) have also demonsrated an effect of uric acid on the reduction of neural damage induced by peroxynitrite, considered responsible for processes of cell damage in, *inter alia*, stroke, Alzheimer's and Parkinson's diseases.
In a twin study, uric acid levels were positively associated with IQ (intelligence quotient) of subjects (Park et al., op. cit. Giorgi et al. 2015). However, genetic evaluation of uric acid levels in different families implied that polymorphisms in purine metabolism pathways could be the link with the inheritance of IQ. Inouye et al. (1984): Heritability of plasma uric acid levels, corrected for age and sex and standardized, was estimated at 0.8 in twin families (consisting of twin parents, spouses and children). Significant correlation was detected of IQ on corrected and standardized uric acid levels in twin children. The results indicate a genetic basis of blood uric acid level, which may have resulted from polymorphisms in purine metabolism pathway, the end product of which is uric acid in man. ***The significant correlation between plasma uric acid level and IQ suggests a contribution of partly common gene loci to the two quantitative traits. Uric acid as an endogenous cortical stimulant promoting the full expression of IQ rather than causing it per se***.

Hyperuricemia and disease.

Hyperuricemia has been linked to a variety of disease conditions (Kutzing & Firestein 2008), including gout, hypertension, cardiovascular diseases, myocardial infarctions, stroke, renal disease and metabolic syndrome (Choi et al. 2005a; Choi et al. 2005b).

According to De Giorgi et al. (2015), Hippocrates defined gout as 'arthritis of the rich', distinguishing it from 'arthritis of the poor' (rheumatic fever). He also hypothesised that gout could depend on social differences such as related to better nutrition and living conditions. This association was later confirmed by the higher incidence of gout in people with higher social status. Gout became known as the disease of 'kings and popes'. Popes – Bonifacius VIII, Pius III, Julius II, Julius III, Clement VIII, Innocent XI, Clement XII, Pius VIII; prominent religious personalities – Martin Luther, John Calvin, John Wesley, cardinals Giovanni de Medici, Leopoldo de Medici; kings or emperors – Alexander the Great, Ceasar Augustus, Charles the Great, Charles I, John II, Francis I of Bourbon, Charles V and Phillip II of Habsburg, Charles II, Charles III of Lorraine, Catherine of Lancaster, Louis XVIII, Stanislaus Leczinsky, king of Poland, George IV, Napoleon Bonaparte, queen Anne of England; noble houses – Duchy of Lorraine, Habsburg, Medici, Bourbon; also manifesting in prominent philosophers and scientists, including Voltaire (Francois-Marie Arouet), Immanuel Kant, Gottfried Leibniz, Isaac Newton, Galileo Galilei, Charles Darwin, Carl Linnaeus and Thomas Sydenham (De Giorgi et al. 2015).

The Engish physician Thomas Sydenham was the first to describe the association between gout, hyperuricemia and a high standard of living (Sydenham 1683, op. cit. Giorgi et al. 2015). The emergence of gout often corresponds to periods of societal wealth (Golden Age of Greece, Roman Empire, industrialization of Europe in the 18th and 19th centuries) and during the last century throughout the world; correlating with rising rates of obesity, hypertension, metabolic syndrome, chronic kidney and cardiovascular disease (Johnson et al. 2009).

Choi et al. (2005a): Gout is associated with conditions such as insulin resistence syndrome, hypertension, nephropathy, and disorders associated with increased cell turnover. Hyperuricemia commonly develops only in humans. The absence of of uricase (uric acid generated during purine metabolism undergoes oxidative degradation through the uricase enzyme when this enzyme is present), combined with extensive reabsorption of filtered urate, results in particularly high urate levels in human plasma. Un-physiologically high uric acid levels (hyperuricemia) nevertheless represent health risks (gout, nephrolithiasis, hypertension, cardiovascular disorders). Urate balance: hyperuricemia results from urate overproduction, underexcretion or often both in

combination. Purin precursors come from exogenous (dietary) sources or endogenous metabolism (synthesis and cell turnover). The vast majority of patients with endogenous overproduction of urate have the condition as a result of salvaged purines arising from increased cell turnover in proliferative and inflammatory disorders or from hypoxia.

Fructose is the only carbohydrate that has been shown to exert a direct effect on uric acid metabolism (23). Fructose phosphorylation in the liver uses ATP, and the accompanying phosphate depletion limits regeneration of ATP from ADP. The subsequent catabolism of AMP serves as a substrate for uric acid formation (Fox et al. 1987). Fructose has also been implicated in the risk of insulin resistance syndrome and obesity, which are closely associated with gout (Gross et al., op. cit. Choi et al. 2005a). Increased adiposity and insulin resistance syndrome are both associated with the risk for gout; as are body mass index, waist-to-hip ratio and weight gain (Roubenoff et al., op. cit. Choi et al. 2005a). Weight reduction was associated with a decline in urate levels (Dessein et al. 2000). Hypertension was found to be associated with an increased risk for gout independant of potential confounders such as dietary factors, obesity, diuretic use and renal failure (Choi et al. 2005b).

Dessein et al. (2000): Insulin resistance has been implicated in the pathogenesis of gout. Weight reduction associared with a change in proportional macronutrient intake, as recommended for counteracting insulin resistance, reduced serum uric acid levels and dyslipidaemia. A low carbohydrate, high protein and unsaturated fat diet is recommended for gout patients, since these all enhance insulin sensitivity and promote the reduction of serum uric acid levels. Avoidance of weight gain with dietary intervention enhancing insulin sensitivity. Dietary restriction (1600 kcal/day) with 40% derived from carbohydrates, 30% protein and 30% fat. Replacement of refined carbohydrates with complex ones and saturated fats with mono- and poly-unsaturate ones; as recommended for insulin resistance, lowered serum uric acid levels (Dessein et al. 2000). High adiposity and weight gain are strong risk factors for gout in men. Weight loss is protective. Close associations have been reported between hyperuricemia and all components of the insulin resistance syndrome (including hyperinsulinema, hypertension, dyslipidemia, obesity). A large study demonstrated BMI (body mass index) has the strongest correlation with hyperuricemia (Dessein et al. 2000).

Metabolic performance *versus* disease vulnerability trade-off.

Sautin & Johnson (2008): Uric acid, a major antioxidant in human plasma, is associated with disease conditions linked to oxidative stress such as obesity, hypertension and cardiovascular disease (the oxidant-antioxidant paradox). An explanation for this paradox is that ***elevated uric acid represents an attempted protective response***. The authors review evidence that uric acid may either function as an antioxidant (primarily in plasma) or pro-oxidant (primarily within the cell). In spite of its antioxidant properties, at least among modern *Homo sapiens*, raised levels of uric acid levels are associated with hypertension (Johnson et al. 2003, op. cit. Sautin & Johnson 2008; Johnson et al. 2005, op. cit. Sautin & Johnson 2008), metabolic syndrome, visceral obesity (Masuo et al. 2003, op. cit. Sautin & Johnson 2008), insulin resistance (Zavaroni et al. 1993, op. cit. Sautin & Johnson 2008), dyslipidemia

(Zavaroni et al. 1993, op. cit. Sautin & Johnson 2008) , diabetes type 2 (Nakanashi et al. 2003, op. cit. Sautin & Johnson 2008), kidney disease (Johnson et al. 2003, op. cit. Sautin & Johnson 2008) and cardiovascular and cerebrovascular events (Alderman et al. 1993, op. cit. Sautin & Johnson 2008; Johnson et al. 2003, op. cit. Sautin & Johnson 2008). Oxidative stress and oxidative modifications of proteins and lipids is common for all these diseases (Furukawa et al. 2004, op. cit. Sautin & Johnson 2008; Wellen & Hotamisligil 2005, op. cit. Sautin & Johnson 2008; Houstis et al. 2006, op. cit. Sautin & Johnson 2008). Hyperuricemia induces endothelial dysfunction by decreasing bioavailability of nitric oxide in endothelial cells (Khosla et al. 2005, op. cit. Sautin & Johnson 2008). Uric acid can act as pro-oxidant and proinflammatory factor *inter alia* by forming free radicals in a variety of radical-forming systems (Maples & Mason 1988, op. cit. Sautin & Johnson 2008). A variety of ROS are involved in redox-dependent signal transduction, immune defense and/or oxidative damage (Lambeth 2004, op. cit. Sautin & Johnson 2008). On the other hand, uric acid has an important antioxidant function as powerful scavenger of carbon-centred and peroxyl radicals in the hydrophilic environment (Muraoka & Miura 2003, op. cit. Sautin & Johnson 2008): oxidant-antioxidant paradox. Also, uric acid acts as a molecular signal alerting the immune system to dying cells (Shi et al. 2003, op. cit. Sautin & Johnson 2008).

De Oliveira & Burini (2012): High plasma uric acid levels are a risk factor for *inter alia* metabolic syndrome and cardiovascular disease. High plasma uric levels are caused by either lowered excretion or higher synthesis or both. Higher waist circumference and BMI (body mass index) are associated with higher insulin and leptin production, both reduce uric acid excretion. The synthesis of fatty acids (tryglicerides) in the liver is associated with *de novo* synthesis of purine, thereby accelerating uric acid production. ***There is still no consensus whether uric acid is a risk factor or an antioxidant protective response. It seems that acute elevation is a protective factor, whereas chronic elevation represents a risk for disease***. Hyperuricemia is *inter alia* associated with renal and cardiovascular disease, hypertension, obesity and metabolic syndrome (Johnson et al. 2003, op. cit. De Oliveira & Burini 2012). Uric acid is an end product of purine metabolism and has high antioxidant capacity (considered responsible for two-thirds of total plasma antioxidant capacity: Sautin & Johnson 2008). Diseases resulting from innate purine metabolic errors would also result in hyperuricemia (Alvarez-Lario & Macarron-Vicente 2010, op. cit. De Oliveira & Burini 2012). Hyperuricemia is seen as a prognostic indicator of renal disease, diabetes, cardiovascular disease, inflammation and as a determinant of metabolic syndrome (e.g. Onat et al. 2006, op. cit. De Oliveira & Burini 2012).
Fruit and vegetables, in addition to flavonoids, contain nutrients that may affect total plasma antioxidant capacity (TAC). Rather than being linked to specific substances, increased TAC would be the result of elevated uric acid resulting from fructose metabolism (Lotito & Frei 2006, op.cit. De Oliveira & Burini 2012). Uric acid is associated with the metabolic syndrome (Sui et al. 2008, op. cit. De Oliveira & Burini 2012) and its components (obesity, dyslipidemia, hypertension, increased C-reactive protein, endothelial dysfunction). Production of urate, a potent soluble antioxidant is increased in hypoxic conditions (Baillie et al. 2007, op. cit. De Oliveira & Burini 2012). Uric acid also has a direct effect on the inhibition of free radicals protecting the cell membrane and DNA (Kutzing & Firestein 2008) and antioxidant activity also occurs in the brain, providing some protection against neurodegenerative disorders (Scott & Hooper 2001, op. cit. De Oliveira & Burini 2012). Obesity and muscle mass reduction are associated with low-intensity chronic inflammation and uric acid levels may then

be increased in order to protect the organism against the resulting moderate oxidative stress. Diesease conditions such as hypertension, metabolic syndrome, preeclampsia, cardiovascular and renal disease are associated with oxidative stress and hyperuricemia (Gersch et al. 2009). The authors conclude that under conditions of oxidative stress, uric acid forms intermediates by reacting with peroxynitrite. Such reactive intermediates were considered to represent an explanatory link on how uric acid contributes to the pathogenesis of associated diseases.

Nasri (2016): Abnormally high levels of uric acid are referred to as a health problem arising from their role in systemic diseases including cardiovascular disease, chronic kidney disease, hypertension, type 2 diabetes, ischemia, Alzheimer's disease and Parkinson's disease. Although uric acid is known as index of chronic disease, it is also referred to as an antioxidant index; ***as well as a main marker of inflammation in various organs*** (Weiner et al. 2008, op. cit. Nasri 2016). Several studies reported that high uric acid level is linked to a possible cause of disease development and in these stidies it was conluded that the high uric acid level is responsible for the outbreak and development of diseases (Jossa et al. 1994, op. cit. Nasri 2016; Bos et al. 2006, op. cit. Nasri 2016). On the other hand, at least half of the plasma antioxidant capacity arises from serum uric acid (Ames et al. 1981). It is thus not clear whether the elevated uric acid concentration in serum participates in the development of diseases or it is an index of diseases.

Oxidant-antioxidant paradox. **Sautin & Johnson (2008) consider *elevated uric acid levels to represent an attempted protective response***. They reviewed evidence that uric acid may either function as an antioxidant (primarily in plasma) or pro-oxidant (primarily within the cell); the latter being consistent with uric acid ***a main marker of inflammation in various organs*** (Weiner et al. 2008, op. cit. Nasri 2016).
Following from the considerations by *inter alia* Sautin & Johnson (2008), De Oliveira & Burini (2012) and Nasri 2016, it is here concluded that increasing uric acid levels initially represent an antioxidant protective response to developing chronic disease states (within-cell pro-oxidant inflammatory response and an antioxidant role of serum plasma) and chronically elevated uric acid levels subsequently then participate in the progression of such disease states.

Elevated uric acid levels support sympathetic ANS performance (Table 2.3.2a: Autonomous Nervous System: staying power, endurance, cognition, assertiveness: testosterone-supported functionality), but when these remain chronically elevated due to persistent requirements for health-promoting oxidant-antioxidant protective responses (as would be required in subjects with high PIE loadings: 2.1.2), ongoing population density stress effects and other challenging impacts, parasympathetic ANS performance functionality is compromised (such as

recuperative rest and efficient nutrient-energy assimilation and storage required for the maintenance of a healthy normo-adaptive body condition: Table 2.5.1.5c). Sympathetic overdominance notably compromises female reproductive success (Table 2.3.2b) which is underpinned by parasympathetic functionality (Table 2.3.2a; MacLean 1990, Knaul 1985).

Efficiency of energy metabolism and plasticity costs in terms of health.

Fructose raises uric acid, inducing metabolic syndrome in animals (Nakagawa et al. 2006). The mechanism by which uric acid mediates features of metabolic syndrome is likely due to the ability of uric acid to block some of insulins actions by reducing endothelial nitric oxide as well as due to direct effects of uric acid on the adiposyte (Sautin & Johnson 2008). The fructose-induced metabolic syndrome is mediated by uric acid. Lowering uric acid was found to both prevent and treat early features of metabolic syndrome (Nakagawa et al. 2006). The mechanism was shown to be mediated in part by inducing endothelial dysfunction that impairs insulin action, as well as direct action on the adipocyte (Nakagawa et al. 2006).

Johnson et al. (2011): The mutation of uricase that occurred during food shortage and global cooling in the Miocene resulted in a survival advantage for early primates, particular in Europe. Today the loss of uricase functions as a thrifty gene, increasing our risk for obesity and cardiorenal disease. Uric acid is a product of purine metabolism generated during the breakdown of nucleic acids (DNA, RNA) and ATP; uric acid can also be generated from proteins. Subjects with higher levels of uric acid are at increased risk for developing gout and kidney stones. Elevated uric acid also predicts the development of obesity, metabolic syndrome, diabetes, fatty liver, hypertension, and cardiovascular and renal disease (op. cit. Johnson et al. 2011). The key question now was which biological benefits has uric acid and why was the uricase mutation naturally selected for in the human species and some other primate species. The authors hypothesised that the uricase mutation benefitted survival by augmenting the fat storing properties of fructose present in fruits (Johnson & Andrews 2010).

Uric acid thus plays a role as a mechanism for amplifying fructose effects on fat formation. Fructose has a superior ability than glucose to increase fat stores, including those in the liver, visceral fat and triglycerides; thus effective in building body condition for times of food shortages (Tappy & Le 2010). Given the characteristics of fructose-uric acid metabolism, the loss of uricase would potentiate the ability of fructose to increase fat stores. Therefore the uricase mutation could have provided survival advantage for Miocene apes during the progressive food shortage that occurred in Europe due to global cooling (Johnson & Andrews 2010).

Johnson & Andrews (2010): The observation that fructose increases fat stores independently of energy intake (Nakagawa et al. 2006) suggests that it must have specific metabolic mechanisms for driving fat accumulation. Whereas the phosphorylation of glucose is tightly controlled so that ATP depletion does not occur, fructokinase will rapidly phosphorylate fructose, resulting in the transient depletion of ATP in the cell with the generation of AMP. AMP is then degraded to generate uric acid, rising both within the cells and in the circulation. Recent evidence suggests that it is the increase of intacellular urice acid that is largely responsible for increasing fat stores. Johnson & Andrews (2010) and others have found that uric acid induces intracellular oxidative stress in a variety of cells, altering mitochondrial function in a way secondarilly stimulating fat synthesis. We further found that uric acid augments the ability of fructose to induce fat stores. Purine-rich foods and fructose are the two major preferrd foods of early hominoids (Marshall & Wrangham 2007: fallback foods). The primary consequences of loss of uricase are a higher baseline level of uric acid, as well as less ability to maintain uric acid within set levels following exposure to diet. The absence of uricase can dramatically enhance the effects of these foods to raise uric acid levels. Metabolic effects of fructose: rise in plasma triglycerides, induction of insulin resistance, increase in blood pressure and weight gain. Recent studies suggest that the uricase mutation enhanced the ability of fruits to enhance fat storage which would have been of survival advantage during periods of food storage, particularly as occurred with increased seasonality in Europe. The dramatically increased intake of added sugars parallels the rise in and obesity, insulin resistance and diabetes (Johnson et al. 2009).

The loss of the uricase gene provided survival advantages in the context of feast-famine alternations, but incurred health impediments under conditions of uninterrupted feast conditions. Accordingly, the loss of uricase seems to underpin a 'thrifty gene' effect, as proposed by Neel (op. cit. Johnson & Andrews 2010). The thrifty phenotype hypothesis is further outlined by Hales & Barker (2001). Refer to Section 2.2.1a.

Accordingly, uric acid as performance catalyst, supports efficiency of energy storage (peak metabolic performance) under conditions of feast-famine alternations (plasticity gains), but incurs plasticity costs i.t.o. health maintenance under prolonged feast conditions, when intensified LHS trade-off constraints take effect (intensified performance-maintenance trade-off relationships as patho-information-engram loads accumulate under conditions of uninterrupted relative affluence/procursive impacts: 2.1.2).

Also, as outlined above (oxidant-antioxidant paradox), uric acid acts as performance catalyst for functionality in sympathetic ANS mode. When too high (sympathetic overdominance), this is at cost of parasympathetic functionality,

compromising health (increased incidence of disease states), especially in in high performers (more so in males) and in respect of female reproduction.

Intensified LHS-mode trade-off Pm vs pM:

We have a LHS trade-off between energy allocation to high performance functionality (metabolic efficiency for e.g. performance: cognition/energy storage) and allocation to maintenance (including health-sustaining processes: prevention and elimination of allostatic load, i.e. patho-information-engram loading epigenetically inherited and produced during the course of life). Initially individuals exhibiting high performance (aristocrats, high social status, performers of high educational status and of high leadership competence or competence in general), as generally associated with wealth, can combine high performance (male competiveness, female reproduction) with sustaining maintenance functions (LHS-mode PM: Section 2.2.2e). However, under conditions of transgenerationally uninterrupted affluence, PIE loads accumulate, which disrupt PIE load-eliminating maintenance processeses (such as autophagy). Under conditions of pre-existing PIE loadings and associated compromised functional efficiency, the trade-off beween high performance realization and the maintenance of health is intensified. High performance (*inter alia* supported by performance catalysts such as uric acid) then becomes associated with a greater preponderance of illness states (see above), disproportionally affecting the wealthy and high performers, especially male high performers (2.2.2j).

d) Plasticity and resilience in health and disease

Plasticity (as genetically-based heritable characteristic: Pigliucci 2007) allows for high performance capacity realization; but the higher the plasticity scope, the lower is the capacity of resilience (involving protective factors/processes curtailing vulnerability to negative experiences under adversity: Pluess & Belsky 2013). A high plasticity scope underpins high performance breadth permitting both high P performance/fast LHS-mode and high M maintenance/slower LHS-mode expression. Resilience capacity, on the other hand, underpins invariant high P performance/fast LHS-mode realization in order to cope with and minimizing vulnerability to experienes of adversity. (Plasticity is here defined as flexibility in adaptability of an organism to environmental changes

or challenges; whereas resilience relates to the capacity of endogenous protective factors and processes to prevent an individual from succumbing to or being harmed by some contextual adversity through the ability to restore or maintain any pre-perturbation functional state).

Health status affects the intensity of LHS trade-off constraints (Doblhammer & Oeppen 2003). Good health status apparently mediates a dampening of LHS trade-off relationships. For example, the fertility-longevity trade-off is absent in individuals of good health status (Doblhammer & Oeppen 2003); implying a weakening of trade-off relationships in respect of performance-maintenance/fast-slow LHS-mode expression.

Doblhammer & Oeppen (2003): The generally observed positive relationship beween parity and late-life mortality (fertility-longevity trade-off) is confounded by the health status of individuals since both parity and late-life mortality are affected by health in a manner dampening the parity-mortality trade-off. The authors found that in a model controlling for health effects, a positive relationship between parity and longevity emerged. Health-based dampening of the fertility-mortality trade-off thus underpins negative trade-off relationships relationships between fertility and mortality; i.e. a positive association of fertility and longevity (Voland & Engel 1986, op. cit. Doblhammer & Oeppen 2003; Müller et al. 2002), thus allowing for a positive association of fertility and longevity. (**AS: as applicable to populations with a predominance of the LHS-mode PM: 2.2.2e**). For historical populations divergent results regarding the (usually positive) relationship between fertility and mortality are recorded. Often positive fertility-mortality trade-off relationships are documented (Korpelainen 2000; Lycett et al. 2000), particularly so for contempory populations (op. cit. Doblhammer & Oeppen 2003). (**AS: as applicable to populations subject to LHS-modes P > M and M > P: a shift from relatively high, but declining fertility and high mortality towards low fertility and increased longevity during the first demographic transition: 2.2.2e**).

As plasticity underpins both high performance scope and responsiveness to health-impacting insults, a compromised health status is thus implicated to result in an increased intensity of the trade-off between investment in performance expression and for health-maintenance requirements (accentuated P-M trade-off). Such would notably be the case for individuals with a poor health status due to functional inefficiencies of the energy metabolism resulting from progressive PIE load accumulation (lowered functional energetic potency: 2.1.2). Minimal P-M trade-off constraints would be applicable in individuals subject to the PM-mode life history strategy which is prevalent under conditions of balanced feast-famine alternation (2.2.2e).

Plasticity-resilience LHS trade-off constraints are further unpacked with reference to relevant interactions outlined by Pluess & Belsky (2013).

Pluess & Belsky (2013): Here the concept of *vantage sensitivity* is advanced, reflecting variation in response to exclusively positive experiences as a function of individual endogenous characteristics (the emphasis is placed on the elucidation of *endogenous* factors associated with variability in response to *positive* influences).
Manuck and associates (Manuck 2011, op. cit. Pluess & Belsky 2013; Sweitzer et al. 2012, op. cit. Pluess & Belsky 2013) introduced the term vantage sensitivity. Vantage is short for advantage and implies benefit, gain or profit and is also defined as 'a position, condition, or opportunity that is likely to provide superiority or an advantage (Houghton Mifflin 2000, op. cit. Pluess & Belsky 2013). Vantage sensitivity relates to the notion that some individuals are more sensitive and positively responsive to environmental advantages to which they are exposed. The following concepts characterize variability in response to positive experiences: (a) *vantage sensitivity* reflects the general proclivity of an individual to benefit from positive and presumptively well-being- and competence-promoting features of the environment, just as *vulnerability* depicts the tendency to succumb to negative effects of adversity; (b) the degree of *vantage sensitivity* is a function of the presence of *vantage sensitivity factors* (i.e. promotive factors) just as *vulnerability/risk factors* increase vulnerability to negative effects of adversity in the diathesis-stress framework; (c) vantage resistance describes the failure to benefit from positive influences, just as *resilience* characterizes resistance to negative effects of adversity in the diathesis-stress framework; and (d) the degree of *vantage resistance* is a function of the presence of *vantage resistance factors* or absence of *vantage-sensitivity* ones, just as *protective factors* increase *resilience* to negative effects of adversity in the diathesis-stress framework.

According to the differential-susceptibility hypothesis, individuals generally vary in their developmental plasticity regardless of whether they are exposed to negative or positive influences. Both models accounting for environmental impacts, the differential susceptibility (Belsky & Pluess 2009) and the biological sensitivity to context (Boyce & Ellis 2005) models, share the notion that some individuals are disproportionately susceptible to both positive and negative developmental experiences and environmental exposures (Ellis et al. 2011a). The theoretical framework of *differential susceptibility* regards more susceptible individuals as not just especially vulnerable, but more generally developmentally plastic (Boyce & Ellis 2005; Ellis et al. 2011a). Accordingly, those disproportionately likely to be adversely affected by negative experiences and exposures are also likely to benefit more from supportive and enriching ones.

Vantage sensitivity should not be equated automatically with differential susceptibility. Whereas some individuals might be more sensitive to the benefits of a supportive or enriching environments as a function of vantage-sensitivity factors, the same individual attributes may not make them more susceptible to the negative effects of contextual adversity (thus not in line with differential susceptibility). A further distinction between the two concepts emerge when we consider that individuals may be both highly responsive to environmental support (i.e. showing increased vantage sensitivity) and unresponsive to and protected from adversity (i.e. showing increased resilience), and this could be due to the very same endogenous characteristics. For example, children with high IQs tend to be more resilent in the face of adversity (e.g. Masten et al. 1999, op. cit. Pluess & Belsky 2013). Vantage sensitivity is exclusively

about the positive benefit derived from an enriching or supportive experience, whether reflected in the reduction of problems or dysfunction (e.g. depression, antisocial behaviour) or the enhancement of competence/well-being (e.g. prosocial behaviour, academic achievement). Thus, whereas some individuals may be disproportionately likely to be affected positively and negatively by, respectively, positive and negative contextual conditions, others may only be susceptible to positive influences; thereby manifesting vantage sensitivity rather than differential susceptibility.

Resilience reflects the absence of problematic functioning despite exposure to contextual adversity. Whereas resilience is what protective factors and processes engender by preventing an individual from succumbing to or being harmed by some contextual adversity (Rutter 1987, op. cit. Pluess & Belsky 2013), vantage sensitivity refers to promotive influences (Sameroff 2000, op. cit. Pluess & Belsky 2013) and is about individual benefit, more than others, from a positive environmental experience or exposure. Vantage sensitivity is about variation in the promotion of well-being or competent functioning when exposed to an experience presumably having a beneficial effect, whereas protection (resilience) is about not having the well-being or competence undermined when subject to negative experiences. (**AS: Combination of vantage sensitivity, based on plasticity scope, and protective resilience; low plasticity-resilience trade-off constraints: low plasticity and low resilience costs. Underpinned by LHS PM realization: Table 2.2.2b**).

The concept of resilience reflects protective responses within a diathesis-stress framework and refers to individual differences in response to adversity.

The concept of vantage sensitivity pertains to individual differences in response to positive contextual conditions as a function of promotive factors. Differential susceptibility, on the other hand, is based on the view that the same factors that increase vulnerability to adversity will also increase vantage sensitivity in positive environments (**AS: high plasticity/low resilience; plasticity-resilience trade-off**) and that factors that make some resilient to adversity will also make them less responsive to positive experiences (**AS: high resilience/low plasticity**).

Pluess & Belsky (2013) have outlined the interrelationships between vantage sensitivity and differential susceptibility; thereby providing a basis for the clarification of a trade-off relationship between plasticity and resilience. Under the concept of vantage sensitivity individuals may be both highly responsive to to environmental support (i.e. showing increased vantage sensitivity) and unresponsive to and protected from adversity (i.e. showing increased resilience); this being due to same endogenous characteristics (plasticity-resilience combination). Conversely, the concept of differential susceptibility implicates high plasticity-resilience trade-off constraints; as the same factors (a) that ***increase vulnerability*** to adversity will also ***increase increase vantage sensitivity*** in/to positive environments (plasticity) and (b) factors that make some ***resilient*** to adversity will also make them less responsive to positive experiences (be associated with ***low vantage sensitivity***). Plasticity costs are thus manifested in increased vulnerability, and resilience costs through lowered vantage sensitivity.

When subject to the LHS-mode PM, trade-off constraints (e.g. Doblhammer & Oeppen 2003; 2.2.2e) are minimized, implicating *inter alia* reduced trade-off constraints between plasticity and resilience. High inherent plasticity scope and resilience capacity are combined under the LHS-mode PM, but differential susceptibility applies as and when the efficiency of endogenous energetic functionality declines due to patho-information-engram load accumulation (2.1.2). Then plasticity, when underpinning high P realization (relating to *inter alia* to competitive and reproductive performance) also involves higher vulnerability to negative experiences/adversity, manifesting in higher P *versus* health trade-off constraints (costs of plasticity). Differential susceptibility, as elucidated by Pluess & Belsky (2013), is then applicable. Furthermore, as higher plasticity costs are constrained through resilience, resilience costs are incurred, manifesting in, *inter alia*, an associated narrowed plasticity scope for fast versus slow LHS-mode expression (e.g. accentuated fast versus slow LHS-mode trade-off). This implies that the capacity for early fertility realization is at the expense of later life fertility realization (as associated with a narrowed scope for fast-slow LHS-mode expression). Resilience costs are then manifesting through *inter alia* a narrowed childbearing age range.

2.2.2 Life history strategies: contextual framework for health and fertility

a) Life history strategies: conceptual framework

Table 2.2.2a Life History Strategies: Conceptual Framework
Life history traits and trade-off relationships Availability of resources in any given environment are finite. Time, effort and energy invested to one purpose diminishes the time, effort and energy available for another. Variations in life history characteristics such as age at first reproduction, reproductive lifespan and number and size of offspring, reflect reflect different resource investment allocations (in terms of time, effort or energy expenditure) to competing life functions. **A fundamental trade-off relationship exists between current production functionality P (current/early life reproduction and competitive capacity underpinned by high metabolic turnover realization and sympathetic ANS functional expression) and maintenance M functionality promoting later life performance (growth/size, health, body condition, longevity; underpinned by slower/lower metabolic turnover realization and parasympathetic ANS functionality)**.

Reproductive value (RV) models the trade-off relationships between reproduction, growth and survivorship. The reproductive value of an organism is defined in terms of its expected contribution to the population through both current and future reproduction (Fisher 1930): RV = Current Reproduction + Residual Reproductive Value (RRV). The residual reproductive value represents a future reproduction of an organism throygh its investment in growth and survivorship. Higher investment in current reproduction is traded off against growth and survivorship and thus future reproduction; whereas investments in growth are expected to yield benefits of higher fecundity and more reproductive events in the future (Jasienska 2009).
r/K selection reproduction strategies Basically following Stearns (1977), organisms that are r-selected have a high growth rate (r) and produce a high number of progenywith minimal parental care (mature rapidly and have an early age at first reproduction; have a large number of offspring at any given time; high mortality rates but low offspring survival rates; and minimal investment in parental care: fast LHS realization). Contrastingly, K-selected organisms are geared to subsist near the carrying capacity of their environment, producing relatively low offspring numbers over a longer time span; with high parental investment (mature more slowly with a later age at first reproduction; have few offspring at a time and more reproductive eventsspread out over a longer time span; low mortality but higher offspring survival rates; high parental investment: slow LHS realization).
A central trade-off relationship exists between somatic (growth and maintenanceof the body) and reproductive (producing offspring) investment (e.g, Hill & Kaplan 1999). Optimal life history strategies allowing for fitness maximization, encompass multiple generation, as natural selection, acting on life history traits, designs for the most optimal group of traits and use of energy (Stearns 1976). Numerous trade-off relationships exist (2.2.2b), notably between maintenance and growth, longevity and fertility, current and future reproduction, offspring quantity and quality, growth and current reproduction, survival and current reproduction; and fast versus slow life history strategy realization (2.2.2d).
Life history strategies are shaped in response to conditions of resource/energy availability (current and anticipated) in a manner optimising the use of resources, optimally balanced in respect of allocation to performance and maintenance in order to maximise fitness. Both ***exogenous*** conditions of resource availability and ***endogenous*** factors of genetically- or epigenetically-based resource use capacities/efficiencies are involved in the cueing of life history strategies. ***A life history strategy amounts to a blueprint for optimal investment allocations of endogenous and exogenous energy availabilities towards the maximization of fitnesss. Such operational blueprints are part of biocybernetic systems of organisms*** (this section: 2.2.2e)

Worthman and Kuzara (2005) applied life history theory to identify key trade-offs in adaptive strategies constraining developmental design based on using environmental information to guide ontogeny and the establishment of cost-benefit trade-offs that weigh early survival advantage against future costs. From overviews of gestational biology and postnatal physiologic, cognitive-affective and behavioural effects of gestational stress, a central shared role of the hypothalamic-pituitary-adrenal (HPA)

axis is evident. Beyond its generally accepted role as mediator of stress responses, the HPA axis seems to function as an ***agent of resource allocation linking conditions of gestation, postnatal environments, and functional and health-related outcomes*** (Worthman and Kuzara 2005). According to the interpretation of Pluess & Belsky (2011), prenatal programming provides a forecast of the postnatal environment in the context of prenatal stress promoting developmental plasticity. Particularly in individuals carrying plasticity genes, prenatal stress would lead to negative behavioural outcomes when the postnatal environment is experienced as harsh, unpredictable, uncaring or generally adverse (cueing to fast LHS-mode in response to harshness/unpredictability); but result in positive outcomes in their absence (cueing to slower LHS-modes). Children prenatally programmed for postnatal plasticity which encounter a positive environment instead of the predicted negative one would develop differentially, nevertheless supporting ultimate reproductive fitness in different ways in different environments.

Worthman and Kuzara (2005): Life history analyses involve both mortality (juvenile and adult) and fertility as primary constraints on life history organization (); subject to selection pressures driving age-specific and fertility operating synergistically on life history characters; including target age at maturity, adult size, reproductive patterns (frequency, litter size, parental care) and senescence. These factors set cost-benefit trade-offs for allocation of two critical resources: time and energy (Worthman and Kuzara 2005). These two resources are allocated among three domains, growth, reproduction and maintenance. Capacity for adaptation (plasticity) is revealed by the norm of reaction and reflected in the range of phenotypes expressed by particular genotypes across a range of operating conditions (Stearns and Koella 1986, op. cit. Worthman and Kuzara 2005). The norm of reaction reflects organism-environment interactions which result in change by design/adaptation, as well as inevitably associated random effects (tolerable costs). Adaptation in this context can be defined as an evolved response to circumstances benefitting fitness, but incurring tolerable costs chronically borne through functional impairments and/or increased maintenance costs (in lieu of plasticity costs). Variability in birth weight attributable to malnutrition is a reflection of resource restriction or unpredictability in utero, which is associated with poor to uncertain maternal nutrition and/or poor maternal health. Fetal responses to such conditions of resource restriction involve energy sparing and reallocation by decreasing maintenance in favour of sustained productivity of fetal growth and reallocation of resources to critical systems, notably the developing brain. The relative costs of growth and reproduction are increased as a consequence of fetal responses to such conditions; and short- versus log-term trade-offs accentuated. Mortality risks shift as a result of these fetal adaptations which adjust trade-offs to favour current over future survival and to anticipate chronic environmental risk. When the expectations of resource adversity are met postnatally, the delayed costs of the enhanced capacity to function under poor conditions (incurred by reduced maintenance, such as accelerated ageing) are offset. However, under conditions of post-natal resource abundance health

may be good and lifespans long, but the deferred costs will then manifest in the form of *inter alia* the increased risk of obesity and other forms of metabolic dysfunctionalities (Worthman and Kuzara 2005).
Worthman and Kuzara (2005) point out that cortisol plays a central role in mediating the allocation of available resources (energy, time) among competing demands (immediate, intermediate, long-term); attesting to the regulatory and integrative functions of the HPA axis in the context of resource allocation. The HPA axis, reflected through cortisol and its actions, emerged as a key player of neuro-endocrine systems in the implementation of life history.
The development of the fetal HPA axis during gestation is buffered by adaptations that reduce the normal negative feedback of cortisol on this axis by mechanisms of fetal buffering, and placental/maternal mechanisms which buffer the fetus against maternal cortisol. Nonetheless, particularly under conditions of increasing population density stress and associated increased levels of crowding, social stratification, social fragmentation and work-related stresses, pressures of psychosocial stress have been increasingly impacting on the mother-fetus unit. Stressful early environments have been shown to induce changes in cognitive style and capacity (attention regulation, memory, learning), emotion regulation (anxiety, moodiness, irritability) and social relationships (novelty aversion, avoidance and/or aggressiveness). Such impacts of early stress compromise future performance and (mental) health. ***From the adaptationist life history perspective, early development under resource restriction implicates a trade-off between early fitness benefits through survival versus later fitness costs in terms of reproduction and health*** (Worthman and Kuzara 2005).

b) Allocation trade-off relationships

Hill & Kaplan (1999): Life history theory focuses on fertility and mortality, since fitness, measured as the intrinsic rate of increase, is derived from summing reproductive output of each year lived. Natural selection is therefore expected to shape the timing of events associated with energy production and mortality hazards; such as growth, maturation, reproduction, maintenance and death (Hill & Kaplan 1999). Evolution by natural selection is the result of a process in which genetic entities/forms compete to harvest energy from the environment and convert that energy into replicates of themselves. Those forms which perform such processes most efficiently will prevail through time. Harvesting energy and converting the harvested energy into offspring involves challenges which are time-dependant. Time is a resource that can be converted into energy through work. Allocation of energy to growth involves certain benefits (increased capacity of energy capture per unit of time; larger body size increasing associated with increased success in intrasexual competition). Associated benefits also accrue to investments in maintenance, since building and safe-guarding physical condition requires health-promoting maintenance processes. We thus have a tri-partite trade-off among reproduction, growth and maintenance (Gadgil & Bossert 1970, op. cit. Hill & Kaplan 1999). Maintenance and growth promote fitness through their impacts on future reproduction (time-dependant reproduction) and we have a trade-off between current (energetically costly process rate-dependant; fast life history taits) reproduction and (time-dependant; slow life history traits) future reproduction. The trade-off is the result of reproductive effort realized during the current interval reduces reproduction at future intervals (reduced future reproduction; reduced probability of living healthily to older ages). Maintenance and growth (size) have their effects on fitness as a result of their impacts on future reproduction. A trade-off arises because

expenditures for current reproduction compromize future reproduction by having impacts which reduce future fertility or survival. According to the concept of embodied capital (Kaplan 1996, op. cit. Hill & Kaplan 1999), development resembles a process in which individuals and their parents invest in a stock of embodied capital; which in a physical sense is organized somatic tissue. Functionally, embodied capital involves fitness-promoting capacity traits such as strength, coordination, immune function and knowledge. These traits affect the profitability of allocating time and other resources to alternative fitness-promoting activites (resource acquisition, defense, mating competition, social dominance and parenting). As embodied capital stocks depreciate over time due to physical entropic forces, allocation to maintenance should also be considered to represent investments in embodied capital (Hill & Kaplan 1999). Own embodied capital results from parental investment in the prior generation. Investments in survival-related capital (defense, maintenance processes: tissue repair, immune functions) determine life time income benefits by increasing the expected life span over which benefits can accrue. However, having descendants requires reproduction and the optimization problem acted upon by natural selection is about the allocation life time income among investments in growth, maintenance (survival/longevity) and reproduction at each age, maximizing the time-discounted surplus energy for reproduction over the life course (op. cit. Hill & Kaplan 1999). Accordingly, the optimization problem for the parent thus is the allocation of investments in fertility and in the embodied capital of the offspring, maximizing total life time allocations by offspring to their own reproductive effort. Provided that individuals in each generation allocate investments in own- and and offspring-emdodied capital optimally, the multigenerational fitness of the lineage is maximized (Kaplan 1996).

Kaplan & Lancaster (2003): Natural selection acts on variability of traits (and their associated gene codes) of individual organisms within populations. Traits will increase in relative frequency to the extent that they impart characteristics to the individual organism supportive of maximizing their long-term production of descendants through time. In this context, fertility is the most direct component in fitness maximization; subject to two main trade-offs: the trade-off between present and future reproduction and the trade-off between quantity and quality of offspring. In organisms engaging in repeated reproduction events, some energy is invested in the current reproductive phase and some is diverted to maintenance, providing the basis for future reproduction (trade-off: current versus future reproduction). Natural selection on both offspring number and investment per offspring is expected to maximize the long-term production of descendants (number of offspring that survive and reproduce). Kaplan & Lancaster (2003) introduced the concept of *embodied capital* involving the processes of growth, development and maintenance; representing organised somatic tissue (various organs, especially the brain) and functional components such as strength, immune function, skill, knowledge; which require investment in maintenance for their sustained functional integrity. High maintenance investment requirements *inter alia* associated with a large brain and long development periods (exposure to environmental information) require specializations toward a slow life history strategy. Thus, the present-future reproductive trade-off relates to optimal investments in own (parental) embodied capital versus reproduction and quantity-quality (mating-parenting) trade-offs in terms of investments in embodied capital of the offspring versus their numbers. With increasing time spent growing and learning, natural selection favours investments in survival capacity/longevity in order to realise associated benefits over the course of life. Any investments that produce increased energy capture rates later in life (e.g.

learning) select for additional investments supporting attainment of advanced ages. Models of embodied capital show that ecological conditions and investments that increase the likelihood of survival to older ages also induce greater selection for income-related embodied capital.

Feeding niche specialization of humans (high quality, nutrient-dense, large, valuable food packages), notably procured through hunting, promoted cooperation between men and women and high levels of male parental investment favoured sex-specific specialization in embodied capital investments and complementarity in male and female inputs. In human females there are physiological and behavioural adaptations which are consistent with an evolutionary history involving male parental investment: food provisioning by males during pregnancy when females reduce their metabolic rates for efficiency of fat storage and during lactation women in foraging societies reduce their work effort and focus on high quality child care (Ellison 2001, op. cit. Kaplan & Lancaster 2003). Congruent with the sensitivity of the regulation of female reproduction to energetic condition, high work loads of females typically affect female fecundity and fertility negatively (op. cit. Kaplan & Lancaster 2003). In males, when production is determined by work effort and ability, a comparatively low variance in the food production by males is encountered and together with the importance of male food provisioning, monogamy is favoured; which was/is the predominant form of marriage among foragers (Kaplan & Lancaster 2003; for Germanic tribes refer to Geist 1978). This is congruent with the critical importance of maternal energetics for reproductive success (Table 2.3.2a: Ellison 2008; Jasienska 2003).

Costs and benefits of different life history strategies are related to individual characteristics and local circumstances; and develop through a combination of genetic variation and phenotypic plasticity, responding to environmental conditions (Ellis et al. 2009). Natural selection then favours adjustments in life history strategies through mechanisms based on phenotypic plasticity, within the species-typical range, in response to environmental conditions. Many allelic variations are maintained within populations, resulting in the development towards different sets of life history trade-off constraints, therby increasing phenotypic diversity. Thus, in response to socoecological conditions, those resource trade-off allocations between growth and maintenance, and growth and reproduction which are favoured by selection result in enhanced inclusive fitness.

Trade-offs between maintenance and growth. Maintenance involves energy allocated to survival capacity and demands; energy needed to stay alive and maintain basic functioning (e.g. brain metabolism, digestion, immune function, cellular/DNA repair, pathogen and predator defense). Quality and quantity of maintenance investments dertermine probability of death (health and longevity). Immune function is a major component of maintenance (McDade 2003), as is cellular/DNA repair, and trade-offs between maintenance and other life history functions such as growth and reproduction are of central importance in shaping life history strategies. Energy allocation to faster growth means earlier maturation, greater future capacity to produce larger and resilient offspring; but bigger individuals have higher maintenance costs (higher total energy requirements) and accordingly greater vulnerability to malnutrition and impaired reproduction during periods of negative energy balance (Kuzawa 2005). In response to energy conditions experienced during pregnancy and early childhood, trade-off settings between growth and maintenance are established. For example, poor maternal nutritional status and resource restrictions *in utero* would result in resources being more allocated towards maintenance at the cost of investment into growth. The resultant energy-sparing phenotype would typically economize body maintenance costs, resulting in slower growth, delayed sexual maturation, low gonadal steroid production, smaller adult body size and low fecundity (Kuzawa 2005; Walker et al. 2006). Such trade-offs arising during the prenatal period between the demands of maintenance and growth would shape developmental trajectories strongly influencing life-long life history strategies (Ellis et al. 2000). Kuzawa & Quinn (2009). Worthman & Kuzara (2005)

Increases in height and weight over the past 150 years were paralleled by improved nutrition and life expectancy (Samaras et al. 2003). This was seen as a positive trend, supported by some studies who found that taller people were healthier, suffering fewer heart attacks and strokes (op. cit. Samaras & Elrick 1999). However, negative correlations between greater height and longevity, as confirmed by many researchers in recent years (op. cit. Samaras et al. 2003; reviewed in Samaras & Elrick 1999) have emerged. Accordingly, individuals with higher, larger bodies have higher death rates (shorter lifespans) and more diet-related chronic diseases. Conflicting findings usually resulted from confounding effects of socioeconomic status, higher body weight for height, excess nutrition or other lifestyle factors. Also, Samaras et al. (2003) suggest

that differences in longevity of individuals relate to their height differences; and, with men being taller than women, they have a lower life expectancy at birth.

Height serves as an index of early nutrition and adult body weight. Samaras et al. (2003) summarized key findings showing a positive association between height and all-cause, cardiovascular disease and cancer mortality (90 studies, reports and populations). The review by Samaras et al. (2003) clearly shows a predominance of a negative relationship between height and longevity and a positive association with height and the incidence of cancer. In a recent review papers on cancer in relation to birth weight, growth rate and height were evaluated (Okasha et al. 2002, op. cit. Samaras et al. 2003). Their conclusion was that higher birth weight and height in children were positively related to the incidence of cancer in childhood and adulthood.

Overnutrition proxied by high birth weight is associated with obesity later in life Martorell et al. 2001 (op.cit. Samaras et al. 2003). Breastfeeding has a protective effect. However, birth weight and adult body mass index was largely accounted for by the weight of the mother and fetal growth indexed by birth weight relative to parental body size was unrelated to adult obesity. Thus, maternal weight or body mass index as such represents a risk factor for adult obesity, rather than birth weight (Martorell et al. 2001, (op.cit. Samaras et al. 2003). Rapid linear growth in childhood increased the risk of obesity in adulthood, especially for males with low birth weight (Parsons et al. 2001).

Increses in height and weight over the past 150 years were paralleled by improved nutrition and life expectancy (Samaras et al. 2003). This was seen as a positive trend, supported by some studies who found that taller people were healthier, suffering fewer heart attacks and strokes (op. cit. Samaras & Elrick 1999). However, negative correlations between greater height and longevity, as confirmed by many researchers in recent years (op. cit. Samaras et al. 2003; reviewed in Samaras & Elrick 1999) have emerged. Accordingly, individuals with higher, larger bodies have higher death rates (shorter lifespans) and more diet-related chronic diseases. Samaras & Elrick (1999). Reviewed the literature pertaining to interactions between height (body size), longevity and the incidence of chronic disease. They also reviewed publications showing the opposite pattern than found to be the predominant (e.g. Fogel 1994, op. cit. Samaras & Elrick 1999; Fogel 2004). However, overwhelming evidence supported that shorter stature and lower body weight were associated with better health and longevity.

In the review by Samaras et al. (2003), height served as an index of early nutrition and adult body weight. Samaras et al. (2003) summarized key findings showing a positive association between height and all-cause, cardiovascular disease and cancer mortality (90 studies, reports and populations). The reviews by Samaras et al. (2002; 2003) clearly show the predominance of a negative relationship between height and longevity and a positive association with height and the incidence of cancer. Samaras & Elrick (1999) state that an overabundance of energy-rich food seemingly promoted this modern increase in body size, but at the same time resulted in an increased incidence of chronic diseases (op. cit. Samaras & Elrick 1999). Notably, shorter people haver significantly lower mortality risk from cancer (*inter alia* Hebert et al. 1997, op. cit. Samaras & Elrick 1999). Albanes et al. (1988, op.cit. Samaras & Elrick 1999) suggested that excess nutrition early in life plays a role in human carcinogenesis. According to Micozzi (1993, op. cit. Samaras & Elrick 1999) stature is a measure of nutritional exposure during childhood and adolescence which predisposes to the long-term risk of chronic diseases. Studies also found reduced life expectancies with increasing BMI (e.g. Lindsted et al. 1991, op. cit. Samaras & Elrick 1999). Thus, maternal weight or body mass index as such represents a risk factor for adult obesity, rather than birth weight. Rapid linear growth in childhood increased the risk of obesity in adulthood, especially for males with low birth weight (Parsons et al. 2001).

Furthermore, the secular increase in body height which has been observed in developed countries during the past 150 years is being attributed to improving living conditions and nutrition, as well as growing heterozygosis (Wolanski 1980, Terrenato & Ulizzi 1983, op. cit. Salaris et al. 2012). In-depth studies (World Cancer Research Fund and the American Institute of Cancer Research 2007, op. cit. Salaris et al. 2012) on health and nutrition found that populations living before the Industrial Revolution were shorter and lighter than those of today and chronic diseases were relatively rare. A global shift toward urban living and industrialization resulted in greater height and weight, paralleled by an increase in chronic diseaeses. Malnutrition and childhood diseases can stunt growth and have long-term health disadvantages. Nonetheless much research shows that many short populations that follow their traditional diets are often free of contempory Western diseases.

Samaras & Elrick (1999): Reviewed the literature pertaining to interactions between height (body size), longevity and the incidence of chronic disease. They also reviewed

publications showing the opposite pattern than found to be the predominant (e.g. Fogel 1994, op. cit. Samaras & Elrick 1999; Fogel 2004). However, overwhelming evidence supported that shorter stature and lower body weight were associated with better health and longevity. In apparent contradiction, increasing body size over time (past 150 years) is associated with increasing life expectancy, this being attributed to improved living standards (reduced malnutrition and communicable diseases). An overabundance of energy-rich food seemingly promoted this modern increase in body size, but at the same time resulted in an increased incidence of chronic disaeases (op. cit. Samaras & Elrick 1999). Notably, shorter people haver significantly lower mortality risk from cancer (*inter alia* Hebert et al. 1997, op. cit. Samaras & Elrick 1999). Albanes et al. (1988, op.cit. Samaras & Elrick 1999) suggested that excess nutrition early in life plays a role in human carcinogenesis. According to Micozzi (1993, op. cit. Samaras & Elrick 1999) stature is a measure of nutritional exposure during childhood and adolescence which predisposes to the long-term risk of chronic diseases. Studies also found reduced life expectancies with increasing BMI (e.g. Lindsted et al. 1991, op. cit. Samaras & Elrick 1999). Nevertheless, tall people with a low BMI may live longer than short people with high BMI values. Eiben & Bodzar (1990, op. cit. Samaras & Elrick 1999) revealed that there were 60 % more Hungarian centenarians during 1870-1930 than during 1940-1987. (AS: Delayed onset of demographic transition: LHS-mode PM).

Samaras et al. (2002) presented a broad range of evidence confirming the inverse relationship between body size and longevity, based on research in respect of both humans and animals. Several biological mechanisms potentially explaining this inverse relationship were reviewed: including the entropy theory (Samaras 1974, op. cit. Samaras et al. 2002), increased cell number exposed to damage and transmutation, reduced cell duplications left in adults of larger size after cell duplication potential has been used up in attaining full body size, and smaller organs in comparison to body weight (*inter alia* relatively greater work load on heart). Body weight is only one risk factor in respect of longevity. Others include socioeconomic status, BMI, body type, dietary practices, lifestyle factors, exercise, genetics and the quality and availability of medical care.

Salaris et al. (2012). A secular increase on body height has been observed in developed countries during the past 150 years and this is being attributed to improving living conditions and nutrition, as well as the increasing incidence of heterozygosis (Wolanski 1980, Terrenato & Ulizzi 1983, op. cit. Salaris et al. 2012). The authors investigated the relationship between individual height and survival at older ages for conscripts born between 1866 and 1915 in an inland village of Sardinia, Italy (Villagrande Strisaili: Blue Zone population). The results showed that short conscripts (< 161.1 cm) generally had higher survival rates than their taller counterparts (≥ 161.1 cm). Biological explanations for greater longevity of shorter people were discussed: Caloric restriction; shorter bodies have fewer cells (greater exposure to free radicals and carcinogens); more potential cell reproductions over a lifetime (larger bodies are at a disadvantage

since they use up more cells in the initial production of a bigger body and in the daily replacement of damage and dead cells); lower DNA, cell and tissue damage (Giovannelli et al. 2002, op. cit. Salaris et al. 2012); greater hart pumping efficiency (De Simone et al. 1997, op. cit. Salaris et al. 2012: the pumping efficiency of the left ventricle dereases in proportion to heart mass); desirable levels of biochemical biomarkers; and rapid growth reduces longevity (Rollo 2007, op. cit. Salaris et al. 2012: slow and protracted growth supports longevity).

A secular increase on body height has been observed in developed countries during the past 150 years and this is being attributed to improving living conditions and nutrition, as well as growing heterozygosis (Wolanski 1980, Terrenato & Ulizzi 1983, op. cit. Salaris et al. 2012). In-depth studies (World Cancer Research Fund and the American Institute of Cancer Research 2007, op. cit. Salaris et al. 2012) on health and nutrition found that populations living before the Industrial Revolution were shorter and lighter than those of today and chronic diseases were relatively rare. A global shift toward urban living and industrialization resulted in greater height and weight, paralleled by an increase in chronic diseaeses. Malnutrition and childhood diseases can stunt growth and have long-term health disadvantages. Nonetheless much research shows that many short populations that follow their traditional diets are often free of contempory Western diseases.

Longevity-fertility trade-off patterns.

Kemkes-Grottenthaler (2004): A gradual transition from high to low fertility/mortality ensued over the past 150 years. Parity often displays an association with increasing mortality for high-parous women (Lund et al. 1990, op. cit. Kemkes-Grottenthaler 2004). According to Westendorp & Kirkwood (1998, op. cit. Kemkes-Grottenthaler 2004) lifespan is negatively correlated with family size, a result which also supports predictions based on evolutionary models of ageing (Doblhammer & Oeppen 2003). Higher fertility regimes thus affect maternal longevity prospects and also familial child survival. With onset of the demographic transition, longevity of women was predominantly contingent on the maternal component, but to a lesser extent of men (Westendorp & Kirkwood 2001). The maternal contribution to offspring lifespan is estimated to be higher than the paternal contribution and that the parental component is larger in daughters than sons; indicating a direct effect on progeny ageing along the female line. Such selection for female lifespan seemingly represents an effective strategy for improved reproductive success.

Higher mother-daughter correlations may be linked to the mitochondrial theory of ageing, which postulates that damage to mtDNA and organelles by free radicals leads to loss of mitochondrial function and cellular energy. Natural maintenance systems of the body may postpone aspects of ageing (Kirkwood 2002). On an ultimate level,

selection for maternal longevity may be a more efficient strategy for improving offspring survivability than selection for female reproductive span. Primate evidence shows that an elongation of life time is positively correlated with longer reproductive life, more offspring and higher reproductive success (op. cit. Kemkes-Grottenthaler 2004). Selection may favour stronger mothers (Korpelainen 2000) and reaching old age may be a by-product of these genetic forces, which also maximize the female reproductive period (Perls et al. 1997; Perls et al. 2002).

Doblhammer & Oeppen (2003): After statistical correction for the effects of differences in health and mortality selection before the age of 50, a strong and significant positive correlation was found between parity and late-life mortality for British peerage women. This is consistent with other studies where the generally observed positive relationship between fertility and late-life mortality (fertility-longevity trade-off) was similarly detected; in historical (Korpelainen 2000; Lycett et al. 2000) as well as contempory populations (Doblhammer 2000).
On the fertility-longevity trade-off: The generally observed positive relationship beween parity and late-life mortality (fertility-longevity trade-off) is confounded by the health status of individuals since both parity and late-life mortality are affected by health in a manner dampening the parity-mortality trade-off. The authors found that in a model controlling for health effects, a positive relationship between parity and longevity emerged. For historical populations divergent results regarding the (usually positive) relationship between fertility and mortality are recorded: sometimes negative relationships (Voland & Engel 1986, op. cit. Doblhammer & Oeppen 2003; Müller et al. 2002); but mostly positive relationships (Korpelainen 2000; Lycett et al. 2000), particularly so for contempory populations: op. cit. Doblhammer & Oeppen 2003).

Trade-offs between current and future reproduction. Trade-off settings between maintenance and growth established during childhood furthermore determine trade-off relationships between current and future reproduction. A metabolic trade-off setting supporting current reproduction is in a trade-off relationship with optimal future reproduction since the former is costly in terms of reduced number, quality or survival of future offspring and reduced growth and survival of the parents. Long-term fitness is the expected relative contribution of an individual to the gene pool in the longer-term future (Harpending & Rogers 1990). This long-term fitness is dependant on on a life history strategy (LHS) combining reproductive output (number of offspring) and wealth or status transmitted from parents to offspring, contributing to fitness by retaining reproduction-supportive competence through increased competitive performance capacity. This involves a trade-off between reproductive output and precondions for

successful reproduction of offspring (LHS with fewer offspring, more wealth per offspring and reduced probability of falling into wealth-deficit conditions no longer permitting reproduction). For this LHS to maximize long-term fitness requires

circumstances of a destitute class not permitting reproduction and the likelihood that the poorer, many offspring falling into such a class. Studied a system with three social classes, the poorest of which had very low single generation fitness. The class with the highest single generation fitness does not have the highest long-term fitness. The authors suggest that this system represents a useful model for understanding changes in the reproductive behaviour during the demographic transition in Europe.

Trade-offs between growth and current reproduction.

There is also a trade-off between metabolic energy investment in current reproduction and that invested in the continued growth of an organism. The human life course represents an extreme example of an evolved trade-off involving the combination of prolonged growth and delayed reproduction; suggesting that large body size and accumulated skills and knowledge compensate for reduced reproductive output due to adolescent mortality and reduced total reproductive output of lineages through shorter generation times.

Trade-offs between survival and current reproduction. A further core element of the current-future trade-off involves trade-off allocations between survival and reproduction. An organism investing in its own survival (body maintenance and offspring survival) will have to trade this off against investment in current reproduction. For example, for historic upper class British families, Doblhammer & Oeppen (2003) documented a negative within-person correlation between number of births and late-life survival (longevity); after correcting for variation in the health and mortality of the women during their childbearing years. This trade-off may be obscured by between-person comparisons where a person in good physical condition and ready access to food, shelter and kinship support may grow up faster to achieve larger adult size and have more, higher quality children than another subject to deficits of such resources. Stressful conditions often result in individuals to allocate energy to survival at the cost of current reproduction. Early pregnancy loss among mothers with high cortisol levels (Nepomnaschy et al. 2006) or suppression of ovarian hormonal functioning in women experiencing negative energy balance (Ellison 2003; Ellison 2008) represent examples of reproduction/survival trade-
offs.

Trade-offs between offspring quality and quantity. Over both developmental and evolutionary time, energy constraints predispose an organism towards investing in

either a relatively small number of high quality offspring or a large number of lower quality offspring (Stearns 1992, op. cit. Ellis et al. 2009). Higher quality offspring, the product of greater investment per child, tend to be healthier and have better developmental and survival outcomes. It is contended that maternal fitness is maximized by the optimal division of reproductive investment between offspring number and offspring quality. Regarding resource-poor landless families in pre-industrial Finland (1709-1815) maternal fitness returns were reduced with increased maternal fecundity (Gillespie et al. 2008). This resulted from the average offspring contribution to maternal fitness declining with increasing maternal fecundity. In contrast, for land-owning families, recruited offspring fecundity increased with increased maternal fecundity. Unaffected by socioeconomic status, the proportion of offspring recruited decreased with increasing maternal fecundity. Subsequent offspring fecundity however increased with increasing maternal fecundity in land-owning families, but remained constant in landless families; implying a trade-off between offspring quality and quantity in the case of families of lower socioeconomic status (Gillespie et al. 2008).

c) Harshness-Unpredictability

Following current life history theory, two primary environmental parameters indirectly influence the evolution of life history strategies: degree of harshness and degree of unpredictability (Ellis et al. 2009). Absolute values of mortality/morbidity are important/relevant indicators of environmental harshness. Unpredictability of environments reflect the degree of stochasticity (unpredictable variation) in environmental risk (harshness). Since such risks are generally spatiotemporally inconsistent and thus largely unavoidable in scenarios of unpredictability (Ellis et al. 2009).

Effects of harsh environments. Morbidity and mortality cues during development represent information calibrating life history strategies. For example, Wilson & Daly (1997) revealed that in neighbourhoods where individuals had shorter life expectancies (e.g. higher homicide rates) also had the lowest median age of women giving birth. This shows the consistent association between involvement in violence (as either perpetrator
or victim) and faster life history strategies (early sexual activity, multiple sexual partners, adolescent childbearing) (op.cit. Brumbach et al. 2009).

Effects of unpredictable environments. Environmental unpredictability cues life history development towards higher offspring numbers and diversity (spreading the risk: diversified bet-hedging), i.e. towards a faster life history strategy. Some distinctions between the effects of harshness and unpredictability have been decribed (Ellis et al. 2009), but harshness and unpredictability generally have similar effects on the development of life history strategies; being associated with faster life history strategies (Ellis et al. 2009; Brumbach et al. 2009). Unpredictability and harshness in adolescence have effects leading to faster life history strategies in young adulthood. A slow young adult life history strategy was associated with adolescent sexual resrictiveness, low levels of young adult social deviance and better adolescent health. The research findings of Brumbach et al. (2009) suggest that it is not general stress, but specificall harshness (mortality risk) and unpredictability (stochasticity) of the environment that form the primary influences towards the development of slow or fast life history strategies. In the face of chronic long-term uncertainty/harshness, organism can better maximize their fitness through resource allocation favouring a fast life history strategy: many offspring, quicker maturation and reproduction at an earlier age (at the cost of growth/size, offspring quality and somatic maintenance investment, thereby compromising health). As revealed by Brumbach et al. (2009), male and female life history strategies operate in conformity, while mean-level differences do occur. Males on average pursue faster life history strategies than females, but with similar dynamics of the strategies pursued. This is congruent with shorter life spans in males (Ellison 2008; Table 2.3.2a: Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution).

Chisholm et al. (2005): Selection always favours organisms leaving more descendants (since fitness is always relative), but since the required resources needed for achieving this are always limited it is not possible to maximise all components of fitness simultaneously, trade-offs are inevitable. A central trade-off in this context is that between current and future reproduction (increasing current/short-term reproduction is at the expense of reproduction in the future). Every else being equal, increased current/early reproduction is optimal under conditions of risk and uncertainty due to inadequate or uncertain resource availability. Maximising current reproduction through intensified fertility (early age of menarche, early age at first birth) in uncertain environments and associated unpredictability of socio-emotional stability minimises the probability of lineage extinction under such conditions (op. cit. Chisholm et al. 2005). Whereas stress of malnutririon and disease delays menarche (involving metabolic, immune and endocrine control) psychosocial stress induces early menarche (psychoneuroendocrine control systems). Psychosocial stress (which may be

experienced as insecurity, arousal, anxiety, fear, anger, grief, hopelessness) would tend to activate the hypothalamic-pituitary-adrenal (HPA) system; resulting in altered levels of stress hormones, especially cortisol (which may have long-lasting/permanent deleterious effects). Chronic activation of the HPA system has been implicated in the early activation of the hypothalamic-pituitary-ovarian system which controls onset of puberty in women (op. cit. Chisholm et al. 2005). The associated altered settings represent phenotypic mechanisms entraining reproductive strategies in the adult-phase contingent on environmental cues under which they had been developing. Chisholm et al. (2005) found significant negative correlations between total early stress and age at menarche, age at first birth and expected life span. Insecure forms of adult-progeny attachment were associated with total early stress, earlier ages of menarche and first births and lower expected life span. Early stressors manifesting in mother-father violence, father absence/no father figure/divorce-separation, mother personality, father personality or mother-father relations were generally associated with lower age at menarche, lower mean age at first birth, adult-progeny attachments being less secure and lowered mean expected lifespan. As early stress indexes environmental risk and uncertainty it can be considered adaptive for women experiencing such stress to maximise current reproduction. Although father absence is one of a range of early stressors, Ellis et al. (2003) conclude that father absence is important in its own right and not just a proxy for its many correlates. However, Chisholm et al. (2005) caution that father absence can only be considered as one early stressor amongst many others affecting age at menarche, age at first sex, adult attachment and expected lifespan. Also, a full understanding of the mechanisms involved furthermore has to accommodate that time preferences regarding reproductive activities are similarly affected by father absence in both prepubertal boys and girls.

Exposure to father absence was strongly associated with elevated risks for early sexual activity and adolescent pregnancy.

Boothroyd & Cross (2017): Principal component analysis in relation to father absence revealed two main axes of variation: a general reactivity factor (aggression, impulsivity, fear) and a masculinity factor (high scores on masculine traits, low fear and physical/verbal aggression). The general reactivity factor was weakly associated with father absence in women. Participants who reported poor childhood relationships with their parents showed higher reactivity, but not higher masculinity. These results suggest that findings linking father absence to reproductive development trajectories may have arisen from a greater propensity towards externalising and reactive behaviour rather than a change in reproductive development as such.

According to Draper & Harpending (1982) humans evolved psychological mechanisms where father presence during childhood acts as a cue for life history strategies. Father presence implicates an environment requiring two parents for child survival and cultural

success, thereby cueing development of a parenting investment strategy (delayed maturation, stable relationships; AS: sustained fertility); whereas father absence would cue for a mating investment strategy (early maturation, short term partnerships, high

early fertility; AS: opportunistic, current fertility). Father absence is associated with with less responsive care since the time and attention of mothers would be divided between earning a living and child care. Father absence is considered a risk factor for undesirable developmental outcomes such as early sexual activity, teenage pregnancies and unstable marriages later in life (*inter alia* Ellis et al. 2003). Father presence/absence may cue reproductive strategies (Draper & Harpending 1982) or may alter parental care patterns influencing development (Ellis et al. 2003). Direct parental care may be limited by pair-bond dissolution and changes in caretaking arrangements (Quinlan 2003). In this context, studies found that children with two parents spent more time at home and with their mothers than father-absence children, reduced parental supervision in single-mother housholds and shorter duration of breastfeeding among father-absent children (op. cit. Quinlan 2003).

The biological stress response is implicated to link direct parental care to reproductive development (Belsky et al. 1991). Unresponsive parenting is positively associated stress levels in children (as indicated by cortisol) and children of single mothers tend to have elevated cortisol levels (op. cit. Quinlan 2003). These findings suggest that the stress response is involved as mediator towards adjusting life history strategies in reaction to early experience (Worthman 1999, op. cit. Quinlan 2003).

Belsky et al. (1991) posit two divergent developmental pathways considered to promote reproductive success within the contexts in which they have arisen. One pathway being characterised by stressfull rearing environments in childhood, the development of insecure attachment to parents associated with subsequent behaviour problems, early pubertal development and precocious sexuality in adolescence and unstable pair bonds and limited investment in child rearing in adulthood. The other pathway is characterised by opposite characteristics.

The results of the study by Quinlan (2003), assessing associations of father absence, timing of parental separation and changes in caretaking emvironment with female reproductive development, suggest that the quality of direct parental care during early childhood underpins differences in female reproductive development. Divorce/separation between birth and 5 years predicted early menarche, first sexual intercourse, first pregnancy and shorter duration of first marriage. Early parental separation (0-5 years) was associated with shorter duration of first marriage. Multiple changes in childhood care taking environments had similar effects. Accelerated

reproductive development decreased as the number of changes decreased. Living with either mother or father after separation had similar effects on reproductive development (Quinlan 2003). Generally, single and two-parent families have different patterns of parental care which result in different reproductive strategies. In conclusion, reproductive development is considered sensitive to direct parental care and variations thereof may be at the basis of causal links between environmental risks (stress impacts) and life history strategies. In two-parent households the ability to provide direct care is enhanced (Quinlan 2003).

d) Fast-slow life history strategy syndromes

McDade et al. (2016): Immune defenses are costly and maximizing investments in immunity and long-term survival may not necessarily maximize reproductive fitness. Trade-offs are thus inevitable as organisms pursue to allocate limited resources across the life cycle in order to maximize reproductive fitness within a given ecological context. Under high risk circumstances (**AS: harshness and unpredictability: 2.2.2c**) the prediction is to invest more of limited resources into processes facilitating current reproduction, with relatively less resources allocated to maintenance (Kirkwood & Rose 1991, op. cit. McDade et al. 2016). Associated fast life history strategies typically involve shorter life spans, earlier reproduction and the production of many offspring with relatively lower survival rates. Conversely, when extrinsic mortality risk is low, greater investment in maintenance and the soma is predicted, facilitating a slow life history strategy characterized by longer life span, but reduced expenditure on growth or reproduction; implying the production of fewer offspring with higher levels of parental investment and survival (Charnov & Berrigan 1993, op. cit. McDade et al. 2016). Immunity represents a primary physiological system playing an essential role in survival and accordingly a major component of maintenance effort. Significant trade-off constraints thus occur between immune defenses and investments in reproduction.

Following Ellis et al. (2009), life history theory involves the explanation of the evolution and development of overarching **resource allocation trade-offs** pertaining to individuals during the course of their lives (growth versus maintenance, current vesrsus future reproduction, offspring quality versus quantity: reproductive rate versus longevity/growth/body size: link to nutrition: Table 2.5.1.2e). These trade-off relationships are expressed in integrated sets of life history traits constituting life history strategies of individuals/lineages as adjusted in response to environmental opportunities and risks encountered and recurrently adjusted to enhance inclusive fitness over evolutionary history (Ellis et al. 2009). Species-typical life history strategies are represented by a combination of modal life history trade-offs over its

natural selective history. Adaptive individual life history strategies then involve both genetic diversity and evolved mechanisms of phenotypic plasticity allowing individual adjustments to environmental conditions and constraints (external and internal). Life history traits are generally correlated and through optimized assemblages of trade-offs form coherent and coordinated life history strategies which determine the optimal allocation to competing demands of growth, reproduction and maintenance (Ellis et al. 2009). Generalized patterns exist in the coordinated directionality of trade-offs in respect of specific life history traits; resulting in clusters of correlated life history traits positioned
on a continuum described as 'fast' to 'slow' (Ellis et al. 2009); also sometimes referred to in terms of quantity-quality or r-K continua.

Systematic within-species variation in life history strategies, through evolutionary and developmental processes, give rise to individually differentiated life history strategies adaptively coordinated with levels of harshness and unpredictability of local environments (Ellis et al. 2009).

The effects of environmental harshness on the the fast-slow differentiation of life history strategy modes, as outlined by the above authors, can be summarized as follows. Under conditions of high levels of morbidity-mortality (extrinsic/intrinsic), which increase or disproportionately influence adult mortality, selection favours faster life history strategies. With this strategy the risk of mortality prior to reproduction is reduced, thereby increasing the chances of contributing offspring to the next generation. Fitness is enhanced by trading off growth (and the benefits of reproduction at a larger size) for earlier maturation and reproduction (including selection for offspring quantity rather than quality). Whenever incremental changes in parental investment /offspring quality reduce juvenile morbidity-mortality, natural selection favours slower life history strategies.

Low rates of environmental harhsness combined with conditions of resource-abundance select for faster life history strategies (greater reproductive effort and productivity). With decreasing environmental harshness, population density-dependant effects increasingly act as selective agents. With increasing population density approaching environmental carrying capacity, intraspecific competition increases, selection then favouring slower life history strategies. Conditions of relatively high population density

favour high competitive ability in offspring (high quality offspring: high maintenance investment associated with slower LHS expression) in order to be able to monopolize contested resources in saturated environments.

Fast life history strategy expression underpins high performance (P) capacity (P based on high metabolic turnover functionality: early and high rates of reproduction and peak male competitive performance). Slow life history strategy expression underpins fitness benefits over time based on efficient maintenance securing fitness benefits into the future (health, extended growth-size/storage, longevity). Fundamental life history trade-off: high performance/low maintenance (fast LHS) *versus* high maintenance/low performance (slow LHS).

Brumbach et al. (2009). Variation in human (mammalian) life history strategies can be described to occur on a slow to fast continuum (Promislow & Harvey 1990, op. cit. Brumbach et al. (2009). At any given point of this continuum, life history traits cluster to form coherent, integrated sets. At the faster end of this continuum we have short gestation times, early reproduction, relatively smaller body size, large litters, high mortality rates and lower longevity. Life history traits at the slower end of this continuum are associated with slow rates of reproduction and population turnover: fewer children, greater energy investment per child (offspring quality) and longer life spans. Supporting pychosocial traits include commitment to long-term relationships, long-term thinking rather than focus on short-term gains, planning for the future of their children through the accumulation of resources and providing for enhancement of the social status of their offspring, and offspring health (Figueredo et al. 2006b). Slow life history strategies are characterized by life history traits such as longer life span, high quality offspring and long-term planning and parental investment. Furthermore, certain value systems and personality traits are manifested and associated with particular life history strategies (Figueredo et al. 2006a); implying that cognitive and behavioural life history traits are similarly essential to human reproductive strategies than purely biological indicators (Brumbach et al. 2009).

Voland (1998). Humans, like all other organisms, are expected to maximise their inclusive fitness subject to the socioecological constraints to which they are exposed.

In this context, life histories evolve in order to maximise the contribution of genetic material to the following generations. Two main types of investments are involved: somatic investments in growth, development differentiation and maintenance, thereby accumulating reproductive potential and increasing residual reproductive value; and reproductive effort: exploiting existing reproductive potential, thereby decreasing the residual reproductive value of the individual. Reproductive effort thus entails costs and natural selection optimises the way in which reproductive effort is allocated in order to result in maximum inclusive fitness over the cource of life of the organism. Under conditions of resource limitations, trade-off constraints develop when two or more traits are limited by the shortage of the same resources. The central trade-off is beween reproductive effort (current reproduction/offspring quantity) and somatic effort (future reproduction/offspring quality).

Whenever living conditions of the mother, especially nutritional circumstances, are conducive to thriving offspring, early sexual maturity and early commencement of reproduction will be advantageous; through transferring their developmental lead into increased reproduction. Under favourable resource conditions, early age at menarche is positively associated with fecundity, fertility and life time reproductive success, as indicated by the number of surviving children (op.cit. Voland 1998). On the other hand, late age at menarche correlates positively with, *inter alia*, interbirth intervals, and the probability of sterility (op.cit. Voland 1998). Late sexual maturity is then associated with reduced lifetime fitness.

Psychosocial stress in childhood and youth (caused by uncertain resource availability conditions or parental pair-bond instability) signal to female offspring an unpredictable life perspective where somatic expense is of less value than advanced sexual maturity and reproductive activity. Average age at marriage for both men and women was relatively high in preindustrial times; linked to a requirement for economic independence of young married couples. Thus, under economically more favourable conditions, people married younger and more frequently, especially also noted for peasant families. For preindustrial societies, early age at first reproduction appears to be a good indicator of female lifetime reproductive success (Käär et al. 1996, op. cit. Voland 1998).

The physiology of reproduction responds sensitively to changing living conditions as reflected in psychogenic stress (Wasser 1994) or state of net energy balance (Table;

Ellison 2008). Energetic stress may result from the variability of food availability (energy intake) and the variability of energy expenditure (work load; high metabolic rate settings). Maximum reproductive performance (early onset, short birth interval, many offspring: maximum fertility) is costly in terms of maximum offspring fitness (requiring maintenance investments; successful raising and social placement of offspring); thus involving a trade-off between the quantity and quality of offspring. Natural selection for maximum fitness involves maximisation of offspring production, maximization of their survivorship and/or maximisation of their social and material endowment (op. cit Voland 1998).

In natural fertility populations the fertility *versus* late-life mortality trade-off (negative relationship between fertility and longevity) is mediated by health status Doblhammer & Oeppen (2003). Accordingly, good health status positively affects both fertility and survival (life span) and can thus result in a dampening or elimination of this trade-off; permitting the concurrence of relatively high fertility and longevity (as applicable to traditionally healthy populations: Section 2.5.1.2). Exemplifying this, Müller et al. (2002), for historical French-Canadian cohorts (1600-1800s), found that increased fertility was linked to increased post-reproductive survival and that the extended postreproductive life expectancy was tied to late births.

Korpelainen (2003): According to the Darwinian theory of evolution all organisms, including humans, are expected to maximize their fitness within relevant socioecological constraints (Voland 2000). Children produced at an early age contribute more to fitness of the female parents than children produced later in life (Stearns 1992, op. cit. Korpelainen 2003). An indicator of fitness, life time reproductive success (LRS) does not take variation in generation length into account. The indicator of fitness λ includes rate measures sensitive to both reproductive quantity (LRS) and timing (parental age of reproductive events): McGraw & Caswell 1996 (op. cit. Korpelainen 2003). Thus the combination of early reproduction and high LRS implies high fitness (λ).

e) Life history strategy modes and the procursion sequence: LHS-explanatory framework

1) Life history strategies as operational blueprints of fitness maximization

Life history strategies are shaped in response to conditions of resource/energy availability (current and anticipated) in a manner optimising the use of resources, optimally balanced in respect of allocation to performance and maintenance in order to

maximise fitness. Both ***exogenous*** conditions of resource availability and ***endogenous*** factors of genetically- or epigenetically-based resource use capacities/efficiencies are involved in the cueing of life history strategies. ***A life history strategy amounts to a blueprint for optimal investment allocations of endogenous and exogenous energy availabilities towards the maximization of fitnesss. Such operational blueprints are part of biocybernetic systems of organisms.*** High endogenous energy utilisation efficiency (as prevalent with low/absent patho-information-engram loads, i.e. minimal procursion impacts undermining health status: 2.1.2) attenuates performance-maintenance trade-off constraints. Following Doblhammer & Oeppen (2003), the fertility *versus* late-life mortality trade-off (negative relationship between fertility and longevity) is mediated by health status; since ***good health status positively affects both fertility and survival (life span) and can thus result in a dampening or elimination of this trade-off and other trade-off constraints such as relating to performance-maintenance trade-off relationships***.

Minimum fast-slow LHS trade-off constraints support fitness maximization. According to the theory of evolution of organisms, including humans, are expected to maximize their fitness within relevant socioecological constraints (Voland 2000). Children produced at an early age contribute more to fitness of the female parents than children produced later in life (Stearns 1992, op. cit. Korpelainen 2003). As indicator of fitness, life time reproductive success (LRS) does not take variation in generation length into account. Thus, as an appropriate indicator of fitness λ includes rate measures sensitive to both reproductive quantity (LRS) and timing (parental age of reproductive events: McGraw & Caswell 1996, op. cit. Korpelainen 2003). Thus high fitness (λ) is achieved through the combination of early reproduction (fast-LHS mode expression) and high LRS (slow-LHS mode realization), as clarified by Korpelainen (2003).

2) Life history strategy LHS-mode PM

LHS-mode PM: Capital P refers to efficient functionality of high performance metabolic processes, *inter alia* supporting early reproduction, competitive capacity (functionality in sympatgetic ANS mode); whereas capital M refers to high efficiency of maintenance processes; supporting *inter alia* later life performance and health maintenance. The LHS-mode PM accommodates both efficiency of P and M LHS functionality as associated with minimized P-M trade-off constraints (as sustained under the resource/energy use efficient (RUE/EUE) metabolic resource use mode

(222f). Pm performance functionality supports the optimal utilization of available resources (fast-LHS-mode Pm) and pM functionality supports survival-promoting processes relating to health maintenance, body condition and longevity (slow- LHS-mode Mp). Food resource conditions are biocybernetically aligned with the LHS-mode PM when produced under growth-curbed circumstances (high nutrient concentrations supporting Pm functionality for maximum resource us, but biocybernetically slow-growth food sources, supporting pM functionality); favouring a minimised Pm versus pM trade-off. Good pM functionality (transient famine conditions providing for *inter alia* autophagic processes, thereby preventing the accumulation of patho-information-engram loads), but also good Pm functionalty (fertility). The LHS-mode PM typically applies to traditionally healthy-living populations (THL populations: Section 2.5.1.2, 2.5.1.2b/d).

The LHS-mode PM thus permits both Pm functional efficiency (e.g. male psychological/physical performance/female reproductive performance) and pM functional efficiency (health/longevity: parasympathetic ANS functionality), as experienced by historical and THL (traditionally healthy-living) populations. Thus, under circumstances involving transient energy resource deficits (inducing DR-dietary restriction-autophagy: 2.2.2f), such as experienced in earlier historic times and by traditionally healthy living (THL) populations (2.5.1.2), the accumulation of patho-information-engram loads is largely prevented (2.1.2); underpinning the LHS-mode PM (P-M trade-off constraints weak or absent) and the combination of both fertility and longevity is sustained.

Diet effects (Table 2.5.1.2e): a high metabolic turnover-boosting nutrient-dense diet underpins increased fast LHS expression (LHS-mode Pm > Mp: increased fertility-longevity trade-off); whereas a diet of growth-curbed plant items (nutrient-poor, arid, cool temperature growth) favours slower LHS-mode PM (reduced fertility-longevity trade-off constraints).

The LHS-mode PM is the primordial LHS-mode (Table 2.2.2b) under K-selection in the peri-artic zone subject to pronounced low-temperature seasonality and a spatiotemporally clumped resource base (variable, but seasonal superabundance); as underpinned by the peri-arctic metabolic performance mode (Table 2.5.1.1a; characterized by high plasticity benefits: adaptability to

high resource level fluctuations; productivity over time uncoupled from resource availability levels and enhanced stress tolerance capacity, supporting size, energy storage, health, longevity; but incurs relatively high plasticity costs associated with high BMR settings/requirements).

Cold adaptation (*vide* Wallace 2005; 2.3.3b) is an integral part of the peri-Arctic metabolic performance syndrome (Section 2.5.1.1; Table 2.5.1.1a). Of importance in this context is that in cold-adapted uncoupled mitochondrial DNA variants, fast-slow LHS trade-off constraints are attenuated, particularly so when associated with endogenous energetic efficiency (low levels of patho-information engram loads) as manifesting in the LHS-mode PM), characterized by combined Pm (performance vitality) and Mp capacities (health and longevity); based on reduced P-M trade-off constraints (Doblhammer & Oeppen 2003).

Table 2.2.2b Life History Strategy PM
Primordial LHS-mode under K-selection in the peri-artic zone subject to pronouced low-temperature seasonality and a spatiotemporally clumped resource base (variable, but seasonal superabundance) as underpinned by the peri-arctic metabolic performance mode (characterized by high plasticity benefits (adaptability to high resource level fluctuations; productivity over time uncoupled from resource availability levels and enhanced stress tolerance capacity, supporting size, energy storage, health, longevity: minimized P-M trade-off constraints) and plasticity costs (high BMR settings/requirements) Table 2.5.1.1a)
Reduced fast-P *versus* slow-M LHS trade-off constraints (cold adaptation and homozygosity): Cold adaptation (*vide* Wallace 2005) is an integral part of the peri-Arctic metabolic performance syndrome (Section 2.5.1.1; Table 2.5.1.1a). Of importance in this context is that in cold-adapted uncoupled mtDNA variants, fast-slow LHS trade-off constraints are attenuated, particularly so when assocated with endogenous energetic efficiency (as associated with low levels of patho-information engram loads). LHS-mode PM characterized by combined Pm (performance vitality) and Mp capacities (health and longevity); based on reduced Pm-Mp trade-off constraints (2.2.2e; Doblhammer & Oeppen 2003). Accordingly, the greater the extent of cold-adaptation (partially uncoupled OXPHOS mtDNA mutations re Wallace 2005), as required in increasingly colder, more northern regions, (a) the higher the predominance of slower LHS-mode expression and also (b) the lower any fast-slow LHS trade-off constraints (Table 2.3.3b), particularly in healthy individuals (low PIE loadings; LHS-mode PM). Furthermore, pronounced homozygosity as exhibited in higher latitude populations (Table 2.3.3b) involve mechanisms relating to the predominance of slow life history strategy-mode expression, indicative of slower rates of ageing, seem to be involved. Slow-LHS expression typically manifests in late female reproductive realization, slow somatic ageing and longevity; but subject

to reduced plasticity costs due to attenuated fast-P *versus* slow-M trade-off constraints. When subject to the LHS-mode PM trade-off constraints are minimized (222e; Doblhamer & Oeppen 2003), implicating reduced trade-off constraints between plasticity and resilience. High plasticity scope and resilience capacity are thus combined under the LHS-mode PM (2.2.1d).
Circumstances underpinning/conducive to the maintenamce of the LHS-mode PM: Environments subject to cold sesasonality (cold adaptation at high latitudes/altitudes); a locally-derived diet biocybernetically in alignment with such environments and associated peri-arctic metabolic performance mode (2.5.1.1a; Table 2.5.1.1a); and lifestyle factors involving annual seasonal fasting; and endogamy (homozygosity). These circumstances are typically manifest in THL (traditionally healthy-living) populations (2.5.1.2).
Diet effects: A high metabolic turnover-boosting nutrient-dense diet (Table 2.5.1.2e) underpins increased fast LHS expression (LHS-mode Pm > Mp: increased fertility-longevity trade-off); whereas a diet of growth-curbed plant items (nutrient-poor, arid, cool temperature growth) favours LHS-mode PM (reduced fertility-longevity trade-off constraints). CR (caloric restriction effects) or polyphenols (hormetic energy deficiency signals/metabolism under stress: growth-curbed conditions) induce Sirtuin activation, thereby optimizing energy metabolism with the involvement of autophagy (2.5.1.4c) and healthy-ageing benefits from Sirt1 activation by CR or polyphenolic CR mimetics (such as polyphenolics) are physiologically linked to autophagy and thus associated with an improved efficiency in energy utilization, closely resembling the benefits of calorie restriction (2.5.1.4c). Basis of LHS-PM (minimized P-M and fast-slow LHS trade-off constraints), as supported/conserved by growth-curbed/stressed plant foods (high polyphenol-antioxidant contents); underpinning LHS-mode PM. Autophagy PM-capacity counteracting patho-information engram (PIE) load accumulation (2.1.2a/d: thus maintenace of health and vitality).
Two main physiological LHS-PM subtype settings are differentiated: LHS-PM/**MP dispersal type** (*sensu* Geist 1978) with **generalist P-M plasticity** and LHS-**P(M) maintenance type** (*sensu* Geist 1978) with **P-capacity specialist resilience** (predominance of the HMT-mode: Table 2.5.1.2e)

3) Transitional LHS-modes Pm > pM, pM > Pm and pM↑.

Small letters m and p refer to relatively reduced allocation priorities of the Pm (predominance of performance) and pM (predominance of maintenance) trade-off combinations respectively.

Transitional LHS modes come into play when circumstances underpinning population equilibrium carrying capacity change/are disturbed under either one of two scenarios: I) a population under resource stress sets off into dispersal migration towards new, largely unoccupied areas with relatively/marginally higher resource availability levels

(historical population migrations/expansions); involving LHS-modes Pm > pM, pM > Pm; or

II) conditions of sustained resource surpluses arise (notably industrialization), setting in motion a resource use reactive LHS sequence facilitating maximum resource use resulting in increased population concentrations (e.g. urbanization) with associated progressively increasing levels of population density stress. Involving LHS-modes Pm > pM (1) → pM > Pm (2); mP↑ (3); pM↑ (4); as manifesting during demographic transitions (2.2.2e:5).

LHS-mode Pm > pM. Use of transient resource surplus conditions (fertility and longevity trade-off). Strong performance expression (Pm) at the expense of maintenance (pM): reproduction-longevity trade-off. Pm mode expression predominant over maintenance investment. In Pm mode, resource use of relative resource abundance (feast) is maximised to support fast-type LHS processes (strong fertility-longevity trade-off; early reproduction, short birth intervals; male competitive performance); but when not interrupted by transient phases of resource deficits (famine) such performance realization is at the expense of maintenance processes (accentuated Pm-pM trade-off). Low pM expression then progressively compromises health and leads to the accumulation of patho-information-engram loads. This furthermore reinforces Pm-pM trade-off constraints. ***Reproduction > longevity***: Reproduction at the cost of longevity (high fertility/high mortality; but both progressively decreasing with increasing patho-information-engram accumulation).

LHS-mode pM > Pm. This denotes a LHS-mode where energy allocation to maintenance processes progressively overrides investment to performance capacity (reduced performance expression); and may arise whenever the demand for maintenance processes increases (increased patho-information-engram loads) and as functional inefficiencies due to accumulated patho-information loads accentuate the performance/maintenance trade-off, with performance vitality being increasingly compromised/reduced (lowered fertility and mortality; longevity comparatively less negatively affected than fertility). ***Longevity > reproduction***: Maintenance/longevity at the expense of fertility.

Evolved psychological mechanisms monitor the availability of physical resources and social circumstances (social support, sociopsychological stress) which provide cues for the most appropriate LHS (fitness maximising). The optimal response under conditions

of prevaling resource abundance (feast conditions) requires the maximum utilization of such resources for the realization of reproductive success (LHS-mode Pm > pM): high fertility-high mortality/shorter lifespan (fast-type LHS strategy). Endogenous factors, such as health status, affect the metabolic efficiency of resource utilization/processing: the lower the health status (accumulated patho-information-engram load), the greater the Pm-pM trade-off. Under conditions of sustained resource abundance, the build-up of patho-information-engram loads (accentuation of Pm-pM trade-off) results in a progressive shift from the LHS-mode Pm > pM to the LHS-mode pM > Pm (from fast-type to slow-type life history strategy: from early to late fertility realization; ***from early to later life performance***: lower mortality; relatively longer lifespans).

During the associated phase of advanced progression of procursive sequencing (patho-information-engram accumulation) and responding to *inter alia* population density stress (especially stress during childhood), a psychological state of readiness for coping with crises is imbued, resulting in a state of chronic sympathetic nervous system arousal (low fight-flight response threshold: 2.3.2a). The associated overarousal of the sympathetic nervous system increases energetic demands and stress proneness, both compromising female reproductive success (suppressed parasympathetic functionality compromizing female reproduction: Table 2.3.2a: Autonomic nervous system).

4) LHS functionality types

Two functionality types are here identified according to LHS trade-off constraints outlined in ths section. **Pm-types** (extremized LHS-mode Pm > pM expression) realize enhanced performance capacities at the cost of compromised maintenance capacities (which include health-supporting processes). **Mp-types** (extremized LHS-mode Mp > Pm expression) realize enhanced maintenance investment at the cost of compromised performance capacities (including competitive and reproductive vitality). Due to fast (early reproduction)-slow (later life reproduction) LHS trade-off constraints (early reproduction at the cost of later life reproduction), extremized Pm-type or Mp-type expression negates fitness maximization (*vide* Korpelainen 2003).

5) LHS-mode sequence: Pre-transition (PDT), first demographic transitition (FDT) to second demographic transition (SDT)

LHS-modes: PDT: PM; FDT: Pm > pM (1) → pM > Pm (2); FDT → SDT: mP↑ (3); SDT: pM↑ (4). (2.3.3e; Table 2.3.3n).

Table 2.2.2c Fundamental divergence of life history strategy settings at population-eqilibrium carrying capacity and during demographic transitions

[a] TFR [b] (Ig Marital fertility)	
(0.7-0.8) 1700-1800	LHS-mode PM M(P) ↔ P(M)
4-5 (0.7-0.8) 1800-1890	
3-4 (0.5-0.7) 1890-1910	LHS-mode Pm > pM(1)
2-3 (0.2-0.4) 1920-1940	LHS-mode pM > Pm(2)
	LHS-mode Pm↑ (3)
1.7-2.1 (1955)	
	LHS-mode pM↑ (4) Fast-LHS → Slow LHS
1.2-1.9 (1980+)	

LHS-modes (Table 2.3.3b; Table 2.3.3o)	Subhaplogroup LHS PM settings N-M(P), C-PM, S-PM, E-P(M)	Pm > pM (1), pM > Pm (2), Pm↑(3), pM↑(4)
Northern (N), Central (C), Southern (S), Eastern (E) Europe		
Functional context	At population-eqilibrium carrying capacity (PECC)	During phases of population increases in response to persistent in situ resource overabundance and mounting population density stress
Energy resource use strategies (2.2.2f) Resource use efficient (RUE) *versus* resource use reactive (RUR)	Nutrient-recycling, efficient metabolic resource use strategy	Adaptive resource re-allocation resource use strategy (responsive to feast *versus* famine conditions; providing for population increase capacity during feast conditions at the cost of pronounced unbuffered population declines under 'space famine' conditions (persistent overpopulation and associated sociospatial density stress)
Vantage sensitivity or differential susceptibility (2.2.1d) (plasticity-resilience trade-off constraints)	LHS PM-based vantage sensitivity (low plasticity-resilience trade-off)	Differential susceptibility: the same factors that increase vulnerability to adversity will also increase vantage sensitivity in positive environments (plasticity) and that factors that make some resilient to adversity will also make them

		less responsive to positive experiences (plasticity-resilience trade-off: high plasticity/low resilience)
Supporting energy use metabolic modes	Energy use efficient EUE-LHS-PM mode	Energy use reactive EUR-LHS-energy use metabolic mode: high-level use of nutritional resources
P-M trade-off constraints: P(max. performance) *versus* M performance	Absent or relaxed	Increased. P_{max} performance specialism *versus* M performance specialism
Performance specialism *versus* tolerance generalism	P-M tolerance generalism	P_{max} performance specialism M performance specialism
Associated dynamics of patho-information-engram loading (2.1.2a; 2.2.2f) and chronic disease accumulation		
Autophagy as healing process	Functional	Blocked
Accumulation of patho-information-engram loads	Minimal or absent	Ongoing
[a] TFR [b] (Ig Marital fertility): [a]TFR = total fertility rate = number of births in a given year by the average number of women of reproductive age.[b]Marital fertility Ig = fertility relative to an observed maximum, that of a twentieth century religious group, the Hutterites, who married early and prohibited contraception).		

LHS-mode PM (Table 2.2.2b): Minimal trade-off constraints between performance expression and maintenance functionality due to absence of patho-information-engram loading under conditions of intermittant dietary restriction. Doblhammer & Oeppen (2003): In natural fertility populations the fertility *versus* late-life mortality trade-off (negative relationship between fertility and longevity) is mediated by health status. Good health status positively affects both fertility and survival (life span) and can thus result in a dampening or elimination of this trade-off; permitting the concurrence of relatively high fertility and longevity (as applicable to traditionally healthy populations: 2.5.1.2). This is consistent with the absence of an early fecundity-longevity trade-off in French-Canadian populations of the 17th and 18th centuries which had not yet reached the phase of demographic transition (Le Bourg et al. 1993).

Traditional patriarchy involved distinct gender role differentiation, but equal status of men and women. It embraced a patriarchal and a matriarchal component: specialised male functionality (protection, provisioning) and specialised female functionality (reproduction, rearing) respectively; supporting complementary efficiency within the family unit. Maximization of fitness is achieved as both female and male physical, metabolic, endocrinologic and psychological specializations are optimally realised (Section 2.3.2c; Table 2.3.2b). Under the LHS-mode PM both male and female

functional vitality prevails (weak performance-maintenance trade-off: minimal patho-information-engram PIE-loading).

Adaptive mutations are clinically relevant as became apparent from studies which correlated mtDNA (mitochondrial DNA) haplogroups with longevity and degenerative diseases (Wallace (2005). Specific mtDNA lineages were found to promote longevity (De Benedictis et al.1999; Rose et al. 2001; Niemi et al. 2003). Some of the same variants associated with increased lifespan and protection against certain diseases, increased the predilection of developing other degenerative diseases. Following Wallace (2005), cold-adapted mtDNA uncoupling mutations would generate less ATP per calorie consumed and would thus be more prone to clinical problems due to energy insufficiency. However, individuals with uncoupled mitochondria subject to energetic sufficiency would burn calories rapidly to generate both the required ATP plus increased heat; resulting in ETCs (mitochondrial electron transport chains) of uncoupled individuals to be more oxidized, thereby minimizing the production of mitochondrial ROS (favouring health and healthy ageing in such individuals). Such mtDNA haplogroups harbouring adaptive mtDNA uncoupling adaptations can thus have reduced rates of ageing and neurodegenerative diseases (reduced mitochondrial reactive oxygen species, associated low levels of oxidative stress and less proneness to somatic mtDNA mutations). Thus, cold-adapted uncoupled mtDNA variants, when assocated with endogenous energetic efficiency (low levels of patho-information engram loads) are manifested in the LHS-mode PM, characterized by combined Pm (performance vitality) and Mp capacities (health and longevity); based on reduced Pm-Mp trade-off constraints (Doblhammer & Oeppen (2003). There are benefits of the associated plasticity (wide adaptability amplitude) underpinning adaptability to current challenges (wider range of Pm *versus* Mp realization; sustaining stability through change/adaptability). With more pronounced inherent cold-adaptivity (Table 2.3.3b), notably as experienced in more Nordic countries, greater plasticity of LHS-mode expression is realized due to attenuated fast-slow LHS trade-off constraints, *inter alia* supporting a wider childbearing age span.

Both male and female fitness is ensconced in monogamous family units (female fitness benefits through the monopolization of male protection and provisioning and male fitness through the monopolization of the reproductive capacity of the attached female).

The male is safe-guarding his mating contribution and functional role efforts to actually benefit his own genetic progeny through a defended family unit (patriarchal family household); thus with interference competition supported by adequate levels of male competitive performance capacity (Table 2.3.2b; Table 2.3.3m).

Due to minimal P-M and fast-slow LHS trade-off constraints, the combined realization of P and M competencies are achieved.
Performance (P) realization under circumstances requiring resource use maximization (surplus resource/nutrient use), as supported by faster-type LHS expression. Supporting interference competition ability in both males and females in respect of upholding breeding and resource territoriality (inter-male interference competition: family territoriality and inter-female competition through matriarchal household territoriality).
Realization of maintenance (M) capacities under conditions requiring slower-type LHS expression such as coping with pronounced periarctic conditions (cold seasonality at higher latitudes or altitudes: e.g. northern Sweden, Alpine regions; Traditional healthy-living Blue Belt populations); with later life reproductive performance prevailing, whilst male competitive vitality is sustained in the absence of fast-slow LHS-mode trade-off constraints under the LHS-mode PM. Cold climate adaptability assovciated with slower-LHS realization; as also later life female reproduction (wide childbearing age spans).

Unfolding of the procursive LHS-mode sequence during the course of demographic transitions:

LHS-mode Pm>pM (1): (Fast LHS-mode Pm > pM (1) setting)
Life history trait combination congruent with energy investment optimization in response to prevailing circumstances. Performance (P) expression maximizing surplus resource use and competitive prowess under conditions of high interference competition requirements (high population density stress), but costly in terms of health and fertility (accentuated P-M trade-off: plasticity scope costs). Fast LHS Pm > pM setting supporting Pm-type expression and early life fertility as underpinned by high metabolic turnover functionality; requiring a ***fast-LHS setting*** promoted and actuated by births in spring (2.2.2g). A fast LHS setting implies that lactation occurs during

spring when high metabolic turnover food is available, promoting high metabolic performance (2.2.2j), high rates of reproduction (Table 2.5.1.2e) and individual development (*vide* Geist 1978: 2.2.2j). This is combined with pregnancy during autumn/winter, when conditions are favourable for somatic metabolic investment (size, energy storage, longevity), *inter alia* cued by low metabolic turnover food availability (Table 2.5.1.2e), providing fat resources during lactation for newborns converting stored fat and breastmilk into ketones (Cunnane and Crawford 2003), which represent key building blocks for brain structures.

Use of uninterrupted resource affluence (feast) via LHS-mode Pm > pM at the expense of pM capacity (autophagus self-healing patho-information-engram-clearing processes: activated under conditions of resource deficits, i.e. transient famine). First stage of procursive load accumulation; but which had started already earlier in time in high SES individuals (2.2.2j). Central to the elimination and prevention of the accumulation of patho-information-engrams are autophagous maintenance processes (catabolic) which cannot occur under conditions of chronic overfeeding (feast > famine conditions) and procursive stress impacts (2.1.2). Circumstances of uninterrupted food availability and increased population density stress generally co-occur, resulting in ***procursive overload*** (progressively reduced metabolic functional efficiency). As a result, the performance-maintenance trade-off increases in intensity, which is associated with an elevated P/M realization ratio: stress proneness, sympathetic ANS overarousal (yang, male functionality) at the expense of parasympathetic functional efficiency (yin, female functionality: 2.3.2a; Table 2.3.2a).

Intensified P > M trade-off constraints: growth > maintenance, fertility at the cost of longevity (relatively high mortality; reduced life expectancy; current reproduction at the cost of survival/future reproduction). Fast ageing: increasingly costly in respect of health and health-based fertility. High male competitive performance expression (interference competition): both male and female fitness maximization within the defended monogamous family unit (perceived as a childbearing territory). Prevalence of high performance realization (Pm-types: interference competition manifesting in patriarchal family territoriality).

LHS-mode pM>Pm (2): (Fast LHS-mode pM>Pm:2 setting)

With increasing patho-information-engram load accumulation and associated decline in metabolic functonal efficiency (endogenous energy deficits) and associated

increased performance-maintenance trade-off constraints, performance capacity is increasingly compromised and a greater demand for maintenance processes arises (*inter alia* self-healing processes in order to cope with chronic disease loads). In response to these changing energy investment demands the appropriate LHS-mode pM > Pm is associated with declining Pm-type expression and increased investment in maintenance (later life performance/extended life span, fertility postponement, longevity).

Representing a LHS optimization shift to LHS M > P in order to reduce high P-HMT plasticity scope costs: high costs associated with high metabolic turnover functionality. Shift to later age fertility realization (postponement); less health-compromizing lower metabolic turnover functionality; supporting quality rather than quantity of offspring. Continuation of fast LHS setting supporting sustained P capacity realization. However, due to continued Pm-type competence requirements in the face of persisting population density stress, a fast LHS setting is sustained (fast LHS-mode pM > Pm (2) setting). Fast LHS pM > Pm setting as characteristically associated with increased maintenance investment underpinning a shift to later life fertility (postponement) and increased life expectancy incurs trade-off costs manifesting in reduced P-vitality and reduced early fertility.

LHS-mode mP↑(3). Eastern European countries. **I**nherent LHS setting E-P(M): H (early life performance). Inherent resilience of the prevalence of P-HMT functional expression, supporting early fertility realization unconstrained under densely packed conditions (Eastern European marriage pattern: 2.3.3b:7). Resilience reflects the absence of problematic functioning despite exposure to contextual adversity; it is about not having a particular competence compromised when subject to perturbing influences.

With onset of the demographic transition, resource use reactive responses to relative resource abundance, the LHS-mode mP↑(3) represents LHS-mode P-HMT (high metabolic turnover) specialism (in support of peak performance). Resilience in sustaining P-HMT functionality is diminished and P-M trade-off constraints intensify. Vulnerability to exogenous stress/harshness (anomy) increases as LHS-mode settings shift to converge towards those of LHS-mode M↑:4. Accentuation of fast-type LHS-mode P-HMT expression (2.2.2c/d) coping with anomy underpins low well-being

scores (in contrast to north-western European countries subject to LHS-modes M>P and pM↑:4).

Energy allocation demands for responding to exogenous impacts (harshness/unpredictability: Eastern European countries) > endogenous maintenance requirements (as in Western/Northern European countries). Early reproductive realization at the expense of later reproductive success (strong trade-off between current and future reproduction: 2.2.2c/d). Conditions of socioeconomic/psychological harshness cue for persistence and accentuation of the LHS-mode Pm>pM (fast-type LH strategy: early life performance/reproduction; manifesting in LHS-mode mP↑(3) expression in eastern European countries). Inherent resilience in coping with anomie and population density stress effects in eastern European countries based on an inherent predisposition for fast-LHS mode realization (Table 2.3.3b).

LHS-mode pM↑ (4). (Fast to slow LHS-mode M↑:4 setting)

Energetic allocation trade-off constraints due to low endogenous efficiency of energy processing on the basis of high accumulated patho-information-engram loads. Strong trade-off between P performance capacity and demands for maintenance due to accumulated high patho-information-engram loadings (2.1.2a). Maintenance energetic investment overriding investment in performance capacity. Extreme trade-off between pM and Pm at the expense of Pm (performance vitality). Disproportionately compromised male performance vitality. Stress tolerance refers to the capacity to maintain performance under adversity, but is energetically costly. Stress resistance is the capacity to cope with stress, minimizing stress impacts, through down-scaling of performance capacity/expression.

Due to advanced patho-information-engram load accumulation (procursive overload), resulting in low functional vitality (endogenous energetic constraints) a high demand for maintenance processes continues to prevail; inducing even greater accentuation of maintenance processes (M): allocation of energy to survival at the expense of current/early reproduction (trade-off between current and future reproduction: 2.2.2d); but supporting survival (longevity) and later life reproduction (postponement and recuperation of fertility through births at maternal ages above 30 years). Diminished Pm-type expression (reduced male P-vitality); but some sustained P expression capacity through continued fast LHS setting required for coping with prevailing population density stress.

Trade-off settings between maintenance and performance (growth, reproduction) established during childhood furthermore determine trade-off relationships between current and future reproduction. A metabolic trade-off setting supporting current reproduction is in a trade-off relationship with optimal future reproduction since the former (early reproduction peak) is costly in terms of reduced number (reduced reproductive time span), quality or survival of future offspring and reduced growth and survival of the parents. Fitness measure λ (Korpelainen 2003) involves both fertility timing (tempo) and life time reproductive success (quantum: LRS – life time reproductive success). Subject to an accentuated fast-slow LHS trade-off, early fertility realization compromizes individual fitness in terms of the quantum component). Highest fitness is achieved with the lowest intensity of this trade-off, that is, with the longest childbearing age span (2.3.3d). Late life fertility realization compromizes individual fitness in terms of the tempo component; but late fertility realization (postponement and recuperation) is facilitated by a genetic predisposition towards slow life history modes as adapted to cold/cool seasonal climatic conditions (2.3.3b; Table 2.3.3b).

Due to an advanced state of patho-information-engram load accumulation and associated reduced functional energetic vitality (resulting from the effects of prolonged procursive impacts due to transgenerationally uninterrupted food abundance and population density stress), the chronic immune system dysregulation (CISD) syndrome has become pervasive (2.2.2i); which *inter alia* implicates that sympathetic over-dominance at the cost of parasympathetic functional efficiency takes effect (Table 2.3.2a). Particularly chronic stress under conditions of compromised vitality (low response reaction thresholds) results in the fixation in a state of sympathetic over-reactivity; thereby compromising parasympathetic functionality (female reproductive success and efficient food digestion). Low vitality in males and associated low reaction response thresholds result in over-expression of allostasis (sympathetic over-reactivity), which leads to further negative allostatic load health effects (Table 2.1.2b). Female allostasis under sympathetic overdominance (energy-expensive) underpins female competitive assertiveness, but at the cost of allostatic load effects (suppressed parasympathetic functionality: compromised energy balance/body condition for female reproductive vitality; stress proneness: low response reaction thresholds). Declining gender role differentiation and its negative demographic effects result (Table 2.3.2b:

Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution).

Low male competitive performance vitality leads to reduced male role competence and scramble competition as a relatively favourable alternative mode of competition (also for females). Under such circumstances, extra-marital childbearing and cohabitation tend to prevail. A mixed system of procreation within the family unit or cohabitation is usually established; with high performance types (usually of higher socioeconomic status) pursuing procreation within the family unit (patriarchal) and lower performance types realising childbearing within alternative household types (often matriarchal). Prevalence of Mp-types: scramble competition for material resources and sexual partners (2.2.2e).

Inherently, individuals of higher socioeconomic status are generally endowed with greater plasticity, but lower resilience capacity, whereas those of lower SES have greater resilience, but lower plasticity scope of LHS-mode expression (2.2.1d; 2.2.2k). (2.2.1d: Plasticity is here defined as flexibility in adaptability of an organism to environmental changes or challenges; whereas resilience relates to the capacity of endogenous protective factors and processes to prevent an individual from succumbing to or being harmed by some contextual adversity through the ability to restore or maintain any pre-perturbation functional state).

As a result of low functional energetic potency due to progressively accumulated PIE loads, an accentuated P-M trade-off (2.1.2; 2.2.1d) is increasingly prevalent in this phase (the SDT: LHS-mode M:4). In high SES individuals (inherently endowed with high plasticity in respect of both P- and M-type LHS-mode expression, but reduced resilience capacity: 2.2.1d), an accentuated P-M trade-off results in extremized P-type and M-type expression. Extremized P-types are in high performance LHS-mode (HMT: high metabolic turnover), at the expense of health (2.2.1; 2.2.2j). Extremized M-types exhibit low P-vitality and LHS M-LMT mode realization (late fertility realization). High P-HMT capacity realization involves fast life history strategy expression involves (2.2.2d: Fast-slow life history strategy syndromes); manifesting in early life fertility realization (many offspring, quantity rather than quality of progeny, early onset of reproduction).

Testosterone plays an important role in the cognitive performance of especially men (Trumble et al. 2015); and performance capacity in in general; but consistently high

levels of testosterone are difficult to maintain under conditions of low energetic surplus (low performance vitality), as applicable under the LHS-mode pM↑. Testosterone-linked P performance is underpinned by LHS P-HMT realization. In general, an increasing proportion in populations of female extremized P-types (performance assertive; associated with compromised fertility) and male extremized M-types (low P-vitality; less and less capable/willing of engaging in interference competition and maintaining family-based childrearing), are emerging. Diminishing male-female role differentiation in the context of psychosocial incoherence is typically reminiscent of the state of affairs emerging in populations subject to chronic population density stress (Table 1.2a; Knaul 1985).

Summary: LHS-mode pM↑(4)

I) LHS optimization shift from predominantly fast to slow-LHS settings

High PIE loading: low P vitality; strong P-M LHS-mode trade-off constraints. Responding to high maintenance demands resulting in further intensified LHS P-M trade-off constraints, supporting slow LHS-mode traits: long-term view; offspring quality > quantity and enhanced later life performance: longevity, fertility postponement and fertility recuperation at maternal ages > 30 years. Plasticity gains of persistent fast-M LHS setting: sustained relatively high performance capacity realization (plasticity scope allowing for combined Pm-type and pM-type expression). Plasticity costs: reduced capacity of resilience under adversity; such as *inter alia* population density stress affecting fertility negatively). Low SES: Responding to *inter alia* high population density stress in predomintantly fast LHS-resilience mode (Fast LHS-mode: early life performance vitality supporting early life fertility realization. Resilience gains: enhanced coping capacity in the face of economic or social adversity; minimized vulnerability to experienes of adversity; relatively higher reproduction rates subject to conditions of population density stress than in high SES individuals. Resilience costs associated with accentuated fast LHS expression: poorer health status and associated higher mortality rates; restricted later life performance: reduced childbearing age span).

Subject to divergent demands for LHS-mode optimization, differentiation into **LHS-mode phenotypes** became manifest.

HMT-Pm-type performance realization. Higher SES: higher inherent P capacity and higher inherent plasticity scope (2.2.1c; 2.2.2d). Sympathetic ANS performance (Table 2.3.2a); realization of achievement-orientated behaviour (2.2.1c: competitiveness, social dominance, endurance, cognitive competence, assertiveness); representing plasticity benefits, but associated with plasticity costs. Plasticity benefit-costs trade-off constraints: compromised parasympathetic ANS functionality (low energy efficiency for the maintenance of normoadaptive body condition: Table 2.5.1.5c and reduced reproductive success, especially in females: Table 2.3.2b). High P/low health-low fertility trade-off combination.

LMT-Mp-type realization: Somewhat reduced high P/low health-low fertility trade-off constraints in comparison with Pm-type expression (reduced plasticity P benefits and reduced M costs in respect of health and fertility). Mp-type realization (realization of enhanced maintenance investment at the cost of compromised performance capacity: 2.2.2e); but some later life fertility sustained.

II) Accentuated fast-slow LHS-mode trade-off constraints

Accentuated P-M trade-off constraints results in extremized P-type and M-type expression. Extremized P-types are in high performance LHS-mode (high metabolic turnover) at the expense of health (2.2.1; 2.2.2j). Extremized M-types exhibit low P-vitality and specialized M-LHS-mode realization (late fertility realization). Increasing proportions of males and females manifesting as low P-vitality males and assertive/low fertility females, respectively; *inter alia* reflected in diminishing gender role differentiation.

III) Psychosocial incoherence

Increasing prevalence of a state of psychosocial incoherence in populations.

Disintegration of traditional social institutions (family/church), dominance hierarchies (largely based on SEP: socioeconomic position) and traditional value systems (based on duty rather than rights). Refer to Surkyn & Lesthaeghe (2004: 2.3.3a) and Table 2.3.3m for characteristic sociobiological features of LHS-mode pM↑:4 (2.2.2e).

IV) Chronic immune system dysregulation

On the basis of low endogenous energetic efficiency due to advanced patho-information-engram accumulation, immune system functionality has become

dysregulated; manifesting in the ***chronic immune system dysregulation*** (**CISD**) syndrome (2.2.2i). This manifests as chronic systemic low-grade inflammation *vide* Ruiz-Núñez et al. (2013); and sympathetic ANS (autonomous nervous system) over-dominance (2.2.1a; Table 2.3.2a). The dysregulated immune system is characterised by functional weakness with low reaction fight-flight thresholds, that is, over-reactive fight responses to weak challenges (allergenic) and flight/escapist responses to strong challenges (non-resolution of acute/subacute disease insults resulting in accumulated chronicity). The associated levels of aggression and escapism furthermore underpin psycho-social incoherence.

f) LHS-settings and metabolic energy resource use modes

It is generally assumed that dietary restriction (DR) extends lifespan (Nakagawa et al. 2012) and reduces fecundity (Moatt et al. 2016); thereby representing a trade-off between longevity and the rate of reproduction/fecundity (refer also to Table 2.5.1.2e). Such trade-off relationships are regularly established, but they are not universal, as highlighted by Jasienska (2009). Dietary restriction (DR) reduces the capacity to respond to environmental challenges (lower BMRs, reduced cold tolerance, reduced immunity, slowed wound healing), reducing survival prospects.

According to the adaptive resource re-allocation hypothesis selection favours the re-allocation of nutrients from reproduction to somatic maintenance and repair under conditions of nutritional deficits, thereby increasing the chances of survival during a famine; thus favouring future relative to current reproduction (Adler & Bonduriansky 2014). This interpretation is consistent with the notion of reproductive suppression being adaptive under conditions of energy deficits (Jasienska 2003). As nutrients become plentiful again, the organism reverses the above mode of resource allocation and resumes reproduction. In fully fed animals nutrient-responsive pathways are activated and cellular recycling and repair mechanisms are inhibited, including autophagy and apoptosis. LHS-mode P > M expression provides for the maximized use of resource surpluses (2.2.2e); but autophagic healing processes are blocked.

Autophagy and apoptosis are two main cellular recycling and repair mechanisms that respond plastically to nutrient availability. Autophagy is intracellular process whereby portions of the cell are sequestered, broken down and recycled, promoting protection

and survival of the cell (for more detail refer to Ravikumar et al. 2010). Apoptosis (programmed cell death) is a systemic process required for normal organismal functioning that also removes cells that are damaged by disease. According to the **adaptive resource re-allocation hypothesis** dietary restriction reduces rates of intrinsic aging due to activated autophagy effects, but at the cost of reproductive output (Adler & Bonduriansky 2014).

Evolutionary theory predicts that selection will strongly favour reproduction early in life, even at the cost of healthy aging and reduced longevity. Adler & Bonduriansky (2014) presented an alternative framework where dietary restriction effects, inducing autophagy and increasing apoptosis (DR autophagy), are interpreted as part of a suite of facultative physiological responses that enables organisms to ***maximize immediate reproductive output even under conditions of reduced resource availability, as well as in times of resource surplus*** (reduced trade-off constraints between P, reproduction and M, maintenance via autophagy; as underpinned by LHS-mode PM). Autophagy is predominantly cytoprotective and beneficial to human health, and reduced autophagy has been associated with accelerated aging (Rubinsztein et al. 2011). However, in the context of an alternative framework (Adler & Buriansky 2014), to the adaptive resource re-allocation hypothesis, emphasis is placed on autophagy as a mechanism by which cytoplasmic molecules can be mobilized to generate energy-rich compounds meeting bioenergetic demands of cells under conditions of declining external and internal resources (autophagy as a dynamic recycling system: Mizushima & Komatsu 2011). Adler & Buriansky (2014) suggest that selection would favour up-regulation of cellular recycling mechanisms under dietary restriction allowing animals to **make more efficient use of limited resources**, possibly allowing for some immediate reproduction. Autophagy frees up stored nutrients in cells, a function that has been suggested to allow the organism to operate at lower resource intake levels and apoptosis recycles whole cells and reduces cell number, allowing the organism to function more efficiently.

A baseline level of nutrients must be available before reproduction is possible. According to the interpretation of Adler & Bonduriansky (2014: **nutrient-recycling, efficient resource use mode hypothesis**), responses to dietary restriction **lower this baseline, making reproduction more attainable under conditions of relative nutritional constraints**. Under this resource use mode, the organism makes more efficient use of incomimg resources, but with a slower conversion rate that is more than

sufficient to accommodate the lower resource intake rate under dietary restriction (energy use efficiency). Processes such as autophagy and apoptosis could accordingly be considered mechanisms of **differential resource allocation**, as under dietary restriction, stored resources are recycled and put to use for survival or reproduction. This form of differential allocations (nutrient-recycling, efficient resource use mode: Adler & Bonduriansky (2014) differs fundamentally from that envisaged under the **adaptive resource re-allocation hypothesis** because it does **not involve sacrificing reproduction for the sake of somatic maintenance** (relaxed P versus M trade-off constraints).

Responses to nutrient availability entail trade-offs. Expressions of autophagy and apoptosis (as under nutrient restrictions) are inversely correlated with nutrient availability, with resulting inhibitory effects on cell growth rate, reproductive rate and environmental stress tolerance (wound healing, cold tolerance, immune function). Under the **adaptive resource re-allocation hypothesis** such trade-off constraints are postulated to be pronounced. Since the stress tolerance capacity (plasticity) of the periartic metabolic performance mode is relatively resource-costly (relatively high BMRs), reproduction is only possible above a relatively high level of resource availability (relatively high reproduction-resource level threshold; high RRT; Table 2.5.1.1a: Reproduction and various levels of resource availability). Reproduction is thus resource level sensitive (relatively high nutritional and space requirements for successful reproduction). The adaptive resource re-allocation explanatory framework is accordingly taken to apply in conjunction with the periarctic metabolic performance mode. Adler & Buriansky (2014) presented an alternative, evolutionary more plausible hypothesis, i. e. that of a highly conserved physiological response to DR (dietary resriction) where the up-regulation of autophagy and apoptosis represents a **nutrient-recycling, efficient resource use mode** that enables organisms to maximize immediate reproductive output under conditions of resource scarcity (amounting to a relaxation of the production *versus* survival trade-off under resource constraints).

The **nutrient-recycling, efficient resource use mode** involves lower reproduction-resource level thresholds (RRT low), implying that reproduction is relatively resource level insensitive (successful reproduction can be sustained with relatively **low nutritional and space resource requirements**). The **adaptive resource re-allocation resource use mode**, on the other hand, involves high reproduction-resource level

thresholds (RRT high), which implicates relatively high resource level sensitivity of reproduction and successful reproduction can be sustained only with relatively **high nutritional and space resource requirements**).

The **differential allocation nutrient-recycling efficient resource use mode** (DR autophagy: adaptive when efficiency of energy resource use at population equilibrium in maintenance mode LHS setting PM outweighs maximization of resource use for population increases in dispersal mode: LHS-mode P > M), differs fundamentally from the **adaptive resource re-allocation resource use mode** (DR starvation: adaptive when responding to alternating feast-famine conditions) because it does **not involve sacrificing reproduction for the sake of somatic maintenance** (Adler & Buriansky 2014). LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated. Reduced P-M trade-off constraints are accordingly associated with the **nutrient-recycling, efficient resource use mode**. This provides for some concurrence/combination of fast LHS P-mode (reproduction) and slow LHS M-mode expression (maintenance of healthy ageing) realization; as underpinned by LHS-mode PM. Plasticity gains at low plasticity costs. This interpretation is supported by DR (autophagy) effects being characterized by combined high metabolism and longevity (e.g. Speakman et al. 2004; Kirkwood & Shanley 2005); i.e. the absence of fertility-longevity trade-off constraints.

Depending on circumstances, relating to environmental resource availabilities favouring either LHS-mode PM (Table 2.2.2b) as opposed to LHS-modes P > M(1), M > P(2) and M(4) with increased plasticity trade-off constraints; either the **differential nutrient-recycling efficient resource use** mode or the **adaptive resource re-allocation feast-responsive resource use** mode may apply within the realm of the peri-arctic metabolic performance mode (2.5.1.1b).

Depending on degree and duration of DR (dietary restriction), it may represent either a state of ***starvation*** (**DR-starvation**) or induce a state of increased metabolic efficiency of energy utilization in association with ***autophagy*** (**DR-autophagy**).
Plasticity of LHS-mode expression provides for LHS-mode P > M realization under feast conditions (with plasticity costs due to P > M trade-off constraints: high reproductive output at the cost of health/longevity: 2.2.2e) and M > P LHS-mode

realization under conditions of increasing population density stress (plasticity costs due to M > P trade-off constraints: survival at the cost of reproductive output and P-vitality, especially in males).

The **nutrient-recycling, efficient resource use mode** enables organisms to maximize immediate reproductive output under conditions of resource scarcity: amounting to a relaxation of the production *versus* survival trade-off under resource constraints (Adler & Buriansky 2014). Following the interpretation of DR effects involving a nutrient-recycling, efficient resource use mechanism (Adler & Buriansky 2014), LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated. This provides for some concurrence/combination of fast LHS (reproduction) and slow LHS (maintenance of healthy ageing) realization.

Based on the insights presented above, two types energy-processing metabolic modes are differentiated: I) a balanced energy use efficient EUE-LHS-PM supporting metabolic resource use mode (minimized P-M trade-off constraints underpinning a high performance and health/longevity combination) and II) an energy use reactive EUR-LHS-P > M metabolic resource use mode (fast LHS extremized, high metabolic turnover HMT-mode); traded off against LHS-mode M expression. Autophagy as component of the metabolic resource use mode is either present (EUE-PM metabolic mode) or absent (EUR-P-M traded off metabolic modes; induced under 'feast' conditions). The latter, the EUR-LHS metabolic energy use modes, as induced by LHS responses to resource surplus conditions, is associated with the accumulation of (epigenetic) patho-information-engram loads, reinforcing P-M trade-off constraints during demographic transition.

I) Energy use efficient EUE-LHS PM metabolic energy use mode.
High P capacity based on energy efficient metabolism (autophagy) of food resources. Reduced P-M trade-off constraints (low plasticity costs). LHS PM (Table 2.2.2b). Reduced P/fast LHS (early-life performance) *versus* M/slow LHS (later life performance, health, longevity) trade-off constraints (reduced plasticity costs). High P performance, health and longevity combination. Energy use efficiency mediated by activated autophagy.

II) Feast-responsive energy use reactive EUR-LHS P > M metabolic energy use mode (from LHS P > M progressively shifting to LHS M > P and LHS M). Maximum P realization (peak P performance) on the basis of maximum resource surplus processing (energy use inefficient: P maximization based on surplus resource use at cost of energy use efficiency). High plasticity costs. High P-HMT*/fast LHS versus M-LMT* LHS trade-off constraints (P at the cost of health/longevity). LHS P > M: fast early life performance realization; shifting to LHS M: later life performance realization. Plasticity of maximum energy dispositioning (autophagy deactivated). *(referring to high and low metabolic turover rates respectively: Table 2.5.1.2e)

As induced by CR stimuli (autophagy), the **energy use efficient EUE-PM metabolic energy use mode**, is characterized by an amelioration of LHS P-fast *versus* M-slow trade-off constraints; allowing for relatively high P (performance vitality) realization with relatively low M (maintenance) trade-off costs; accommodating a P-health and M-longevity combination; as manifesting in traditionally healthy living (THL: 2.5.1.2) populations (Table 2.2.2b; performance vitality in respect of both reproduction-competitive performance and health-longevity sustention).

Following the interpretation of CR effects involving a nutrient-recycling, efficient resource use mechanism (Adler & Buriansky 2014), LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated; promoting fast-slow balanced LHS realization. This provides for some concurrence/combination of fast-P LHS (reproduction) and slow-M LHS (maintenance of healthy ageing) realization. This interpretation is supported by results of Speakman et al. (2004) regarding the 'mitochondrial uncoupling to survive' hypothesis according to which a positive association between high metabolism and longevity is implicated in CR animals. This is also consistent with the finding that, on refeeding, female rodents previously kept on restricted diets were able to reproduce at much later ages than fully fed controls (Holehan & Merry, op. cit. Kirkwood & Shanley 2005).

g) Seasonality of births

Gavrilov & Gavrilova (2011: Siblings born in September-November (autumn: cool season births) had higher chances to become centenarians than those born in March (spring: warm season births). Infants born during the autumn and winter seasons had increased birth weights and gestation ages. According to Gavrilov & Gavrilova (2011) this supports the notion that early-life programming is involved in shaping human aging and longevity. Association of month-of-birth with exceptional longevity appears to have been stronger for earlier birth cohorts born before 1899; this being explained by progressively improving nutrition and sanitation over time. (**AS: Association of cool season births and slow LHS settings**).

Gavrilov & Gavrilova (2011). For persons born during 1880-1890, as recorded by the 1900 US census, an excess of centenarians were born in fall months (September-November). The seasonal pattern of siblings of the centenarians is somewhat intermediate but closer to that of the general population with more births in spring (March-May) and a secondary lower birth peak during the fall months of August to October. Generally, birth during the spring months was associated with decreased chances of survival to age 100 (**AS: Association of warmer season births and faster LHS settings**), whereas birth in fall increased such chances. For persons of the group born before 1899 the chances of survival to 100 were significantly higher for those born in November (**AS: Association of cool season births and slow LHS settings**); compared to those born in March. For later born cohorts the month of birth effect was much weaker (not statistically significant after adjustments for multiple comparisons). Centenarians, their siblings and individuals in the general population show decreased proportions of persons born during the summer months.

In Germany the SoB pattern has almost reversed during the past 50 years. Around 1950 the peak was in February/March (spring), but has since then shifted to September in 1981-1990 (Lerchl et al. 1993). (**AS: Change over to slow-LHS expression during the SDT cueing for autumn births**). A pattern now resembling that as found in the United States of America. The American pattern is characterised by a fall in birth rate in the first six months of the year and a rise during the last six months, peaking in September. In Canada the SoB pattern used to be like the European pattern, but has shifted towards the American pattern (James 1990, op. cit. Winje 2007). Lesthaeghe & Neidert (2009)

(Section 2.5.1.6 Seasonal timimg of births)

Knodel & Wilson (1981) A shift in peak season of second and third term births in Germany from autumn/winter during 1750-1825 to spring births during 1875-1900. Birth peaks changed from autumn-winter during 1770-1825 to spring during 1875-1900 (Knodel & Wilson 1981).
(**AS:** ***LHS-mode PM (1750-1825) → LHS-mode Pm > pM(1) (1875-1900) → LHS-mode pM > Pm(2) → LHS-mode pM↑ (1981-): from slower to faster to slower LHS expression. According to the LHS explanatory framework, seasonality of birth peaks during autumn/winter is cued by slow LHS expression, thus relatively high maintenance investment, and longevity; whereas seasonality of birth peaks during spring supports faster LHS expression, thus relatively high investment in early life performance (high early reproduction and high fertility), but low maintenance investment and longevity***.)

Life history strategy sequence (Table 2.3.3n) and season of birth (1750-1990+): LHS-mode PM: 1750-1825 (slow LHS: autumn/winter) → LHS-mode Pm > pM(1): 1870-1930 (fast LHS: spring) → LHS-mode pM > Pm(2): 1931-1960 (fast LHS towards slow) → LHS-mode pM↑(4): ≥ 1960 (slow LHS: autumn/winter) → LHS-mode M-P: c. 1990+ (slow ↔ fast LHS-mode atumn/winter).

Overall, the results of the study by Gavrilov & Gavrilova (2011) point toward early life environmental conditions having long-lasting effects on aging and longevity in humans (Gavrilov & Gavrilova 2011). These findings are consistent with those reported in a review of seasonality of birth weights globally; with infants born during the fall and winter seasons in European countries to having higher birth weights (Chodick et al. 2009). They are also consistent with those reported by Doblhammer & Vaupel (2001). Adult life expectancy at 50y+ was increased for those born in autumn (Northern hemisphere autumn: October-December; Australia: Southerm hemisphere autumn: April-June). In the NH people, those born in autumn (implying postnatal infant development during autumn/winter) tended to live longer than those born in spring (involving postnatal infant development during spring/summer). The lifespan patterns for British immigrants to Australia is similar to that of other European people (like Austrians and Danes). Congruently, for Australian-borns (Southern hemisphere) the

mean age at death was found to be higher for those born in the Southern hemisphere autumn (second quarter of the year: April-June). Remaining life expectancy beyond age 50 years was taken to be mediated by factors arising *in utero* and during infancy. Doblhammer & Vaupel (2001) pointed out that, according to numerous studies (op. cit. Doblhammer & Vaupel (2001), it can be concluded that spring-born individuals (entering the warm period of the year: LHS-mode Pm > pM) experience increased risks of developing chronic disorders of some kind (e. g. neurodegenerative disorders, insulin-dependant diabetes, lower lifespan of cancer patients). (**AS: *Spring births underpinned by fast-LHS-mode Pm > pM, supporting performance at the expense of maintenance in the associated investment trade-off, resulting in vulnerability to health disorders; especially when the relevant trade-off is accentuated due underlying patho-information-engram loading***).

Increased incidence of chronic disease/disorders in spring-born individuals explained by the association with the fast-LHS-mode Pm > pM(1): accentuated low maintenance/high performance trade-off and spring births (refer also to Castrogiovanni et al. 1998; Winje 2007; Vaiserman et al. 2007; Vaiserman et al. 2009).

Ellison et al. (2005).

Vaiserman &Voitenko (2003): Subjects in the Ukraine born during April-July had the lowest longevity; with increasing longevity with each successive birth-month in the second half of the year, with peak longevity for births in December. Individuals born in April-July experienced fetal life during nutritionally marginal conditions (late autumn to early spring) and passed the first post-natal months under nutritionally favourable conditions and increasing environmental temperatures (**AS: late spring to early summer births: high metabolic turnover food, high protein diet; infancy during times of increasing environmental temperatures**). Such individuals were found to have the shortest longevity (**AS: Association of warmer season births and faster LHS settings**). Greatest longevity was associated with birth in autumn/winter (October-March), with early infancy in a season of relative shortage and low environmental temperatures (**AS: autumn-winter births: low metabolic turnover diet and infancy during times of decreasing environmental temperatures**).

Spring-born dwarf hamster males had higher resting metabolic rates, higher body mass in the middle of the experiment (suggesting fast early growth), larger genitals, higher basal testosterone levels and and a stronger T-cell immune response, but showed a lower adrenocortical response to a social stressor and ACTH stimulation than fall-born males (Rogovin et al. 2014). More rapid development of spring hamsters and higher,

earlier reproductive activity. Photoperiod duration was considered to act as signal factor involved in neuroendocrine regulation of growth, maturation and reproduction. Rogovin et al. (2014) refer to a considerable body of evidence suggesting that the redistribution/allocation of resources among the energy-consuming systems of life maintenance, immune defense and reproduction in the course of their life history is season-dependent. Such allocation patterns are related to day-light duration and mediated by sex hormones (androgens, prolactin), stress hormones (glucocorticoids), melatonin and leptin (op. cit. Rogovin et al. 2014). The outcome of relevant resource allocations is that animals of fall generations grow more slowly, retain signs of physiological youth for longer and reach reproductive maturity later than those born in spring. Increased longevity is associated with a prolonged juvenile period (op. cit. Rogovin et al. 2014). Spring generations served rapid population growth, whereas fall cohorts have a greater capacity for survival in winter. The physiological differences between hamsters born in different seasons were highly conserved (Rogovin et al. 2014). In northern, highly seasonal regions, programming by spring vegetation (sprouting vegetation, high protein levels, high tryptophan levels) to signal genes to switch on behaviours conducive to great individual development, is evidenced (Geist 1978). Protein-deprived baby monkeys were socially less active, were fearful of strange objects (neophobic), had a low level of of manipulative behaviour, performed poorly in specific learning tasks, had greatly reduced sexual behaviour and manifested a greater proportion of their social behaviour as overt aggression (Zimmerman et al. 1973, op. cit. Geist 1978).

Spring-borns are clearly physiologically geared for high-rate metabolic performance (higher resting metabolic rates, fast early growth, higher basal testosterone levels): rapid development higher, earlier reproductive activity (fast LHS-mode expression: high investment in metabolic performance capacity underpinning high rates of early reproduction); whereas fall generations were characterisized by slower growth, prolonged juvenile periods, later reproductive maturity and increased lifespans; thus geared for moderate-rate, extended metabolic performance (slower LHS-mode expression; higher investment in somatic maintenance). This pattern is consistent with the Performance (P) versus S (Survival) trade-off in the context of a productivity-rate versus survival-capacity (lifespan, health maintenance, stress tolerance) trade-off (Table 2.5.1.2e: higher nutrient/carbon diets and progressively increasing ambient temperatures in spring; relatively high carbon/nutrient diets and progressively

declining ambient temperatues in autumn). Spring-borns are accordingly metabolically cued towards high performance rates, especially also for high rates of reproduction (**LHS-mode Pm > pM; Pm-types**), whereas autumn-borns have greater survival capacities, reflected in better health (through somatic maintenance) and longer life span (**LHS-mode pM > Pm: Mp-types**). This trade-off is reduced in traditionally healthy populations with low epigenetic patho-information-engram loads and thus with high functional-energetic capacities capable of maintaining a costly wide-amplitudinal metabolism (Table 2.5.1.1a). The combination of reproductive performance and health/longevity is then achieved (2.5.1.2). (**LHS-mode PM: providing for the combination of high performance/reproduction and high maintenance/health/ longevity**).

In humans subject to environmental seasonality, the role of female energy dynamics underpins autumn conceptions and spring birth peaks (Ellison et al. 2005). Reproductive success/ovarian functionality is sensitive to female energetic conditions (Table 2.3.2b; Ellison 2008). With the presence of an endogenous signal such as day length (a reliable predictor of seasonally changing environmental conditions) selection coordinated reproduction in alignment with environmental conditions of nutrient/energy availability most advantageous for the various reproductive phases (Ellison et al. 2005). Substantial metabolic requirements are associated with pregnancy and lactation; especially the demands due to the relatively large and rapidly growing human brain (Cunnane & Crawford 2003). Maternal metabolism is geared towards fat storage early in gestation (high energy storage demands, supported by low metabolic turnover and aligned diets available during autumn); representing energy reserves to be mobilized during lactation (high metabolic energy flux demands, supported by high metabolic turnover and aligned food items availably during spring). Understanding diet/life history interactions is of importance in this context (refer to 2.5.1.2cd; Table 2.5.1.2d). Under conditions of either high or low energy flux, energy allocation to reproduction is constrained due to high energy expenditure on non-reproductive functions or low energy intake. Since both low and high energy flux reduces the potential for allocation of additional energy to reproduction it is a positive energy balance and moderate energy flux which indicate conditions that favour energy allocation to reproduction. Energy allocation to reproduction is of special importance during early pregnancy when fat is stored in order to cater for the high energy demands during late pregnancy and lactation (Ellison et al. 2005). Pe-pregnancy weight and early

getational weight gain are both predictors of birth weight and hence also infant survivorship (refs).

Under conditions characterized by minimal fast-slow LHS trade-off constraints: **In terms of energetics, pregnancy during winter (low energy flux, energy storage) and births during spring (lactation: high energy flux, energy expenditure), thus represents the optimal baseline metabolic rhythm in female reproduction in this context**.

Fast-slow LHS trade-off constraints: season of birth, cold adaptation and diet.

-Under circumstances of accentuated fast-slow LHS trade-off constraints (high PIE loadings) spring births cue for LHS-mode Pm > pM(1) realization (fast LHS-mode expression: early life performance/reproduction; heightened fertility-longevity trade-off; increased performance-health trade-off).

Diet effects (Table 2.5.1.2e): a high metabolic turnover-boosting nutrient-dense diet underpins increased fast LHS expression (LHS-mode Pm > Mp: increased fertility-longevity trade-off); whereas a diet of growth-curbed plant items (nutrient-poor, arid, cool temperature growth) favours slower LHS-mode PM (reduced fertility-longevity trade-off constraints).

Flouris et al. (2009): In a study carried out in Greece, Flouris et al. (2009) found increased birth weight, gestational age and longevity in individuals born during autumn and winter (**AS: Associated with the slower-LHS-mode setting , i.e. relatively high maintenance investment**). Increased temperature at birth was associated with adverse effects relating to fetal development and longevity (**AS: Spring births associated with the fast-LHS-mode Pm > pM; relatively high performance investment at the trade-off expense of maintenance investment**).

Bobak & Gjonka (2001): In the Czech Republic (1989-1991) most births occurred in the months March to May (spring), with minimum rates in October to December (autumn/winter). This seasonality was most pronounced in mothers aged 25-34 years, for children born as second or third and for married women; but almost absent among unmarried women. Seasonal variation was most pronounced for mothers with university education (**AS: Pm-types: 2.2.2e**) and minimal among mothers with primary education.

Season of birth had been detected to affect reproduction later in life of pre-modern women (Smits et al. 1999; Lummaa & Tremblay 2003). In the rural Saguenay region, Canada, for women born between 1850-1889, summer-born daughters had the lowest and winter-born daughters had the highest fertility (Smits et al. 1999). For the same study population, women born in winter (November-March), early summer (June) or early autumn (September) had the largest number of grandchildren in the following generations (Lummaa & Tremblay 2003). Offspring born in these months married earlier, gave birth to their last child later, had longer reproductive lifespans and had more children raised to reproduce. Transgenerational fitness was influenced by reproductive rates of daughters depending on the months their mothers were born (Lummaa & Tremblay 2003). In this rural region the onset of the fertility transition was relatively late in comparison with most other regions of Western Europe (Dribe et al. 2017). **AS: The described features of reproduction of the Saguenay population correspond with those expected to be prevalent with LHS-mode PM predominance during pre-fertility transition eras (encompassing combined performance and maintenance capacities on the basis of patho-information-engram loadings being low or absent: 2.2.2e)**.

Men born in autumn (October to December) tended to have fewer offspring and a higher probability of remaining childless than those born during spring (March to June: Huber et al. 2004a).

Haandrikman & Van Wissen (2008): The variation in in patterns of human birth seasonality between geographic regions is relatively large. One of the most important in this respect is the identification of the American and European seasonal birth pattern. A 'trough' in April (spring), followed by an increase in the number of birth until the autumn, is a feature of the American pattern. The European pattern of births is characterized by a peak early in the year – usually the spring – and a decreasing number of births in the rest of the year, with the exception of September (Seiver 1985, op. cit. Haandrikman & Van Wissen 2008 op. cit. Haandrikman & Van Wissen 2008; Doblhammer-Reiter et al. 1999, op. cit. Haandrikman & Van Wissen 2008).

The Dutch pattern of births at the beginning of the 20th century shows some resemblance with the European pattern: a peak of births in the beginning of the year, a decreasing number of births in the remaining months, and a peak in September. Around the 1950s, seasonal fluctuations had declined; the peak in the beginning of the year is less pronounced and relatively low number of births in the last months of the year. The Dutch pattern of births in the period 1941 to 1984 followed the European pattern quite closely; with a global peak in spring, a local peak in September, and an October to December trough (see also Lam & Miron 1994, op. cit. Haandrikman & Van Wissen 2008; Lam & Miron 1996, op. cit. Haandrikman & Van Wissen 2008). At present, the pattern has changed: most children are born in August and September. In northern

Europe most children are born in the spring (March and April); in Sweden and Finland the pattern is pronounced, with high spring peaks. In southern Europe the birth peak occurs in summer or late summer, and the seasonal pattern is less pronounced compared with the Dutch case.
The seasonality pattern in the period 1953-1963 is characterized by a concentration of births in spring, followed by a trough, a local peak in September and a relatively low number of births in the period October-January. In the next 10 years (1965-1974), when fertility dropped to the current low level, the seasonal pattern of birth changed considerably. The share of spring births increased at the costs of births in the winter months and the September peak. In respect of the period 1975-2005 (SDT-phase), the peak in births has shifted from spring to summer months, with an obvious peak in September (late summer/autumn). Thus, a significant shift in season of birth had occurred from predominantly spring towards predominantly late summer/autumn (**AS: Consistent with a similar shift recorded by Lerchl et al. 1993 for Germany during 1976-1990; as well as in Norway, Denmark and Sweden: Norum et al. 2014**).
Birth seasonality is parity-specific. The shift in seasonality of births can be attributed to changes in seasonality of parity-specific fertility. The pattern of first births resembles that of all births in the early period (1953-1964). The monthly pattern of births of parity 2 and higher shows less seasonality in this period. Births of higher orders are more frequent in the winter months, while in summer comparatively fewer births of higher orders occur. For the period 1965-1974, less seasonality of births is encountered, with especially fewer births in spring and early summer. However, compared with first births, the pattern of higher order births has changed considerably. The peak of births is in spring, while the December depression has deepened. The deviant pattern for 1965-1974 is thus attributable to the changing seasonality of births of higher orders. In 1975-2005, spring months have changed from favourable to being unfavourable months for first births, with August and September births compensating for the change. Compared with the seasonal pattern of higher order births in previous periods, the 1975-2005 pattern does not show much change although seasonality has increased. Seasonality for second and higher order births is still very strong, with spring months being favourable for childbirth, and winter months being unfavourable.
Seasonality and maternal age (1990-1998). The seasonal patterns differ to a great extent for mothers younger than 30 years and older than 30 years (average age at birth was 30 in 1990-1998). The seasonal pattern of the younger mothers shows a very low number of births in the beginning of the year and a linear increase in the rest of the year with a September peak; while the pattern for older mothers is a decreasing trend across the year, with most births occurring in the first months of the year and a deep winter trough. (**AS: The older mothers of this sample functioned under the fast-LHS M↑4 setting which promotes spring birth peaks; whereas the younger mothers, subject to a slow-LHS M↑4 setting, underpinned autumn birth peaks: Table 2.3.3o**).

It is here contended that the shifting pattern of birth seasonality as identified by Haandrikman & Van Wissen (2008) for the periods 1953-1964, 1965-1974 and 1975-2005, can be explained in accordance with expectations following from LHS settings prevailing during these periods. During the 1953-1964 period the concentration of birth during spring is consistent with the predominance of the fast-LHS M > P (2) setting, whilst the September sub-peak is attributed to the existence of some slower-LHS M >

P (2) phenotypes. During the 1965-1974 period, when fertility had declined to the current low levels, the share of the spring births had increased at the costs of births in the winter months and the September peak. The proportion of mothers in the predominant fast-LHS-mode M > P (2) had increased relative to slower-LHS phenotypes; therewith explaining the enhanced spring birth peak and the relatively depressed September peak. During the period 1975-2005 (Second Demographic Transition-phase), the peak in births has shifted from spring to late summer/autumn. This is consistent with and according to expectation of birth seasonality arising from slow-LHS M↑4 realization (Table 2.3.3o).

Dahlberg & Andersson (2018): Swedish birth rates (1940-1999) showed the typical seasonal variation with high numbers of births during the spring and low numbers of births during the last quarter of the year. The extent of seasonal variation declined during the 21st century so that only minor variation in birth rates between February and September now remains. The pattern of low birth rates at the end of the year remains and has even become more pronounced from the 1980s onwards. The September secondary birth peak disappeared over the last 30 years. From 1980 onwards, the decline in birth rates during the last quarter of the year bescame particularly pronounced among highly educated mothers. Over the 72 years studied, the seasonal variation of first-time mothers declined steadily and has almost disappearedat the end of the study period.

The findings of Dahlberg & Andersson (2018) reveal two basic patterns of birth seasonality over the study periods (1940-1959, 1960-1979, 1980-1999, 2000-2012).
I) Pronounced spring peak and November-December trough, with the pattern relatively sustained over the study periods; II) Relatively weak spring peak, progressively flattening out towards a weak autumn peak during the period 2000-2012. Pattern I reflects that of the higher educated, of mothers of ages 25-29/30-34 years, of parity 2 offspring; and in respect of offspring with same partners compared to offspring with new partners. Pattern 2 reflects that of the lower educated, mothers of ages ≥ 35 years and for third and higher order births. For the population as a whole, seasonal birth variation is consistent with pattern I for the periods 1960-1979/1980-1999 and pattern 2 during 2000-2012.
Pattern I is typically in alignment with P performance requirements as underpinned by a fast-LHS-mode-P > M; whereas pattern II is typically in alignment with M performance requirements, as underpinned by LHS-modes slow-LHS-M4 or slow LHS-M(P). Over time, increasing M performance requirements are reflected in shifts towards LHS M-specialist realization (later life M performance) at the cost of P

performance LHS P-specialist realization (early life P performance); reflecting pronounced P-M trade-off constraints. From fast-LHS M-specialism (spring birth peak) to slow-LHS M(P)-generalism (autumn birth peak).

Pattern I relatively sustained over study period including period 1980-1999 (for western-central European countries where the change over to autumn birth peaks had already occurred from 1980 onwards). Provide link to N country inherent LHS features.

Balan & Jaba (2016): During the period 1996-2012, birth rates of CEE (central-eastern Europe) countries showed one of two patterns. I) From initially high levels before 1996-2000, declining and the rising to higher levels between 2004/2007/2005/2007/2008 and 2009/2010/2011; then declining again (Romania, Hungary, Poland, Slovakia, Lithuania, Croatia); and II) Rising from initially relatively low birth rates (1996) to higher levels between 2007/2008 and 2009/2010/2012, then declining again (Slovenia, Czech Republic, Bulgaria, Latvia, Estonia).

In all these countries (1996-2012), seasonal birth peaks were recorded for the months June-September (late summer/autumn). In the case of the Czech Republic, these findings are in contrast with those of Bobak & Gjonka (2001), which showed that most births (1989-1991) occurred in spring March-May (spring). (**AS: This discrepancy can be explained by pointing out that the fast-LHS-mode M4, underpinning spring birth peaks, seemingly prevailed during the earlier period and that the slow-LHS-mode M4, underpinning autumn birth peaks, prevailed during 1996-2012: refer to Table 2.3.3o**).

European versus American season of birth patterns:

An important geographic variation relates to the divergence of the American and European seasonal birth pattern (e.g. as *inter alia* reported by Haandrikman & Van Wissen (2008): A 'trough' in April (spring), followed by an increase in the number of birth until the autumn, is a feature of the American pattern. The European pattern of births is characterized by a peak early in the year – usually in spring – and a decreasing number of births in the rest of the year, with the exception of September.

Any organism interacts with its environmental biogenic information (*inter alia* contained in food of the local environment, reflecting *subtle organizing energy fields*: Table 2.5.1.2d). An alignment of the genetic-epigenetic and biogenic information systems is established; underpinning maximal performance through specialized adaptation to local conditions. Natural selection seems to favour increased efficiency during even limited times of optimal conditions (specialism) rather than extending the range of conditions (generalism) that support fitness-enhancing activity (Gilchrist

1995). However, a trade-off between maximal performance (functional specialism) and performance breadth (functional generalism) is implicated (Gilchrist 1995). Thus, contrasting **maximum performance specialism** of locally adapted genotypes, a broad tolerance curve function (describing survival rate along a continuous environmental gradient) should evolve to span the range of conditions an organism is likely to experience within a generation (Gilchrist 1995; underpinned by phenotypic **tolerance generalism**) when such genotype variants are confronted with novel biogenic information on invading foreign environments (e.g. Europeans having colonized America). Clear clinal genetic differentiation of native populations along gradients of environmental variation in native environments (**maximum performance specialism**); while any differentiation in introduced species is much weaker; with introduced populations displaying higher average fitness in association with broader environmental tolerances (phenotypic **tolerance generalism**), seems to be a general biological phenomenon (e.g. Alexander et al. 2012).

In order to functionally accommodate novel biogenic information, slow-LHS settings, supporting functional generalism (Table 2.3.3o), are adaptive; which in turn underpin birth peaks in autumn, as reported for America and Europe post-1980; whereas the characteristic European seasonal birth peak was around spring (between c. 1870-1980: Table 2.3.3o).

Chmielewski & Boryslawski (2016): A significant relationship between month of birth and lifespan was found (as studied in Poland). Individuals born in autumn and winter months lived significantly longer than those who were born in the middle of the year (May). Subjects of both sexes born in autumn and winter months were significantly shorter than their peers born around the middle of the year. Longevity/shorter combination. However, according to the results of other studies, the short die young (Kemkes-Grottenthaler 2005): inverse relationship between adult height and age at death. Size up, low age at death. Size down, high age at death. Men were significantly taller than women and lived significantly shorter. Subjects born in autumn lived significantly longer than their peers born in the middle of the year, i. e. in spring and summer months. Similar results were found for Ukraine, Poland, Germany and the USA; with the former two countries having lower life expectancies and greater male-female differences in life expectancies (males < females), than the latter two countries (refer also to Table 2.3.3d). Regarding these results, Lerchl (2004, op. cit. Chmielewski & Boryslawski 2016) noticed the negative correlation between the average life expectancy of subjects and the maximum difference due to the month of birth effect. Also, greater average life expectancy is correlated with lower differences between sexes in amplitude of the analysed effect (refer also to Table 2.3.3d).

According to reported data, in Europe the spring months of birth are the most favourable for adult body height, while birth in autumn and winter months is the least favourable. It turns out that shorter individuals, usually born at the end of the year, live on average longer, which is in line with evidence supporting the inverse relationship between adult stature and longevity (Salaris et al. 2012; Samaras 2014, op. cit. Chmielewski & Boryslawski 2016). Spring-born men taller but at the cost of reduced health-span/longevity (**AS: intensified P-M trade-off constraints**).

Spring births support HMT performance (Table 2.5.1.2e) relative to somatic investment (size/longevity). Reduced P-M trade-off: late age pregnancy (P cueing during SS) under sLHS with births peaks during AU/W (combination of slow LHS and P cueing in fetus during SS)

The results of Huber et al. (2004b) indicated that seasonality of contempory Austrian reproducing women manifests in that women born in the summer months (June-August) had fewer children than those born during other months of the year **(AS: *spring versus autumn: fast and slow LHS-modes respectively*: 2.2.2d/e**).
Women born in/around August (**AS: As associated with/determined by LHS-mode pM > Pm; slow LHS mode phenotypes**) have higher rates of conception failures than those born in/around February (**AS: associated with/determined by LHS-mode Pm > pM; fast LHS mode phenotypes**), who had more successful conceptions (Smits et al. 1999).
Women born during September-December reach menopause at older ages than those born between March and June (Cagnacci et al. 2005). (**AS: Slow LHS mode: 2.2.2d**).

Furthermore, spring peaks in births are stronger among adults with higher and medium education whereas those with basic education are over-represented among the autumn born (Doblhammer & Vaupel 2001). For British-born males, non-manual workers tended to be born in spring and manual workers in autumn and winter (Smithers & Cooper, op. cit. Doblhammer & Vaupel 2001). Spring birth peaks are more pronounced in cases of higher maternal education (university/secondary > apprentice/primary; Bobak & Gjonka 2001).

From the above it emanates that spring-borns represent performance types (Pm-types: **2.2.2e**), while autumn/winter-borns represent maintenance types (Mp-types: **2.2.2e**).

High performance types, as associated with LHS-modes Pm > pM underpinning spring births, are expected to arise from spring births in alignment with high metabolic turnover conditions at birth and early childhood (**AS: Association of warm season births/high nutrient levels during lactation and Pm-types**). **However, associated trade-off costs in terms of reduced maintenance capacities result in high performance types to be more vulnerable to patho-information-engram accumulation and associated disease states (link between performance realization and disease vulnerability: 2.2.2j).**

h) Oxidative stress and performance expression

Wallace (2005): Mitochondria are at the intersection between environmental factors such as calorie availability and cold and the human capacity to cope energetically with environmental challenges in different regions of the globe. Our ancestors had to adapt to two classes of environmental changes: I) short term changes in the availability of calories and climate associated with seasonal variation, and II) long term changes in the nature of calories and average annual temperatures as defined by latitude and geographic zones in which they lived.
For populations living in the colder temperate and arctic zones the ability to uncouple mitochondrial OXPHOS in brain and muscle by induction of mitochondrial proteins was required. Most ancestral populations had to accumulate plant carbohydrate calories and store them as fat during the plant growing season and then to efficiently use the stored fat to sustain their cellular energetics when plants were dormant. This seasonal variation in caloric availability was metabolically managed through the insulin signaling network which coordinately integrated the energy utilization, energy storage and energy-homeostasis tissues (through the hormonal signals of pancreatic α and β cells). This was regulated by cueing the energy-sensing tissues to serum glucose concentrations that oscillated based on the availability of plant carbohydrate calories. When calories were abundant, blood sugar levels were high, insulin was secreted and mitochondrial OXPHOS and associated antioxidant defences were down-regulated in the energy-utilization tissues; and excess carbohydrate calories were stored as fat in energy-storage tissues. As the availability of plant calories declined at the end of the growing season, blood sugar levels declined, resulting in decreased insulin secretion and increased glucagon secretion. The associated hormonal changes triggered the up-regulation of mitochondrial OXPHOS and the associated antioxidant defenses in the energy-utilization tissues, mobilized the stored fats in energy-storage tissues for use as mitochondrial fuel and activated glucose synthesis in order to sustain minimal blood sugar levels. The uncoupling mutations also partially relieved the constraints of the inner membrane electrochemical gradient (ΔP) on electron flow through the ETC (mitochondrial electron transport chain), permitting the ETC to run continuously. This kept the electron carriers oxidized and

minimized ROS production (**AS: when subject to feast-famine alternation underpinning LHS-mode PM: Section 2.2.2e:2**).

Dowling & Simmons (2009): The goal of the review presented was to elucidate the potentially far-reaching effects that highly effective reactive oxygen-containing molecules (ROS: reactive oxygen species) might have in the context of life history strategies. ROS are generated as by-products of vital oxidative enzyme complexes and harnessed for the use as molecular messengers for a wide range of biological processes. At high levels they are known to exert damaging effects through oxidative stress and have been implicated to act as mediators in LHS trade-off relationships (relating to costs of reproduction, immunity; between metabolic rate and lifespan: Sanz et al. 2006, op. cit. Dowling & Simmons 2009). At high levels the highly reactive molecules exert oxidative stress on the cell, thereby invoking changes in gene expression (Apel & Hirt 2004, op. cit. Dowling & Simmons 2009) and may result in cumulative oxidative damage to to DNA, RNA and proteins in cells (Beckman & Ames, op. cit. Dowling & Simmons 2009). Most energy production is generated by oxidative phosphorylation (OXPHOS) involving five enzyme complexes (Blier et al. 2001, op. cit. Dowling & Simmons 2009). These complexes (the electron transport chain) involve transporting electrons through a series of proteins via REDOX reactions. As byproducts of REDOX reactions in the context of OXPHOS, reactive oxygen species (ROS) are produced. When ROS is produced as part of an oxidative burst, harnessed to fulfil a variety of functions, including killing incoming microbes (Apel & Hirt 2004, op. cit. Dowling & Simmons 2009), such oxidative bursts may cause self-harm (autoimmunity since they are non-targeting) if not dealt with effectively by the body (Apel & Hirt 2004, op. cit. Dowling & Simmons 2009).
According to the well-known premise in gerontology dietary caloric restriction extends lifespan (Masoro 2000). It seems however that nutrient restriction rather than caloric restriction is playing a major role in modulating lifespan. Low ratios of protein to carbohydrate correspond with longest lifespans, whereas higher ratios are associated with higher reproductive success; suggestive of a trade-off between slow-type and fast-type LHS expression. This is also consistent with findings that protein rather than caloric restriction decrease mitochondrial ROS production and oxidative damage (Sanz et al. 2004). (**AS: A trade-off relationship between fast LHS (early life performance), high metabolic turnover rates and high ROS production on the one hand and slow LHS (later life performance), low metabolic turnover rates and low ROS production on the other is herewith indicated**). As reproduction is costly, a life history trade-off exists beween current reproduction and future reproductive potential and survival prospects. Also, increases in reproductive effort are associated with an increased susceptibility to oxidative stress (ROS as a cost of reproduction; negative association between reproductive effort and resistance to oxidative stress). This negative association was found to be absent in breeding pairs of zebra finches when supplemented with antioxidant carotenoids in their drinking water (Bertrand et al. 2006, op. cit. Dowling & Simmons 2009). ROS are also harnessed for immune defence (fighting invading microbes as part of an innate immune response) in both plants and animals (Nappi & Ottaviani 200, op. cit. Dowling & Simmons 2009). Use of non-specific reactive metabolites (such as ROS) by the body is associated with the danger of autoimmunity in individuals with insufficient capacity to detoxify surplus ROS (trade-off between the benefits of ROS immune action and the incidence of autoimmunity). Evidence from animal studies links surplus ROS production with decreases in sperm quality (Chen et al. 2013). Males with adaptations to protect their

seminal constituents (sperm and seminal fluid proteins) from the damaging effects of ROS generated during spermatogenesis and sperm motility are anticipated to have a fitness advantage under sperm competition. In general, ROS production appears to be the limiting factor preventing the unconstrained evolution of other life history traits (ROS as cornerstone of life history evolution).

Griskevicius et al. (2013): Investigated the connection between oxidative stress and risk taking (whether resource scarcity cues result in different risk-taking as a function of the chronic level of oxidative stress of an individual). Oxidative stress reflects damage to cellular tissue and DNA due to the production of reactive oxygen species during metabolic processes. Such damage accumulates with age and accumulates rapidly in individuals subject to chronic exposure of environmental toxins or distress (Gangestad et al. 2010). Repairing oxidative stress requires costly maintenance processes (Dowling & Simmons 2009), thereby impacting on LHS energy investment trade-off relationships. Low levels of oxidative stress were associated with less risk-taking; with more risk-taking being associated with high oxidative stress. Individuals with higher levels of oxidative stress responded to resource scarcity with higher risk-taking and those with lower levels with lower risk-taking. (**AS:** ***resource scarcity, but also endogenous resource stress, high PIE loads, accentuating energy investment trade-off constraints regarding LHS traits***).
(**AS:** ***Individuals with low oxidative stress, reflecting higher functional efficiency associated with lower PIE loads and high fight-flight reaction response thresholds, are accordingly expected to act from a position of strength: Win-win behaviour, Invincibility, inter alia implying low risk-taking. Those with high oxidative stress, reflecting functional insufficiency associated with high PIE loads, are expected to respond to challenges from a position of weakness subject to a low reaction response threshold: immediate over-reaction to challenges in order to mobilise maximum aggression-fight or initation of flight; win-lose behaviour***).

Gangestad et al. (2010): Oxidative stress occurs as an organism produces an overabundance of ROS relative to ROS-neutralising antioxidants. Energy production via cellular respiration, results in the creation of reactive oxygen species (ROS: oxygen-containing molecules or atoms possessing unpaired electrons known as radicals) as a byproduct. The electron transport chain involved in oxidative phosphorylation supports efficiency of energy metabolism, but at certain steps electrons are prematurely leaked to oxygen to produce radicals (Valco et al. 2007, op. cit. Gangestad et al. 2010). Aerobic organisms prevent harm due to ROS by special adaptations: enzymes (e.g. superoxide dismutase, catalase), use of dietary antioxidants (e.g. tocopherol) and repair of some ROS-induced damage (Valco et al. 2007, op. cit. Gangestad et al. 2010). Oxidative stress is experienced by an organism when ROS production exceeds antioxidant capacity. Oxidative stress is causally linked to senescence and mutations; and contributing to the pathogenesis of chronic diseases such as cancers, neurodegenerative disorders and diabetes (Valco et al. 2007, op. cit. Gangestad et al. 2010). ROS represent intrinsic costs of energy production (defence against oxidative stress through the production of antioxidants and maintenance repair processes), thereby placing constraints on investment in other life history traits. Limited energy budgets force a trade-off between maintence (somatic effort) and reproductive effort; since a major cost of reproductive performance is the risk of oxidative damage (Dowling & Simmons 2009). ROS-induced costs per unit of energy production represents a component of the efficiency of metabolism.

Gangestad et al. (2010) used fluctuating asymmetry as primary indicator of developmental instability, the imprecise expression of developmental design due to perturbations of development. Oxidative stress is implicated as a process involved in causing developmental instability and linked disease proneness. Female mate choice is implicated to be partly based on male physical features/attractiveness and females may benefit by mating with males with low susceptibility to oxidative stress, as reflected in healthiness and masculinity of appearance (e.g. Rhodes et al. 2007, op. cit. Gangestad et al. 2010). Results: 1) Fluctuating asymmetry significantly and positively predicted oxidative stress; 2) Physical attractiveness significantly and negatively predicted oxidative stress; 3) Healthy appearance and masculine appearance covaried with attractiveness and both were significantly and negatively associated with oxidative stress. These findings are consistent with the interpretation that women evolved to find particular features attractive because they reflect lower oxidative stress levels. As oxidative stress occurs when the production of ROS outpaces neutralizing antioxidant defences, individuals may alternatively experience high levels of oxidative stress because of particularly high rates of ROS production or lower capacities to produce antioxidants (possibly due to lower overall energy budgets).

Kiffin et al. (2005) and Wu et al. (2009) outline the involvement of autophagy in the oxidative stress response.

Kiffin et al. (2005): Both increasing intracellular antioxidant agents and removal of already damaged compoments form part of the oxidative stress response. Evidence supports a protective role of the lysosomal system by elimination of altered intracellular components through autophagy. The oxidative stress response thus involves activation of the main intracellular proteolytic systems, the ubiquitin/proteasome and the lysosomal/autophagic systems. Numerous studies have reported malfunctioning with age in both the ubiquitin/proteasome system and the lysosomes (Cuervo & Dice 1996, op. cit. Kiffin et al. 2005; Cuervo 2004, op. cit. Kiffin et al. 2005; Donati et al. 2001, op. cit. Kiffin et al. 2005; Keller et al. 2004, op. cit. Kiffin et al. 2005). Normal ageing and numerous diseases related to oxidative stress are linked to oxidation-related pathologies where failure of the lysosomal system plays a role (e.g. atherosclerosis, age-related macular degeneration, neurodegenerative disorders and diabetes mellitus).

Damaged mitochondria tend to produce increased levels of reactive oxygen species (ROS), further increasing mitochondrial damage, leading to more oxidant release and additional mitochondrial damage (Wallace 2005). Wu et al. (2009) demonstrated that impairment of autophagy results in the accumulation of damaged and dysfunctional mitochondria and corresponding increase in intracellular ROS levels. Autophagy seems to be required for dietary restriction mediated life span extension (Jia & Levine 2007).

i) Chronic immune system dysregulation syndrome

Ruiz-Núñez et al. (2013) presented a review of lifestyle and nutritional factors underpinning a state of chronic systemic low-grade inflammation (below). Following

on such considerations, the ***chronic immune system dysregulation*** (**CISD**) syndrome, in the context of patho-information-engram load accumulation and life history modes, is defined and developed.

Ruiz-Núñez et al. (2013): Human sensitivity towards insulin resistence derives from rapid brain growth over the past 2.5 million years. An inflammatory reaction is apparently currently associated with the fulfilment of high glucose requirements of our brains; resulting in various adaptations, including insulin resistence, functional reallocations of energy nutrients and changing seum lipoprotein composition. The latter results in redistribution of lipids, modulation of the immun reaction and active inhibition of reverse cholesterol transport for damage repair. With the emergence of the agricultural/industrial revolutions numerous false inflammatory triggers were introduced, resulting in a state of chronic systemic low grade inflammation; eventually leading to typical Western diseases via an evolutionary conserved interaction between the immune system and metabolism. The underlying triggers of the disturbance of the inflammatory/anti-inflammatory balance involve an abnormal dietary composition and microbial flora, insufficient physical exercise and sleep, chronic stress and environmental pollution. Possibly (all) tpically Western diseases are centered on the metabolic syndrome (a combination of of excessive body weight, impaired glucose homeostasis, hypertension, atherogenic dyslipidemia). Systemic inflammation results in insulin resistence and a compensatory hyperinsulinemia in order to keep glucose homeostasis in balance. Glucose homeostasis ranks high in the hierarchy of energy equilibrium, but becomes progressively compromised under continuous inflammatory conditions via glucotoxicity/lipotoxicity or both.
Insulin resistence (reduced insulin sensitivity) is a survival strategy rooted in our evolution during which our brain has grown substantially. Insulin resistance is aimed at *inter alia* the reallocation of energy-rich nutrients because of a chronically activated immune system (Straub et al. 2010; Straub 2011, op. cit. Ruiz-Núñez et al. 2013), limitation of the immune response and the repair of the inflicted damage. The authors contend that our current Western lifestyle is causing many false inflammatory triggers which successively result in a state of chronic systemic low grade inflammation, insulin resistance and the metabolic syndrome, leading to the typically Western diseases of affluence.
The growth of the human brain was enabled by finding a high quality dietary source, easy to digest and containing ample amounts of nutrients. 'Brain selective nutrients' include inter alia iodine, selenium, iron, vitamins A and D, and the fish oil fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Refer also to Leonard et al. (2007, op. cit. Ruiz-Núñez et al. 2013). The reduced carbohydrate intake during the evolutionary transition from vegetarians to omnivores resulted in humans being strongly dependent gluconeogenesis from glucogenic amino acids. This became possible due to the consumption of protein from meat and fish (the 'carnivore connection': Colagiuri & Miller 2002, op. cit. Ruiz-Núñez et al. 2013). Under conditions of severe glucose deficit (e.g. fasting) the energetic needs of the brain are increasingly provided for by ketone bodies from fat (Cahill 2006, op. cit. Ruiz-Núñez et al. 2013; Hadden & McLaughlin 2009, op. cit. Ruiz-Núñez et al. 2013). ***Reallocation of energy-rich nutrients by insulin resistence***: Glucose deficits result in competition between organs for the available glucose. In the case of pregnancy and inflammation, active compartments are competing with the brain for available glucose, that is, the

growing child and the activated immune system. Competition between organs for glucose: fulfilment of the high glucose needs of the brain by the reallocation of energy-rich nutrients is facilitated through insulin resistance. Glucose is saved for the brain, for the fetus during pregnancy and facing infection/inflammation by entering a state of insulin resistance in selected insulin-dependent tissues. Such tissues are thereby forced to switching to the burning of fat (adipose tissue encouraged to distribute free fatty acids, the liver to produce glucose via gluconeogenesis and to distribute triglycerides via very low-density lipoprotein). The characteristics of insulin resistance are considered necessary during post-partum, saving available glucose for the brain while other organs are provided with fatty acids from adipose tissue stores. During infection and inflammation, signals for metabolic adaptation are transmitted by pro-inflammatory cytokines; resulting in isulin resistance, causing reallocation of energy (Integration of inflammation and metabolism: Hotamisligil & Erbay 2008; Hotamisligil 2010). Insulin resistance implies diminished reduction of glucose circulating concentrations by insulin. Insulin has various metabolic functions and some functions are impared by insulin resistance (are resistant), while others remain intact becoming stimulated by hyperinsulinema. The associated compensatory increase of circulating insulin represents an attempt to prevent a disturbance of glucose homeostasis. However, the persistence of compensatory hyperinsulinism is responsible for most, if not all, abnormalities associated with the metabolic syndrome (Reaven 2005, op. cit. Ruiz-Núñez et al. 2013). The promoted reallocation of of energy-rich substrates through insulin resistance (glucose to the brain, fetus and immune system; fat to fetus and the organs which had become insulin resistant) and the compensatory hyperinsulinemia are geared for short-term survival. Their persitance as a chronic state form the basis of ultimate changes that are recognizable as symptoms of the metabolic syndrome including changes in glucose and lipid homeostasis (Straub et al. 2010; Straub 2011, op. cit. Ruiz-Núñez et al. 2013) and increased blood pressure. Reaven (2005, op. cit. Ruiz-Núñez et al. 2013) introduced the term metabolic syndrome, subsequently renamed it the insulin resistance syndrome. According to Ruiz-Núñez et al. 2013, a more fully descriptive and appropriate term would be '***chronic systemic low-grade inflammation induced energy reallocation syndrome***'. Insulin resistance is only one part of the simultaneously occurring adaptations. These currently known adaptations and consequences include I) reduced insulin sensitivity (glucose and lipid redistribution, hypertension); II) increased sympathetic nervous system activity (stimulation of lipolysis, gluconeogenesis, glycogenolysis) and III) increased activity of the HPA-axis (hypothalamus-pituary-adrenal) gland stress axis, mild cortisol increase, gluconeogenesis, cortisol resistance in the immune system); IV) decreased activity of the HPG-axis (hypothalamus-pituary-gonadal gland axis), decreased androgens for gluconeogenesis from muscle proteins, androgen/estrogen disbalance, inhibition of sexual activity and reproduction; V) IGF-1 resistance (insulin-like growth factor-1), no investment in growth and VI) the occurrence of sickness behaviour (energy saving, sleep, anorexia, minimal activity of muscles, brain and gut: Straub 2011, op. cit. Ruiz-Núñez et al. 2013). ***Changes in serum lipoproteins***: Quantitative and qualitative chanes in the composition of serum lipoproteins from an inflammatory trigger are known to have at least three goals (Esteve et al. 2005, op. cit. Ruiz-Núñez et al. 2013; Murch et al. 2007, op. cit. Ruiz-Núñez et al. 2013): I) the reallocation of energy-rich nutrients (fatty acids to insulin resistant organs); II) modulation of the immune response providing protection against invading bacteria, viruses and parasites; III) restoration of the associated inflicted damage. In summary, humans are sensitive to glucose deficits due to the substantial glucose requirements of their large brains and

during starvation, pregnancy and infection/inflammation, insulin resistance and other adaptations take effect in order to facilitate the reallocation of energy-rich substrates to spare glucose for the brain, the rapidly growing infant during the third trimester and our activated immune system. The metabolic adaptations caused by inflammation are designed for the short term. In a chronic state they will eventually cause the metabolic syndrome and its pathological sequelae.

Lifestyle-induced chronic systemic low grade inflammation: Currently the Western lifestyle contains numerous false inflammatory triggers and by a lack of inflammation suppressing factors. An inflammatory reaction is a reflection of an activated immune system which should subsequently be ended. However, many factors of our Western lifestyle jointly result in a state of chronic systemic low grade inflammation. This then results in chronically compromised insulin sensitivity, compensatory hyperinsulinemia and diseases related to the metabolic syndrome. Lifestyle factors can cause inflammation due to an unbalanced composition of the diet (Anand et al. 2008, op. cit. Ruiz-Núñez et al. 2013; Galland 2010, op. cit. Ruiz-Núñez et al. 2013) or non-food related factors (Egger & Dixon 2011, op. cit. Ruiz-Núñez et al. 2013). Dietary pro-inflammatory factors include a) consumption of saturated fatty acids (Jimenez-Gomez et al. 2009, op. cit. Ruiz-Núñez et al. 2013); b) industrially produced trans fatty acids (Mozaffarian 2006, op. cit. Ruiz-Núñez et al. 2013); c) a high omega-6/omega-3 fatty acid ratio (Calder 2006, op. cit. Ruiz-Núñez et al. 2013; Serhan & Chiang 2008, op. cit. Ruiz-Núñez et al. 2013); d) low intake of long-chain polyunsaturated fatty acids of the omega-3 series from fish (He et al. 2009, op. cit. Ruiz-Núñez et al. 2013); e) a low status of vitamin D (Adorini & Penna 2008, op. cit. Ruiz-Núñez et al. 2013); f) vitamin K deficiency (Shea et al. 2008, op. cit. Ruiz-Núñez et al. 2013); g) a low status of magnesium (Laires et al. 2004; Laires & Monteiro 2008; Kim et al. 2010); h) endotoxemia of a high fat/low fibre diet (Cani & Delzenne 2009, op. cit. Ruiz-Núñez et al. 2013); i) consumption of carbohydrates with a high glycemic index and a diet with a high glycemic load (Levitan et al. 2008, op. cit. Ruiz-Núñez et al. 2013); k) dysbalance between micronutrients making up the antioxidant/pro-oxidant network (Benzie 2003, op. cit. Ruiz-Núñez et al. 2013; Vertuani et al. 2004, Pan et al. 2009, op. cit. Ruiz-Núñez et al. 2013); and l) a low intake of fruit and vegetables (Holt et al. 2009; Pan et al. 2009, op. cit. Ruiz-Núñez et al. 2013). In the 'dietary inflammation index' of the University of North Carolina (op. cit. Ruiz-Núñez et al. 2013), magnesium deficits ranked high as pro-inflammatory stimuli in this index (Cavicchia et al. 2009). Indirect diet related factors involved include an abnormal composition of the bacterial flora in the mouth, gut (De Filippo et al. 2010, op. cit. Ruiz-Núñez et al. 2013; Koren et al. 2011, op. cit. Ruiz-Núñez et al. 2013) and gingivae; chronic stress (Black & Garbutt 2002, Garcia-Bueno et al. 2008); (passive) smoking and environmental pollution (Egger & Dixon 2011, op. cit. Ruiz-Núñez et al. 2013); insufficient physical activity (Petersen et al. 2005, op. cit. Ruiz-Núñez et al. 2013; Roubenoff 2007, op. cit. Ruiz-Núñez et al. 2013; Handshin & Spiegelman 2008, op. cit. Ruiz-Núñez et al. 2013) and insufficient sleep (Simpson & Dinges 2007; Irwin et al. 2006, op. cit. Ruiz-Núñez et al. 2013; Irwin et al. 2008, Mullington et al. 2010).

Mechanisms of lifestyle-induced inflammation. Inflammation is an essential process of survival, but the immune system must be carefully regulated in order to limit associated collateral damage (Eisenächer & Krug 2012, op. cit. Ruiz-Núñez et al. 2013). Diets high in refined starches, sugar, saturated and trans fats; and low in long-chain polyunsaturated fatty acid omega-3, low in natural antioxidants and low in in fiber from fruits and vegetableshave been shown to promote inflammation (Giugliano

et al. 2006, op. cit. Ruiz-Núñez et al. 2013; Mozaffarian 2006, op. cit. Ruiz-Núñez et al. 2013; Mozaffarian et al. 2009, op. cit. Ruiz-Núñez et al. 2013).

The authors (Ruiz-Núñez et al. 2013) pointed out that our diet is composed of millions of substances that are part of a biological network (we eat biological systems), the various nutrients of which are balanced and interacting as parts of living organisms. This balance may be found in the reconstruction of the Paleolithic diet (Eaton et al. 1997; Cordain et al. 2000; Eaton & Eaton 2000, op. cit. Ruiz-Núñez et al. 2013).

Ruiz-Núñez et al. (2013) presented the conceptual term '***chronic systemic low-grade inflammation induced energy reallocation syndrome***' in order to accommodate and embrace pathological manifestations such as reduced insulin sensitivity, increased sympathetic nervous system activity, increased activity of the HPA-axis (hypothalamus-pituary-adrenal) gland stress axis (cortisol resistance in the immune system), decreased activity of the HPG-axis (hypothalamus-pituary-gonadal gland axis), IGF-1 resistance (insulin-like growth factor-1) and the occurrence of sickness behaviour.

AS: Following on such considerations, the ***chronic immune system dysregulation*** (**CISD**) syndrome is defined and developed in the context of patho-information-engram load accumulation and life history modes. With declining performance vitality as the LHS-modes pM > Pm(2) and pM↑(4) prevail on the basis of low endogenous energetic efficiency due to advanced patho-information-engram accumulation, immune system functionality becomes dysregulated. This is characterised by chronically activated immune system functionality with low reaction thresholds and restrained maximum performance: activation by relatively small insults (e.g. food item allergies), but attenuated acute reactions (e.g. fever; low capacity for overcoming acute pathogenic insults and preventing these from becoming lodged as patho-information-engrams in the biocybernetic regulation system of the body). This manifests as chronic systemic low-grade inflammation *vide* Ruiz-Núñez et al. (2013); and sympathetic ANS (autonomous nervous system) over-dominance (2.2.1a; Table 2.3.2a). The dysregulated immune system is characterised by functional weakness with low reaction fight-flight thresholds, that is, over-reactive fight responses to weak challenges (allergenic) and flight/escapist responses to strong challenges (non-resolution of acute/subacute disease insults resulting in accumulated chronicity).

Our energetic system (as underpinning the LHS-mode PM under feast-famine conditions) worked well for our ancestors who lived in an environment of periodic carbohydrate surplus and deficiency (Wallace 2005). However, with unlimited dietary calories, including carbohydrates throughout the year, our energy signalling systems remain continuously in the high carbohydrate state (Wallace 2005). As a result, mitochondrial OXPHOS (oxidative phosphorylation) and associated antioxidant defences are chronically down-regulated. Concurrently, due to sedentary life styles, we do not turnover ATP through sustained physical activity. The excess of caloric reducing equivalents in such diets then leads to fat accumulation and obesity, keeping the electronic carriers of our down-regulated ETC (mitochondrial electron transport chain) fully reduced. This results in chronically increased mitochondrial ROS (reactive oxygen species) production and oxidative stress, which damages the mitochondria and mtDNAs (Wallace 2005).

j) Performance types and vulnerability to disease

Two functionality types were identified in Section 2.2.2e in accordance with relevant trade-off constraints: **Pm-types** (extremized LHS-mode Pm > pM expression) realize enhanced performance capacities at the cost of compromised maintenance capacities (which include health-supporting processes). **Mp-types** (extremized LHS-mode Mp > Pm expression) realize enhanced maintenance capacities at the cost of compromised performance capacities (including competitive and reproductive vitality).
High performance types (Pm-types: 2.2.2e), as associated with LHS-mode Pm > pM are expected to be in alignment with high metabolic turnover conditions at birth and early childhood: accentuated fast-LHS-mode Pm > pM realization and associated trade-off costs (2.2.2d) in terms of reduced maintenance capacities result in high performance types to be more vulnerable to disease states; indicating a link between accentuated performance realization and disease vulnerability (2.2.2e; 2.2.2g and 2.2.1c).

Uric acid acts as a perfomance catalyst (Johnson et al. 2009; De Giorgi et al. (2015), *inter alia* reflected in the positive relationship of uric acid with IQ (Sofaer & Emery 1981), achievement-oriented behaviour (Kasl et al. 1970; Lorenzi et al. 2010), school performance and increased locomotor activity (Barrera et al., op. cit. Johnson et al. 2009). Uric acid levels are increased under conditions of emotional and physical stress (Rahe et al., op. cit. Johnson et al. 2009) and are associated with intelligence and

reaction time (Inouye et al. 1984). Kasl et al. (1970) found a positive relationship to college attendance, extracurricular and social activities, and vocational aspirations. Brooks & Mueller (1966) confirmed highly significant positive correlations between uricemia and intensity of activity, professional productivity, organizational skills, placing demands on oneself, breadths and multifacetted nature of activities (2.2.1c).

Heritability of plasma uric acid levels and IQ, corrected for age and sex and standardized, was estimated at 0.8 in twin families (consisting of twin parents, spouses and children), suggesting a contribution of partly common gene loci to the two traits (Inouye et al. (1984). These results indicate a genetic basis of blood uric acid levels (presumably associated with polymorphisms of purine metabolism pathways) and associated **Pm-type** capacities (2.2.1c).

High Pm-type expression, is associated with increased/accentuated P-M trade-off constraints. High P/M realization ratios *inter alia* associated with fast LHS modes, higher education levels, leadership performance and the capacity to maintain performance under adversity (urbanization, population density) require high performance realization (good vitality status) and are thus costly in terms of maintenance (Section 2.2.2e) Accordingly, we have a LHS trade-off between energy allocation to high performance functionality and allocation to maintenance (including health-sustaining autophagic processes; notably supporting recursive deletion of patho-information-engram load accumulations epigenetically inherited: 2.1.3). Initially individuals exhibiting high performance (aristocrats, high social status, performers of high educational status and of high leadership competence or competence in general), who are usually wealthier, combined high performance (male competiveness, female reproduction) with sustaining maintenance functions (LHS-mode PM: 2.2.2e:2). Under conditions of transgenerationally uninterrupted affluence and population density stress (procursive impacts), patho-information-engram (PIE) loads accumulate, which disrupt PIE load-eliminating maintenance processeses (such as autophagy: 2.1.2). The better the basic health status (low patho-information-engram loading), the weaker the P-M trade-off and reduced plasticity-resilience trade-off constraints apply, permitting the coexistence of plasticity and resilience (plasticity-resilience combination). As subject to plasticity-resilience trade-off relationships, high P-type realization is associated with susceptibility/vulnerability to adversity when subject to differential susceptibility constraints (2.2.1d), which would apply in individuals with high patho-information engram (PIE) load accumulations.

Accordingly, under conditions of pre-existing PIE loadings and associated compromised functional efficiency, the trade-off beween high performance realization (high plasticity benefits) and the maintenance of health is accentuated (increased plasticity costs). High performance (*inter alia* supported by performance catalysts such as notably uric acid: 2.2.1c**)** then becomes associated with a greater preponderance of illness states, disproportionally affecting the wealthy and high performers, especially male high performers.

Fitness is maximized when P-M trade-off constraints are minimized (i.e. as prevalent on the basis of a good fundamental health status: 2.2.2e; Doblhammer & Oeppen 2003). Especially for high-SES individuals it is important that high performance realization (underpinned by fast-LHS-mode expression) is not at the expense of life time reproductive success in respect of high quality offspring underpinned by slow-LHS-PM mode realization. Fitness is maximized through the combination of early reproduction and high lifetime reproductive success (Korpelainen 2003), as supported by fast and slow LHS-mode expression respectively. Under high P-M trade-off constraints (accentuated fast-slow LHS-mode trade-off relationship), the associated narrowed childbearing age range negates fitness maximization (2.2.2k).

Skirbekk (2008): The study by Skirbekk (2008) revealed that as fertility declined, a shift from positive to negative/neutral occurred in the status-fertility relationship; i.e. those with high income/wealth/high occupation/social class switch from having relatively many to fewer or equal numbers of children than those of lower status. Education was found to be negatively associated with fertility (1900 onwards). As fertility levels decline, elites are the first in reducing their fertility, resulting in a negative status-fertility relationship. When fertility has declined to be close to replacement level, differences in fertility levels between high and low status groups are generally small, but variable. In such countries as Belgium, Sweden and Germany, a pronounced fertility gap between the high and low educated has been sustained over the past few decades. In general, a status increase from from low to medium and from medium to high was associated with higher fertility until the mid-1700s. From 1750-2006, occupation and social class tended to be negatively related to fertility.
Relative fertility of the high status groups for Europe and North America: variable *d* = (Fertility high status-fertility low status)/fertility low status.
All status groups: *d* = 35.8 (< 1750), -8.2 (1750-1899), -15.1 (1900-1924), -17.0 (1925-1949), -15.5 (1950-1974), -5.2 (1975-1989), -9.0 (1990-2006).
Income/wealth: *d* = 24.3 (< 1750), -45.0 (1750-1899), 6.1 (1900-1924), -12.4 (1925-1949), -13.9 (1950-1974), 2.3 (1975-1989), 6.7 (1990-2006).
Occupation/social class: *d* = 30.9 (< 1750), -4.2 (1750-1899), -22.3 (1900-1924), -45.6 (1925-1949), -6.0 (1950-1974), *na* (1975-1989), -7.9 (1990-2006).
Education: *d* = -35.7 (1900-1924), -25.8 (1925-1949), -21.8 (1950-1974),

-24.6 (1975-1989), -17.8 (1990-2006).
Demand for child quality increased at the expense of child quantity. Empirical results consistently confirmed that the upper classes were forerunners in the decrease of family size.

As outlined in section 2.2.1c, we have a LHS trade-off between energy allocation to high performance functionality (metabolic efficiency for e.g. performance: cognition/energy storage) and allocation to maintenance (including health-sustaining processes: prevention and elimination of allostatic load, i.e. patho-information-engram loading epigenetically inherited and produced during the course of life). Initially individuals exhibiting high performance (aristocrats, high social status, performers of high educational status and of high leadership competence or competence in general), as generally associated with wealth, can combine high performance (male competiveness, female reproduction) with sustaining maintenance functions (LHS-mode PM: 2.2.2e:2). However, under conditions of transgenerationally uninterrupted affluence, PIE loads accumulate, which disrupt PIE load-eliminating maintenance processeses (such as autophagy). Under conditions of pre-existing PIE loadings and associated compromised functional efficiency, the trade-off beween high performance realization and the maintenance of health is intensified. High performance (*inter alia* supported by performance catalysts such as uric acid) then becomes associated with a greater preponderance of illness states (see above), disproportionally affecting the wealthy and high performers, especially male high performers (2.2.2j).

Accordingly, during the course of demographic transitions (2.3.3) the functional vitality of individuals of wealthier lineages (with wealth usually based on genetically inherited Pm-type capacities: 2.2.2k) was disproportionately compromised due to an earlier onset of transgenerational patho-information-engram load accumulation (2.1.2; 2.1.3); as induced by having been subjected to relatively higher levels of resource availabilities and population density stress over time (procursive impacts).

k) Socioeconomic status, health and fertility

McEwen & Wingfield (2003) and others (e.g. McEwen & Gianaros 2010; Bradley & Corwyn 2002) presented evidence for a gradient of progressively lower health states

associated with decreasing socioeconomic status, notably applicable during this stage of the demographic transition (LHS-mode pM↑:4). The association between socioeconomic position (SEP) and health is usually attributed to poverty causing disease, but Charlton (1996) presents an alternative interpretation which considers that added increments of SEP are correlated with added increments of health; following a salutogenic explanation for the causes of health rather than a pathogenic explanation of disease (Charlton 1994, op. cit. Charlton 1996; Charlton & White 1995, op. cit. Charlton 1996).

McEwen & Wingfield (2003): Those at the highest levels of socioeconomic status (SES) had the lowest incidence of osteoarthritis (Cunningham & Kelsey 1984, cit. McEwen & Wingfield 2003), relative prominence of chronic disease (Townsend 1974, cit. McEwen & Wingfield 2003), prevalence of hypertension (Kraus et al. 1980, cit. McEwen & Wingfield 2003) and rates of cervical cancer (De Vasa & Diamond 1980, cit. McEwen & Wingfield 2003). Also, lower education and income levels are associated with increased incidence rates of affective and anxiety disorders (ex McEwen 2000). Abdomal obesity (measured as increased waist-hip ratio WHR; and *inter alia* linked to type 2 diabetes and cardiovascular disease: Brindley & Rolland 1989, op. cit. McEwen & Wingfield 2003) is increased at the lower end of the SES gradient (Larsson et al. 1989, cit. McEwen & Wingfield 2003; Brumner et al.1997, cit. McEwen & Wingfield 2003). Regarding psychiatric disorders there is evidence that low SES is associated with mental distress and depression, as well as disorders such as schizophrenia and substance abuse (Brown & Adler 1998, cit. McEwen & Wingfield 2003). On the question of causality: does SES cause the disorder or does the disorder lead to low SES? In the case of schizophrenia, personalty disorders, substance abuse and cognitive impairment, it seems likely that the conditions themselves lead to a lower SES position (Brown & Adler 1998, cit. McEwen & Wingfield 2003; Dohrenwend et al. 1992, cit. McEwen & Wingfield 2003).

As shown by numerous authors (Cherkas et al. 2006; Adams & White 2004; Adams et al. 2005), a clear link between poorer health states associated with lower socioeconomic status and faster rates of ageing has been established. Fast ageing is linked to fast LHS-mode expression typically associated with lower socioeconomic status (Nettle (2010; Whitehead et al. 2016; Frankenhuis et al. 2016; Grundy & Read 2015; McEwen & Gianaros 2010).

Adams & White (2004): From evidence investigated by Adams & White (2004), socioeconomic differences in health are partly the result of people of lower socioeconomic status ageing faster than those of higher socioeconomic status. (AS: This implies faster LHS and relatively lower investment in maintenance in lower socioeconomic classes and an associated compromised health status).
Cherkas et al. (2006): Low socioeconomic status (SES) is associated with a shorter life expectancy believed to be underpinned by a faster rate of ageing.

Adams et al. (2005): Evidence was found that prostate, colorectal and lung cancers were diagnosed at earlier ages in people from more deprived areas; implicating a link between low SES and faster biological ageing.

Nettle (2010): In deprived neighbourhoods compared with affluent ones in contempory England, age at first birth is younger, birth weights are lower and breastfeeding duration is shorter, and reproductive rates tend to be higher. It is suggested that a fast life history strategy (involving early reproduction and reduced investment per child), as based on phenotypic plasticity, is the adaptive response to such an environmental context; but entailing specific costs to children in terms of health and competence.

Whitehead et al. (2016): Conducted a review investigation pertaining to the question: what theories and conceptual frameworks have addressed the causal associations and pathways connecting the degree of control in the living environment with SES and health-related outcomes. The explanatory model posits that low social position, as associated with lack of resources to cope with demands and social fatalism (low perceived control) results in low control over destiny (actual control over money, power, information, prestige, environment) and mental perceptions of having low control; which in turn, lead to a reduced ability to cope with stressfull environments, reduced power of influence on decision-making, uncertainty about the future (present time preference), aggressive responses, ineffective coping (low self-efficacy) and stress-induced metabolic disturbances; adding up to poorer physical and mental health for people in low social positions (*inter alia* manifesting in heightened chronic stress responses, depression, cardiovascular disease, compromised endocrine and immune function). (**AS: SES gradient: high to low performance/good health combination. Low SES-linked low control capacity → vulnerability to conditions of harshness/unpredictability and experience of such conditions, notably unpredictability → fast LHS response underpinning poor health outcomes**).

Frankenhuis et al. (2016): Review studies which demonstrate present-orientation behaviours (such as vigilance, impulsivity, discounting of future) in response to harsh and unpredictable environmental conditions. It is contended that present-orientation under such conditions represent biological adaptations, despite associated potential harm to health and wellbeing. People in stressful environments have a stronger preference for immediate over delayed rewards; notably early life fertility realization. Natural selection results in developmental mechanisms using individual experience to tailor phenotypes to local conditions and current states (Frankenhuis & Del Giudice 2012, op. cit. Frankenhuis et al. 2016; Bjorklund & Ellis, op. cit. Frankenhuis et al. 2016; Del Giudice & Gangestad 2015, op. cit. Frankenhuis et al. 2016). Shorter reproductive life spans implicate greater benefits of accelerating maturation and earlier reproduction, even if it is at the expense of investment to maintenance (Belsky 2002, op. cit. Frankenhuis et al. 2016; Chisholm 1999, op. cit. Frankenhuis et al. 2016). Present-orientation is considered adaptive (Griskevicius et al. 2011, op. cit. Frankenhuis et al. 2016; Mittal & Griskevicius 2014, op. cit. Frankenhuis et al. 2016) under experience of harshness and unpredictability (such as high mortality and morbidity, unpredictable threats of confrontation and opportunities are fleeting), referring to biological fitness, not health or well-being (Frankenhuis & Del Giudice 2012, op. cit. Frankenhuis et al. 2016).

Grundy & Read (2015): In England, early parenthood and larger family size are associated with less wealth and poorer health behaviours; accounting for much of the association with health. At least partly operating through stress-related physiological dysfunction (allostatic load). Early parenthood (< 20 years for women and < 23 for men) was positively associated with higher allostatic load and long-term illness.
Most studies of contempory populations have found a U- or J-shaped association between number of children born (parity) and later life mortality and health among women, and in some studies also among men; with both nulliparity and high parity (4, 5 or more children) being associated with increased risks relative to having two children (e.g. Doblhammer 2000, op. cit. Grundy & Read 2015; Alonzo 2002, op. cit. Grundy & Read 2015; Grundy & Tomassini 2005, op. cit. Grundy & Read 2015; Hurt et al. 2006, op. cit. Grundy & Read 2015). In Scandinavian populations there seems to be no or a reduced mortality penalty for high parity (Hinkula et al. 2006, op. cit. Grundy & Read 2015; Grundy & Kravdal 2008, 2010, op. cit. Grundy & Read 2015). (**AS: congruent with slow-LHS-mode PM realization of individuals with low patho-information-engram loadings**).
Hank 2010 (op. cit. Grundy & Read 2015): In Western Germany mothers and fathers of four or more children reported better health and no elevation in mortality risk (**AS: congruent with slow-LHS-mode PM realization of individuals with low patho-information-engram loadings**) while in Eastern Germany high parity was associated with increased mortality risks, but not with poorer health (**AS: congruent with slow-LHS-mode P(M) realization of individuals with low patho-information-engram loadings**).
UK studies of associations between parity and various health indicators, such as studies of mortality, generally show disadvantages associated with with nulliparity, high parity or both (Grundy & Holt 2000, op. cit. Grundy & Read 2015; Guralnik et al. 2009, op. cit. Grundy & Read 2015; Grundy & Tomassini 2005, op. cit. Grundy & Read 2015). In a more recent British study it was found that childnessless was associated with faster accumulation of health limitation in women; and that high parity was associated with poorer health outcomes for women and men (Read, Grundy & Wolf 2011, op. cit. Grundy & Read 2015).
Age at parenthood: Studies of age at childbearing consistently show poorer later health and higher mortality among women with an early entry to motherhood (Grundy & Tomassini 2005, op. cit. Grundy & Read 2015); Mirowsky 2005, op. cit. Grundy & Read 2015; Henretta et al. 2008, op. cit. Grundy & Read 2015; Pirkle et al. 2014, op. cit. Grundy & Read 2015). Later health disadvantages of early fatherhood have also been reported (Grundy & Tomassini 2006, op. cit. Grundy & Read 2015; Grundy & Kravdal 2008, op. cit. Grundy & Read 2015; Pudrovska & Carr 2009, op. cit. Grundy & Read 2015). Some studies suggest that late maternity or paternity is related to better later health (Snowdon, et al. 1989, op. cit. Grundy & Read 2015; Yi & Vaupel 2004, op. cit. Grundy & Read 2015). (AS:). In congruence, for Norwegian mortality data, a positive association was established between later age of last birth and lower later mortality (Grundy & Kravdal 2010, op. cit. Grundy & Read 2015).
Leahy & Crews (2012, op.cit. Grundy & Read 2015) reviewed publications which examined the relationships between allostatic load and risk factors, chronic diseases, morbidity and mortality of older people and concluded that allostatic load captured aspects of physiological dysregulation and somatic decline, thus predicting health deterioration (an early indicator of later poor health). The analyses by Grundy & Read (2015) were in agreement with those anticipated from the review by Leahy & Crews (2012, op.cit. Grundy & Read 2015). Number of children 4 relative to 2: positive

association with allostatic load (for men, fathers, women, mothers), also in respect of the incidence of limiting long-term illness; first birth at 23 y: fathers, at < 20 y mothers: positive association with allostatic load (also in respect of the incidence of limitng long-term illness); no educational qualification: positive association with allostatic load (for men, fathers, women, mothers; also in respect of the incidence of limiting long-term illness); currently married: negative association with allostatic load (for men and fathers) and negative association with limiting long-term illness in women and mothers. Number of children 4 relative to 2: negative association with wealth (men, fathers, women, mothers); first birth at < 23 y: fathers, at < 20 y mothers: negative association with wealth (fathers, mothers).

McEwen & Gianaros (2010): Disparities in income education, occupation and other dimensions of SES account for much variance in all-cause and disease-specific morbidity and mortality rate; as well as risk factors for chronic medical conditions (Adler et al. 1994, op. cit. McEwen & Gianaros 2010; Adler et al. 1999, op. cit. McEwen & Gianaros 2010) and psychopathologies of mood (Kessler et al. 1994, op. cit. McEwen & Gianaros 2010; Lorant et al. 2003, op. cit. McEwen & Gianaros 2010). That health and longevity track a socioeconomic gradient cannot be fully explained by material deprivation, illiteracy or restricted availability of quality health care to those occupying lower socioeconomic positions (Marmot 2004, op. cit. McEwen & Gianaros 2010; Sapolsky 2004, op. cit. McEwen & Gianaros 2010). Several conceptual models of SES related health disparities posit that life experiences inherent to socioeconomic position at individual, familial and community levels could negatively influence well-being and increased disease risk through stress-related pathways (Adler 1993, op. cit. McEwen & Gianaros 2010; Marmot 2004, op. cit. McEwen & Gianaros 2010; Sapolsky 2004, op. cit. McEwen & Gianaros 2010; Kelly et al. 19987, op. cit. McEwen & Gianaros 2010). Risky family dynamics (e.g. aggressive and harsh parenting) and associated early life stress may alter risk trajectories for ill health in later life (Repetti et al. 2002, op. cit. McEwen & Gianaros 2010); and individuals living in low SES neighbourhoods are more frequently exposed to stressful life events (Dohrenwend 1973, op. cit. McEwen & Gianaros 2010; McLeod & Kessler 1990, op. cit. McEwen & Gianaros 2010).

Following from our primate inheritance of dominance hierarchies, human societies are stratified according to status (Charlton 1996). Individuals with higher performance capacities and health would occupy positions of higher social standing, with natural selection ensuring relatively higher reproductive success (on average) of those occupying higher-ranking positions than those of lower status. According to the interpretation of Charlton (1996), health is a consequence of access to resources, implicating an association between socioeconomic position (SEP), resources and health (SEP → resources → health → fertility association). Such associations are reflected in agricultural societies where substantial differences in age at death, stature and evidence of pathology between the rich and the poor are evident. This applies as psychological processes firstly translate status into resources and then translate resources into health. Status differentials are thus translated into economic stratification whenever an

economy generates a surplus of resources (Barkow 1992, op. cit. Charlton 1996); resulting in fine-grained differentials in health which are resolvable both between and within social class when SEP is defined in terms of small increments of income, occupational status or educational attainment (Davey Smith et al. 1990, op. cit. Charlton 1996; Feinstein 1993, op. cit. Charlton 1996; Marmot et al. 1984, op. cit. Charlton 1996; Marmot et al. 1991, op. cit. Charlton 1996; Kunst & Mackenbach 1994, op. cit. Charlton 1996; Mackenbach 1994, op. cit. Charlton 1996). With health as one of the pre-requisites for reproductive success, natural selection for capacites to maintain organismal integrity over the childbearing age span is implicated; involving mechanisms for repair of errors in DNA transcription, inter-cellular control mechanisms and processes of organism-wide homeostasis involving immune, endocrine and nervous systems (*vide* Charlton 1996).

However, although substantial inequalities in health prevail, status-based differentials in reproductive success have currently disappeard or reversed in many cases (Symons 1979, op. cit. Charlton 1996; Ridley 1994. op. cit. Charlton 1996; Buss 1994, op. cit. Charlton 1996).

According to the interpretation of Charlton (1996), health is a consequence of access to resources, implicating an association between SEP, resources and health (SEP → resources → health → fertility association). Accordingly health and associated fertility were considered to be based on enhanced access to resources (refer to Rickard et al. 2010). Alternatively, the interpretation presented here is that a positive association between SEP and health underpinned the positive association between SEP/SES and fertility; as long as the LHS-mode PM predominated (High SEP/health → resources → fertility. Low SEP → low resources → resource-constrained lower fertility). This interpretation implies that good access to resources does not necessarily ensure a positive SEP/health association. A break-up of the SEP-health association resulting in progressively lowered fertility manifested during the first demographic transition (Table 2.3.3n: 1870-1930 onwards). Individuals of higher SES were impacted to a greater extent due an earlier onset of patho-information-engram accumulation in high SES lineages (2.2.2j). At this stage resource deficit conditions no longer constrained fertility in lower socioeconomic strata and an inverse association between fertility and SES is commonly observed (Tables).

The declining relative fertility of high SES individuals during the FDT is attributed to a break-up of the SEP-health combination, compromising fertility. An explanation is now required why low SES individuals have (marginally) higher fertility rates than higher SES individuals during the SDT in spite of the higher incidence of disease states being associated with the former (as outlined above).

According to the principle of differential susceptibility (Pluess & Belsky 2013), plasticity of high-SES individuals implies greater sensitivity to adversity, including population density stress (2.2.1d). As population density increases towards environmental carrying capacity, intraspecific competition increases (Geist 1978). The adaptive response to such competitive conditions for higher-SES individuals is to produce high quality competitively competent offspring through slow-LHS-mode realization (fewer high quality offspring; later life fertility realization). Low SES individuals, with greater resilience rather than plasticity, are less vulnerable to psychosocial stress (based on fast-LHS expression coping with harshness and unpredictability; higher quantity of offspring; early life fertility realization: 2.2.2c/2.2.2d) and their fertility expectantly less negatively affected by population density stress.

Low functional energetic potency due to progressively accumulated PIE loads is prevalent during this phase (the SDT: LHS-mode M:4: 2.2.2e), bringing on an accentuated P-M trade-off (2.1.2; 2.2.1d). In high SES individuals (inherently endowed with high plasticity in respect of both P- and M-type LHS-mode expression, but reduced resilience capacity: 2.2.1d), an accentuated P-M trade-off results in extremized P-type and M-type expression. Extremized P-types are in high performance LHS-mode (high metabolic turnover) at the expense of health (2.2.1; 2.2.2j). Extremized M-types exhibit low P-vitality and slow-LHS-mode realization (late fertility realization). In high SES individuals, fertility is reduced in extremized P-types due to associated health constraints and unfavourable conditions for early fertility realization pertaining to high SES individuals. Fertility of extremized M-types is constrained as a result of pronounced fertility postponement, leaving little leeway for fertility recuperation at advancing ages. Reduced reproductive vitality and narrow childbearing age ranges accordingly result in depressed fertility in high SES individuals.

Resilience in coping with harshness and unpredictability of low SES individuals is based on fast LHS realization (2.2.2c: Harshness-Unpredictability); involving high performance (P) capacity (2.2.2d) manifesting in early life fertility realization (many offspring, quantity rather than quality of progeny, early onset of reproduction). Due to low functional energetic potency of individuals applicable in this phase (SDT), accentuated fast-slow LHS-mode trade-off constraints underpin a fixation of an intensified fast LHS-mode in low SES individuals. This then manifests in fast ageing and associated compromised health; but fertility realization is less constrained than in high-SES extremized P- and extremized M-types.

Fitness is maximized when P-M trade-off constraints are minimized, i.e. as prevalent on the basis of a good fundamental health status. Especially for high-SES individuals it is important that high performance realization (underpinned by fast-LHS-mode expression) is not at the expense of life time reproductive success in respect of high quality offspring underpinned by slow-LHS-mode realization. Fitness is maximized through the combination of early reproduction and high lifetime reproductive success (Korpelainen 2003), as supported by fast and slow LHS-mode expression respectively. Under high P-M trade-off constraints (accentuated fast-slow LHS-mode trade-off relationship), the associated narrowed childbearing age range negates fitness maximization.

During the current/advanced stage of the SDT with country-specific TFRs generally below replacement level, the negative relationship between fertility and higher SES is seemingly reversed in Nordic countries when taking education level as proxy for SES. For the years 2007-2011(Eurostat 2013), TFRs (annual averages) of women with low education (ISCED 0-2) ranged between 1.82-1.86, intermediate education levels (ISCED 3-4) between 1.35-1.47 and for those with high educational levels (ISCED 5-6) between 1.53-1.58. Generally, the fertility of women with medium education (ISCED 3-4) had decreased more so than of women with low and high education (Eurostat 2013). In contrast to countries such as Austria, Spain and of eastern Europe (Czech Republic, Slovakia, Slovenia, Estonia, Romania), in Nordic countries of Denmark, Finland and Norway women with the highest education had the highest fertility. This deviation from the general trend of an inverse association of fertility and high SES performance expression during the SDT can be explained by an attenuation

of fast P/slow M-LHS-mode trade-off constraints prevalent in more northern European countries on the basis of inherent LHS predispositions shaped by cold-adaptation and low levels of heterozygosity (Table 2.3.3b), supporting relatively increased childbearing age spans in Nordic countries (2.3.3d).

2.3 Consequences of reduced vitality (reduced functional energetic potency)

2.3.1 Vitality status and brain functional integration

According to MacLean (1990) the brain (triune brain) consists of the reptilian complex, the paleomammalian complex (limbic system) and the neomammalian complex. The reptilian complex is considered responsible for species-typical instinctual behaviour relating to self-preservation (defense, reproduction, territoriality).The paleo-mammalian complex (termed the limbic system by MacLean 1990) is related to behaviour in respect of intra-societal functionality (motivation and emotion relating to rearing and social cooperation/harmony). The functional compex of the neocortex involves, *inter alia*, language, abstract thinking, insight (perception), conceptual thinking, planning ahead and problem solving.

Instinct relates to self-preservation and reproduction (genetic representation into the future); emotion to intra-group altruism and emotional intelligence (intra-group altruism later replaced by diffuse cosmopolitan altruism) and ratio is notably involved in the capacity for problem-solving. Peak realization of these brain functional domains (self-preservation instinct, emotio/altruism and ratio) are potentially subject to conflicting trade-off relationships. Instinct impairment (Instinktabschwächung) and compromised access to intuition (Intuitionsblockierung) are, according to the principles of functional-energetic trade-off constraints, particularly pronounced in individuals with a predisposition to increased capacities in the domains of emotio and ratio.

The realization of a value system with evolution-competent leadership potency requires *inter alia* brain-functional integration based on a relatively high vitality status. Brain-functional integration regarding instinct, emotio and ratio requires sufficient functional metabolic energy which is not available with a low vitality status on the basis of an increased Patho-Information-Engram (PIE) loading (2.1.2). Systems-functional

allocation trade-off constraints (Allokationsabtausch) between instinct, emotio and ratio prevail. For example, functional-energetic metabolic trade-offs between intelligence and instinct (entwurzelte Intellektuelle) or emotion and instinct, results in a weakening or loss of instinct vitality.

Multidimensional cognition

Trade-off constraints are also applicable in terms of cognition at the conscious versus the subconscious level: in low vitality individuals strong cognitive expression/capacity in the conscious domain is at the expense of cognitive performance in the subconscious domain.

Thus, with an increased Pathogen-Information-engram loading and associated endogenous functional-energetic constraints (low vitality status: 2.1.2), a loss of capacity for intuitive-deductive-visionary thinking (syllogistic thinking; strategic long-term thinking) is implicated. Holistic perspectives with intuition and in-depth understanding of complex systems are impaired. Access to intuitive knowledge is in a trade-off relationship with ratio (Laszlo 2014b). Also the loss of the intuitive belief in a higher authority to whose laws our lives/fate is subordinated to (Verflachende Gottgläubigkeit).

Laszlo (2014a): The Akashic paradigm recovers an ancient insight: the presence of a deep dimension in the cosmos (**AS: refer also to Laszlo 2014a: 2.1.2a; Table 2.1.2a**). This A-dimension is the record and the memory of all the things we experience; it connects all things with all other things; it conserves the trace of all that has alreasdy happened and it "in-forms" all that is yet to happen (**AS: "embodied" in the kharmic information entity: 2.1.2b**). In the context of human experience the Akashic deep dimension is a source of intuitions, hunches, creative ideas, and sudden insights.

We have two distinct systems in the brain that process information: the classical neuroaxonal network and the quantum-level microtubular network (Frecska & Luna 2006, op. vit. Laszlo 2014a). The neuroaxonal network gives us the "perceptual-cognitive-symbolic" mode of perceiving the world, and the microtubular network offers a direct-intuitive-nonlocal mode. The perceptual-cognitive-symbolic mode dominates consciousness in the modern world; information processed in the direct-intuitive-nonlocal mode is mostly filtered out.

The sea of Akashic information includes the species-specific pattern that is the natural "attractor" of healthy functioning in the organism. This pattrern results from the long-term interaction of a species with the A-dimension; it is the enduring memory of those interactions; and it codes the generic norms of viable species (see Ságі 1998, op. cit. Laszlo 2014a). For humans beings it is the equivalent of the *Qi* of Chinese medicine, the prana of Hindu philosophy, and the *life energy* of the traditional Western healing arts. Without access to Qi, prana or life energy, errors in cellular and organic interaction, reaction, and transcription would accumulate in the body and would lead

to evermore serious and ultimately terminal malfunctions. This is inevitably the case - for biological organisms on this planet are inherently mortal – but the species-specific "Qi attractor" slows the degenerative processes and enablres the organism to unfold the full potentials of its inherent vitality.
In traditional societies people made more effdective use of the Akashic Qi attractor in maintaining their health. Shamans, medicine men and women, and spiritual leaders were remarkably accomplished in safe-guarding the physical condition of the people in their tribe, village, or community (**AS: vitality-based access to multidimensional cognition**).

2.3.2 Vitality status and energy allocation response modes

a) Fight-flight response modes.

Stress responses. The general adaptation syndrome is triggered by challenge- or stress impulses and involves a response pattern (alarm phase, resistance phase, recovery phase) to these stimuli with attack or flight behaviour. The initial alarm phase in situations of danger then enables peak performance in fight or flight (Selye 1953; Selye 1978). With continuation of the challenging situations or their frequent repetition, interim recovery phases are too short and a state of increasing exhaustion sets in (exhaustion phase: Selye 1953; Selye 1978); with consequences detrimental to health. As a result of a low fight-flight reaction threshold, the sympathetic nervous system functionality dominates at the expense of parasympathetic functionality (reduced stress resistance). A low fight-flight reaction threshold manifests in alternating phases of hyperaggression (fight mode) and flight behaviour. Win-win behaviour, however, requires efficient brain functional integration on the basis of sufficient functional-energetic potency (vitality). An advanced state of recursion healing (Patho-Information-Engram load deletion) promotes increased vitality and therewith kharmapositive win-win behaviour. Individuals with high vitality and thus high fight-flight thresholds were characterized by Geist (1978): High quality individuals will be alert, sensitive, curious, show a readiness to explore, control their behaviour well, rarely panic and learn readily and well. They also, have a higher rate of metabolism, higher threshold of pain and a relatively high rate of food consumption.

Win-win versus win-lose behaviour.
Low vitality often fosters a sense of inferiority (low self-respect accompanied by low respect for others and win-lose behaviour). With a relatively high vitality status the

basic reaction to challenges manifests in non-reaction based on inner harmony and strengh, that is, neither aggression nor flight; but rather the maintenance of position (standing your ground response; Invincibility: Sun Tzu: Art of War). Conflict resolution is pursued in win-win mode. With a low vitality status the body evaluates itself as relatively weak (subconsciously). An associated low fight-flight reaction threshold then results in fight behaviour already at the slightest challenges (exaggerated aggression in win-lose mode) or flight reactions (psycho-allergies; escapism, reality withdrawal). Generally increased inter-personal aggression is observed and leaders primarily apply win-lose strategies in pursuit of their goals. Furthermore, a mode of spontaneous immediate reactivity at low fight-flight reaction thresholds is also associated with a narrowed reality span of individuals in general (reality span: for how long into the future is reality still considered relevant). A short time horizon then predominates (short reality span; time span perception of within which future realities are perceived as relevant to the individual). A low fight-flight reaction threshold tends to induce focusing on the presence (crisis management) at the expense of strategic long-term thinking (recognition of the essential baseline). Competition behaviour: competition within oneself, in pursuit of self-realization of ones own inherent potential (win-win: Invincibility) *versus* competition relative to others; achievement of a competitive advantage (Win-lose: at the cost of *Invincibility* and *Take Whole* principles *re* SunTzu: *The Art of War*); that is, at the cost of the principles and strategies required for successful, long-term national conservation (Volksschutz).

A low fight-flight reaction threshold (due to low vitality: high PIE-loadings) further compromises brain functional integration (2.3.1): when low, we find a spontaneous locking into the fight-flight mode (instinct, self-preservation), thereby initially cutting out any emotional and rational intelligence. Debating individuals with a low fight-flight threshold (low subconscious self-worth perception) experience contrasting opinions as a challenge/attack to their identities (challenges to their self-preservation/self-assertion). Any discussions or negotiations then follow in win-lose mode and remain subjective and unprofessional.

Population density stress. A low fight-flight reaction threshold furthermore results in stress proneness and interpersonal intolerance within society; particularly potentised under population density stress (Knaul 1985). Continuing stress impacts then result in the exhaustion phase (General Adaption Syndrome; Selye 1953); associated with

manifold physical and mental disorders. This is also, *inter alia*, associated with reduced fertility and increased patho-information-engram loading (2.1.2) in respect of the fetus (procursion) during pregnancy, with negative health outcomes during the later course of life of the new-born (2.2.1b). Sympathetic overdrive (autonomous nervous system) and an associated low fight-flight response threshold implies a predominance of the sympathetic performance mode at the cost of parasympathetic functionality (Table 2.3.2a). Insufficient parasympathetic functional efficiency is, *inter alia*, associated with low digestive efficiency, poor sleep quality and compromised female reproductive body condition (Table 2.3.2b).

High population densities provide the setting for intense peer competition and trains children in the art of aggression/overt aggression from an early age onwards, but to the detriment of intellectual development (op. cit. Geist 1978). Other factors that enhance aggression in children are maternal lack of self-esteem, chronic family disorders, punitive discipline, low performance demand on children and low degree of supervision and care by parents (op. cit. Geist 1985).

Summary: Low fight-flight response threshold (low vitality):

- Win-lose behavioural reaction mode (contrsasting win-win behaviour from a position of strength)
- Associated with stress proneness; low interpersonal tolerance and compromised
- Follows from and exacerbates high population density effects.

b) Energy allocation in the sociobiological context.

Sociobiological consequences of reduced instinct vitality. Dominance of win-lose behaviour: intra-societal polarization according to vitality status: conservative *versus* liberal. Conflict between generations (Lorenz (1986; Meves 1984). Meves (1984): loss of values; the road to radicalization, loss of sense of reality; reduced birth rates; drug addiction and confused gender role non-acceptance. Based on extended career experience (Psychagogin), Meves (1981) describes the distress experienced by the youth and the family in modern, highly civilized societies (e.g. behavioural disorderliness of children; adolescent neuroticism; about the difficulty of being happy

under conditions of affluence; levelling of gender differences; weakening of the traditional family model and consequences thereof for children).
A quantum jump of increased Patho-Information-Engram loading from the parental generation in relation to their youth can be identified as causative of the conflict between the generations (Generationskonflikt). (Wertekonservatismus → Werteverlust: Lorenz 1986).

Low vitality in males due to allostatic load effects (2.1.2a: Table 2.1.2b; patho-information-engram load accumulation: 2.1.2), as associated with sympathetic overdominance, is characteristically manifesting in aggressiveness in response to even low-grade challenges or flight behaviour in order to escape from challenges (low fight-flight reaction response thresholds). Female allostasis under sympathetic overdominance (energy-expensive) underpins female competitive assertiveness, but at the cost of allostatic load effects (suppressed parasympathetic functionality: disturbed energy balance/body condition for female reproductive vitality; stress proneness: low response reaction thresholds). Gender role complementarity (win-win patriarchal value system underpinning male protection and provisioning roles) is compromised. Erosion of patriarchal value system in low vitality males (win-lose competition) takes effect, and gender role competitiveness (for power) emerges; overall leading to declining gender role complementarity and differentiation (Table 2.3.2b).

Table 2.3.2a Autonomic Nervous System

The autonomic nervous system (ANS) is part of the peripheral nervous system controlling internal organs and various body functions. It also represents the primary mechanism controlling the figh-flight response (Schmidt & Thews 1989). The ANS has two branches, the sympathetic nervous system (fight and flight) and the parasympathetic nervous system (rest and digest; feed and breed).

Sympathetic-parasympathetic functionality (MacLean 1990)
Parasympathetic functions: **Assimilation of food**, the cranial nerves of the parasympathetic division activate salivation and the secretion of digestive juices (including salivary gland and gastric acid secretion), relax the sphincters separating the various compartments of the gut and induce peristalsis. Following assimilation, parasympathetic activity promotes the **storage of sugar, fat and protein**. (**AS: importance of after-meal resting**). Increases blood flow to the gastrointestinal tract, accelerates peristalsis and mediates digestion of food and absorption of nutrients. Cleaning/eliminative functions (of the gut). Preparation of the organism for **rest and sleep**: parasympathetics slow heart and respiration rates; reduce the stimulating effect of light. Parasympathetic participation/activation in the act of

procreation results in genital tumescence and the production of lubricative secretions.
Sympathetic functions: The sympathetic division comes primarily into play in dealing with exigencies of the external environment. In times of **emergencies or excessive exertion**, the sympathetics call up body resources required for survival; i.a. during combat or vigorous exercise (augmented blood supply to working muscles, increased pulmonary ventilation, increased action of the heart, rise in bood pressure, energy supply through release of glucose, shortened blood clotting time). While the stressful situation continues, sympathetic inhibition results in the cessation of digestive processes. Sympathetic activation of thermoregulation. In the act of procreation, parasympathetic activation results in genital tumescence and the production of lubricative secretions, while sympathetic impulses trigger ejaculation.
Male metabolism: capacity for maximum performance in sympathic mode (HMT; relatively high BMR setting). Female metabolism: capacity for reproduction in parasympathetic mode: low stress, nutrient/fat sorage (LMT; relatively lower BMR setting). There is a trade-off between the capacities for efficient male-typesympathetic and female-type parasympathetic functionality; which is optimized through complemetarity of metabolic gender differentiation for fitness maximisation.
Parasympathetic functions and allostasis Allostasis is the process of adaptation that helps the body to maintain homeostasis. Allostatic load is the cost of excessive adaptation and reflects overactivity of chemical mediators involved in adaptation. It reflects an imbalance in the activity of mediators, e. g. inflammatory cytokines with inadequate glucocorticoids or excess excitory amino acids in brain after stressor; elevated glucocorticoids, insulin, catecholamines in relation to abdominal obesity and Type 2 diabetes. The parasympathetic and sympathetic components of the ANS control the involuntary body functions, whereas the enteric nervous system is involved primarily with the internal regulation of the gustatory processes. Blood pressure change patterns. Blood pressure normally falls during the night (the so-called dipper pattern). In some hypertensive patients the blood pressure does not dip at night (non-dippers) and this represents a form of allostatic load that may contribute to the damage caused by chronic hypertension. Non-dippers: this would be consistent with a failure to reduce sympathetic and to increase parasympathetic activity during the night and with the failure to lower blood pressure. Regulation of satiety via vagus and gut.
McEwen, B., Bullock, K. & Stewart, J. (1999). Parasympathetic function. Summary. Research: Allostatic Load Notebook, MacArthur Research Network on Socioeconomic Status & Health, University of California, San Francisco, USA.

Low fight-flight reaction thresholds, implying a predominance of behaviour in the sympathetic state of the autonomous nervous system (supporting staying power, endurance, assertiveness: testosterone-supported functionality) is suboptimal for female reproduction which is underpinned by parasympathetic functionality (MacLean 1990, Knaul 1985).

c) Gender role specialization and complementarity.

Substantial inherent functional differences exist (*inter alia* hormonally) between men and women (Brizendine 2006, 2010). An evolutionary-competent complementarity of gender roles was/is pre-programmed (Table 2.3.2b). In a state of weakened vitality and associated loss of instinct the respective gender roles are no longer fully accepted and lived, with negative consequences in respect of long-term national survival (Knaul 1985; Declinig birth rates: Meves 1981, Meves 1984).

Cunnane and Crawford (2003): In the past 2 million years the hominid lienage leading to modern humans involved significantly larger and and more sophisticated brains than other primates. According to the interpretation of Cunnane and Crawford (2003) the human brain was the product of having evolved fat babies. Body fat in human babies provides three forms of insurance for brain development: 1) a large fuel store in the form of fatty acids in triglycerides; 2) fatty acid precursers to ketone bodies which are key substrates for brain lipid synthesis; and 3) a store of long chain polyunsaturated fatty acids, particularly docosahexaenoic acid, needed for normal brain development. The role of a high quality diet in human brain development is being increasingly recognized (Leonard et al. 2003): levels of body fatness are relatively high in humans, notably in infancy; providing a ready supply of stored energy to feed the relatively large brain. Fire and cooking in order to make plant food (especially underground storage organs) more digestible, thereby providing more usable calories than if the same food had been consumed raw. Resulting in a substantial increase of food availability (Wrangham et al. 1999). A high quality diet involves more fat and meat (higher concentrations of nutrients and energy) and less plant material. Genes controlling fetal fat deposition needed to be expressed because fat deposits are needed as insurance for the developing brain (Cunnane & Crawford 2003). This required long-term stability in the maternal nutrient and energy supply during pregnancy and lactation.
Humans respond to their environment with adaptive forms of energy storage in order to increase reproductive success (providing for the costs of reproduction in human females includes the production of a mature follicle, preparation of the endometrium for implantation, gestation and lactation). The energetic costs of late gestation and lactation are provided for through anticipatory adipose storage. Such fat stores are are primarily mobilised during the third trimester to support fetal adipose accumulation

and brain growth and after birth for lactation (Ellison 2008; Table 2.3.2b). The probability of conception is thus highest when females are in positive energy balance when gaining weight, but less so when losing weight or maintaining a steady weight but are subject to conditions requiring high levels of energy expenditure. Positive energy balance and lower energy flux result in higher ovarian steroid levels, correlating with higher conception rates (Jasienska et al. 2006; Jasienska 2003).

Humans have evolved a large and energetically expensive brain (Leonard et al. 2003). According to Cunnane and Crawford (2003) the fattest infants become mentally the fittest adults, implying that the impact of infant nutrition has lifelong consequences. Human newborns and exclusively breastfed babies are in a metabolic state of ketosis (Cunnane and Crawford 2003). Ketosis is a metabolic state when the body uses fat as fuel in preference to glucose (derived from carbohydrates and sugar). The body makes ketones from fat when dietary glucose is low. Ketones are then used as fuel to produce energy and the brain. In the second half of pregnancy ketones supply as much as 30% of the energy required by the foetal brain, implying that ketones are essential for foetal brain development (Cunnane and Crawford 2003). After birth, newborns adapt to using their fat stores as their primary fuel source and begin to produce more ketones; converting stored fat and breastmilk into ketones (Cunnane and Crawford 2003). Ketones provide them with energy between feeds and play a role as key building blocks for brain structures. Breastmilk is high in fat (55%, 39% carbohydrates, 9% protein). Exclusively breastfed babies are in a state of mild ketosis. Breastfed babies experience better cognitive performance, a lower incidence and severity of infectious diseases, lower rates of sudden infant death syndrome, certain cancers, food allergies, asthma, diabetes and obesity. Infants should be exclusively breastfed for the first six months and breastmilk should be the main source of nutrition for the first year of life (World Health Organization. 2015. Breastfeeding). Human brain development during gestation and the first few years of life is enhanced, since during this phase the brain is best at processing /utilizing ketones (Prins 2008).

Table 2.3.2b Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution (Ellison 2008)
High metabolic costs and physical activity compete for energy available for reproduction. High basal metabolic rates, typically associated with the periarctic metabolic performance syndrome (Table 2.4.1.1a), are energetically costly in absolute terms (costs associated with large body size, pronounced

muscularity, high costs of thermoregulation). Relatively small differences in body size (lower by 5-10 kg) can result in substantially reduced metabolic costs (Snodgrass & Leonard 2009). Sex-based division of labour, by transferring more of the energetic burden of physical activity to males (low metabolic costs of reproduction) supports conservation of metabolic energy for females, with comparatively high energy requirements for reproduction (reviewed by Ellison 2008).

Multiple variables are involved in female reproductive capacity and fat stores, energy balance and energy flux (rate of energy turnover) influence ovarian function and fecundity. Fat stores (energy status) represent the amount of stored energy that can be mobilized for reproductive processes. Energy balance relates to the net residual of energy intake minus energy expenditure that can potentially be allocated to reproduction and energy flux refers to the absolute level of energy turnover. Ovarian function is highly sensitive to energetic conditions, that is, relatively small changes in energy expenditure, energy intake or energy stores have been linked to rapid responses in ovarian hormone levels. This responsiveness to energetic parameters serves to optimize energy allocation to reproduction through synchronization of conception with favourable energetic conditions of maternal energy availability; thereby supporting reproductive success. The association of calorie restriction, weight loss and emaciation with menstrual disruption is well documented. At the other extreme, obesity is associated with anovulation and menstrual irregularity (op. cit. Snodgrass & Leonard 2009).

The review by Ellison (2008) focused on energetic trade-off constraints between reproductive effort and other demands for metabolic energy (metabolic energy availability as opposed to energy available from the environment).

1. The fecundity of non-pregnant, non-lactating women is sensitive to metabolic energy availability.
2. Early fetal loss is sensitive to metabolic energy availability (also to other forms of stress).
3. Fetal growth is sensitive to metabolic energy availability. Considerable evidence suggests that the birth weight of babies at term depends on maternal energy availability. Maternal nutritional status at the beginning of gestation and the rate of fat gain during early pregnancy are strong indicators of fetal growth.
4. Fat storage in pregnancy is a high metabolic priority, establishing reserves to be mobilized in late pregnancy and during lactation. During the final weeks of pregnancy and lactation maternal fat stores are rapidly mobilized to meet the demands of the growing fetus and developing infant. This occurs even in women living under favourable energetic conditions. Growth and development of the human brain is energetically very expensive (Leonard et al. 2003), placing an energetic burden on maternal metabolic energy reserves. The ability to store fat early in pregnancy is accordingly considered critical for reproductive success.
5. The duration of gestation is positively associated to metabolic energy availability (although buffered by offsetting effects).
6. Resumption of fecundity postpartum is sensitive to energy availability.

Energy available early in development may influence reproductive effort in adulthood.

Gender differentiation also manifests in the relative prominence of sympathetic and parasympathetic functionality of the autonomic nervous system (MacLean 1990). Sympathetic functions (MacLean 1990) as supported by metabolic performance based on relatively high BMR settings: The sympathetic division comes primarily into play in dealing with exigencies of the external environment. In times of **emergencies or excessive exertion**, the sympathetics call up body resources required for survival; i.a. during combat or vigorous exercise (augmented blood supply to working muscles, increased pulmonary ventilation, increased action of the heart, rise in bood pressure, energy supply through release of glucose, shortened blood clotting time). While the stressful situation continues, sympathetic inhibition results in the cessation of digestive processes. Sympathetic activation of thermoregulation. Parasympathetic functions (MacLean 1990) are optimized by functionality at relatively low metabolic turnover rate settings: **Assimilation of food**, the cranial nerves of the parasympathetic division activate salivation and the secretion of digestive juices, relax the sphincters separating the various compartmentsof the gut and induce peristalsis. Following assimilation, parasympathetic activity promotes the **storage of sugar, fat and protein**. Cleaning eliminative functions (of the gut). Preparation of the organism for **rest and sleep**: parasympathetics slow heart and respiration rates; reduce the stimulating effect of light.

Following Knaul (1985), research established a relationship between hyperuricemia (enhanced uric acid stimulation of the cerebral cortex). Individuals with hyperuricemia displayed a higher intellectual/mental and generally higher performance; favouring *inter alia* the advancement into higher social positions. When allocated to groups from labourer to solicitor, from teacher to professor and director, uric acid values increased from goup to group. Male values were notably higher than those for females (Knaul 1985). Uric acid values apparently index high metabolic turnover

functionality which forms the basis of enhanced performance in sympathetic mode of the nervous system. Such is supported by a relatively high BMR. In terms of male/female metabolic complementarity: high versus low metabolic turnover performance settings. Male performance capacity in sympathetic nervous system mode (competitiveness, +) versus female reproductive performance, requiring body condtion (based on energy storage) as supported by functionality in parasympathetic mode.
In contrast, male fecundity *per se* is comparatively insensitive to energy availability. However, other features linked to male reproductive success such as body size, muscularity (body mass as a form of somatic reproductive effort), testosterone-based performance capacity under stress and social status require relatively high basal metabolic rates and are thus are energetically expensive; but compromise longevity relative to females. (see also 2.2.1c: uric acid as performance catalist)
As has been outlined, reproduction is very demanding on the energy metabolism in human females (Jasienska 2003). Any demands placed on female physiology resulting in an increase of basal metabolism, such as increased physical activity, results in energy costs at the expense of reproduction. Increased basal metabolism also interferes negatively with fat accumulation during pregnancy (of notable importance for lactation). Such increased basal metabolism of females increases their vulnerability to conditions of energy deficits, inducing reproductive suppression as an adaptiv response (Jasienska 2003).
As indicated above, female reproductive effort is more sensitive to constraints of metabolic energy availability than in the case of males. Also, female fecundity is of greater consequence for population level fertility. Natural seletion favours the optimal allocation of energy and other limiting resources to reproduction. **From the above it can be concluded that inherently differentiated sex-specific metabolic specializations are represented in males and females, with adaptive complementarity and implications for gender role differentiation.**

Huber et al. (2010): For contemporary US women, childnessless decreases with higher income of their husbands. Increased own income of women and age at marriage increased their chances of remaining childless; while higher education of women and higher income levels of their husbands decreased such probabilities. The number of children a woman has is positively associated with the income of her husband, but negatively with her own income. Women older at marriage and with higher educational levels (due to postponement of reproduction associated with longer education and labour force participation) have lower numbers of children. Number of children among highly educated women were positively associated with income levels of their husbands. Women are expected to adjust their reproductive output according to resource availability and preferentially select mates who provide access to more resources (op. cit. Huber et al. 2010). This is borne out by the findings of this study (Huber et al. 2010) and consistent with gender-specific energetic constraints (refer to Table 2.3.2a); underpinning traditional, complementary gender role differentiation (***fitness maximizing gender role complementarity***: males - provisioning and protection; females - having and successfully rearing of children).

The traditional male role is however not only about provisioning, but also protection; implying *inter alia* the minimization of stress to which women may be subjected to. Father absence is considered a risk factor for undesirable developmental outcomes such as early sexual activity, teenage pregnancies and unstable marriages later in life (*inter alia* Ellis et al. 2003). Psychological stress activates the hypothalamic-pituitary-adrenal (HPA) system; resulting in altered levels of stress hormones, especially cortisol (which may have long-lasting/permanent deleterious effects). Chronic activation of the HPA system has been implicated in the early activation of the hypothalamic-pituitary-

ovarian system which, *inter alia*, controls onset of puberty in women (op. cit. Chisholm et al. 2005). Father presence/absence may cue reproductive strategies (Draper & Harpending 1982) or may alter parental care patterns influencing development (Ellis et al. 2003). Studies found that children with two parents spent more time at home and with their mothers than father-absence children. Also, shorter durations of breastfeeding were detected among father-absent children (op. cit. Quinlan 2003).

The biological stress response is implicated to link direct parental care to reproductive development (Belsky et al. 1991). AS: When children experience harshness/unpredictability in their environment (an experience to which children are seemingly partly psychologically shielded against by father presence), a fast LHS-mode is cued (Section 2.2.2c). Unresponsive parenting is positively associated stress levels in children (as indicated by cortisol) and children of single mothers tend to have elevated cortisol levels (op. cit. Quinlan 2003). In addition to more overt forms of pretection provided by males, the role of fathers in minimizing maternal stress during all reproductive/rearing phases is thus of crucial importance for parental reproductive success (refer also to 2.3.2).

In humans the long juvenile period coevolved with other life history traits (such as multigenerational resource flow, grandparental investment, male provisioning and protection: Kaplan & Lancaster 2003; Kaplan et al. 2000); allaying juvenile mortality. This coevolution enabled the long juvenile period required for the development of the powerful human brain.

Importance of family

Gallagher (2002):

d) Evolution-competent leadership

Loss of vitality status has also resulted in the demise of evolution-competent leadership (as based on instinct vitality, brain-functional integration and win-win potency).

Maxwell (2007): In order to attract support a leader must possess charisma (have influence, be respected, magnetism). Who you are is who you attract. People naturally follow leaders who are stronger than themselves. Leaders must be able to make ***intuitive, instinctive*** assessments. Who you are dictates what you see. A leaders potential is determined by those closest to him. Only ***secure*** leaders give power to

others. Leadership is about empowering others (win-win). A ***mindset for victory***. Natural ability and learned skills create an informed intuition that makes leadership issues jump at leaders (**AS: capacities underpinned by brain-functional integration, high fight-flight reaction thresholds and psychological integrity for win-win behaviour re Sun Tzu**).

The majority of people in a population do not think according to a broader spatiotemporal context, that is, they are present-orientated and mainly concerned about their daily existential needs. Evolutionary-competent leaders of a group, by embracing a broader range of survival-promoting issues and longer time horizons, can enhance evolutionary fitness for the group they lead. Evolutionary fitness implies, at the most basic level, that prevailing reproductive patterns pertaining to members of a group provide for the sustained persistence of lineages into future generations.

Evolution-competent leadership is based on *inter alia* instinct vitality, brain-functional integration and win-win potency; i.e. leadership capacities promoting fitness maximization relating to the populations they lead.

Table 2.3.2c Evolution-competent leadership capacity	
Win-win strategies in pursuit of national interests (Table 1.1d: Kharma-positive life mastery *re* Sun Tzu) and social harmony (2.3.2abc).	Domestic- and foreign policy
Long-term time horizon: priority of long-term population preservation of the ethnogenetic-territorial entity	Value system: protection duty over profit pursuit (rights)
Quality of life and environmental conservation (Safeguarding of the ethnogenetic-territorial entity)	Green architecture and technologies, biological agriculture
Facilitation of fitness maximizing behaviour in respect of the ethnogenetic entity	Family and population policies (2.3.3g); amelioration of population density stress; holistic health care

2.3.3. Demographic transitions

Refer to 2.2.2e: Life history strategies: contectual framework for health and fertility.

a) Demographic transitions: patterns and perspectives

Demographic transitions are considered to be central phenomena in the context of the rise and fall of civilizations. In this section summaries are presented of numerous studies and reviews in order to provide a comprehensive overview of characteristics and perspectives held in respect of demographic transitions. Comments are inserted mainly with reference to the Life History Strategy (LHS) explanatory framework (2.3.3e and section 2.2.2e) in parentheses (**AS:**). Highlighting by AS in bold and italics. Two demographic transitions are generally recognized, a first and a second demographic transition (SDT). Refer to Coleman (2004) for placing this differentiation into perspective. The work by numerous authors regarding demographic transitions is summarized and presented below; outlining a varity of demographic patterns, associated proximate associations of socioeconomic, social and ecological factors; and perspectives as to possible causality of these. An explanatory framework seeking ultimate causality is presented in the next section below (**2.3.3e: Demographic transitions: a life history strategy, LHS, explanatory framework**).

Pretransition demographic patterns

Müller et al. (2002), for historical French-Canadian cohorts (1600-1800s), found that increased fertility was linked to increased post-reproductive survival and that the extended postreproductive life expectancy was tied to late births. Thus, a positive association between fertility and longevity was evidenced during pre-transformation years. No effect of sibling death on adult lifespan was detected for the period 1800-1854; but for the period 1855-1880 (when mortality had declined), when sibling death had become a negative predictor of later life survival (Gavrilova et al. 2003). Absence of a mortality-longevity trade-off before c. 1850, but a negative association between juvenile mortality and longevity thereafter.

First Demographic Transition

Dribe et al. (2014, 2017): The progressive fertility decline during the late 1800s and early 1900s has been associated with changes following the transition from an agricultural-based economy to an industrial economy; characterised by a sustained mortality decline, increased levels of urbanization, expansion of education and increasing female employment (op. cit. Dribe et al. 2017; Brown & Guinnane 2002).

The fertility decline was led by the upper and middle classes. Dribe et al. (2017) posed the question whether this pattern was due to socioeconomic factors first affecting the upper and middle classes or whether it was related to diffusion of innovations/ideational changes from upper to lower social strata. Prominent in the literature was the view that higher social status was linked to higher fertility before the fertility transition which changed to a negative association between social status and fertility as the fertility transition progressed (e.g. Borgerhoff Mulder 1998; Voland 2000; Kaplan & Lancaster 2003). This reversal occurred during or even before the demographic transition began (e.g. Skirbekk 2008). Dribe et al. (2017) present a more differentiated perspective on the interplay between socioeconomic status and fertility. They presented the results of investigation of selected case studies focusing on socioeconomic and/or educational differentials in fertility before, during and after the transition. Both parity-specific stopping and prolonging birth intervals were involved in the fertility transition. Upper and middle classes acted as forerunners, while farmers were late in the transition. Farmers and unskilled labourers generally lagged behind in the progression of fertility decline.

Dribe et al. (2017) differentiated between four transition phases: pre-transition (PT) as a phase before any signs of fertility decline, early transition (ET) when the fertility decline had started, but had not spread to the whole population, and during the late transition phase (LT) a general decline of fertility had been ongoing. During the post-transition phase, fertility evened out at low levels, usually around replacement levels (SDT: second demographic transition). Transition phases and associated total marital fertility levels at ages 20-49 (in parentheses) for the case studies represent some variation, the explanation of which provided some more insights regarding the nature of the demographic transition (Data not available for some phase/study site combinations). Scania (Sweden): Pre-transition (PT) 1815-1879 (8.2), Early transition (ET) 1880-1909 (7.7), Late transition (LT) 1910-1934 (4.8), Post-transition 1935-1968 (3.1). Utah (USA): PT 1850-1879 (na), ET 1880-1919 (7.8), LT 1920-1969 (4.4). Alghero (Sardinia/Italy): PT 1866-1915 (7.6), ET 1916-1935 (6.9). Saguenay (Canada): PT 1842-1929 (8.9), ET 1930-1959 (7.2), LT 1960-1971 (3.7). Stockholm (Sweden): PT (na), ET 1878-1909 (6.6), LT 1910-1926 (3.8).

Scania, Sweden: Data from five rural parishes. High fertility levels in the pre-transition phase are closely associated with short time spans between marriage and the start of childbearing. Compared to the other three study populations Scania had the lowest mean marriage to first birth intervals (Mean marriage to first birth interval/inter-birth interval 1.06/2.69 years during the pre-transition phase, progressively increasing to 1.34/3.05 in the late transition phase (Dribe et al. 2017). Elite and middle class families had higher fertility in the pre-transition period, their fertility started to decline in the 1880s, earlier than in lower status groups (Dribe et al. 2014). Low skilled and unskilled workers of Scania and Utah had lower higher-order birth rates (restricted family size) compared to farmers; suggesting some socioeconomic harshness during pre-transition and to some extent also early transition phases. This contrasted the situation in Alghero and Saguenay during the pre-transition phase when low/unskilled workers had similar or relatively higher values of higher-order births than higher socioeconomic groups; suggesting that socioeconomic constraints did not limit their family sizes disproportionately. This changed during the early transition phase when low/unskilled workers tended to have mostly lower levels of high-order births than farmers in Scania, Utah and Saguenay (again suggesting socioeconomic constraints on family size). Farmers and unskilled workers consistently lagged in the fertility decline, notably also during the late and post-transition phases.

Utah, USA: Mean marriage to first birth interval/inter-birth interval were determined for the Utah study population as 1.21/2.01 years during the pre-transition phase, progressively increasing to 2.14/3.46 in the late transition phase (Dribe et al. 2017). Declining fertility was due to longer intervals from marriage to births, longer birth intervals and early stopping. This was found to be the case for all socioeconomic groupings. However, whereas unskilled families in Utah had relatively long intervals from marriage to birth (notably during pre- and early transition phases) compared with short intervals in Scania and Alghero, longer intervals were experienced by the higher status groups in Alghero. Sharp fertility declines relating to both first- and higher-order births between early and late transition phases (fertility decreases of 30-50 % and even more so regarding higher-order births). However, the fertility decline started earlier and proceded more quickly regarding white collar families (delayed age at marriage and longer time between marriage and first birth: Dribe et al. 2014). Highest fertility levels were recorded for farming families.

Alghero, Sardinia/Italy: There were no signs of fertility transition for the cohorts born before 1912 and analyses showed more or less pre-transitional fertility patterns (natural fertility: absence of deliberate fertility control) until the 1930s (Breschi et al. 2014). The fertility decline between the pre- and early transition phases was relatively small (marital fertility at ages 20-29: 7.6 to 6.9). Regarding the total population no indications of family limitation were found (parity-specific control). Mean birth intervals from marriage to first births were comparatively long (1.41/1.64 years) during the pre- and early transition phases compared with those of other study populations. Limitations of number of births as adaptation to resource availability levels was based on controls of marriage behaviour, i.e. late marriage of foregoing marriage. Child survival was generally higher in the upper classes

Saguenay, Quebec/Canada: Analyses of rural parts of Quebec in the Saguenay-Lac-St. Jean region. Onset of fertility transition relatively late in comparison with regions of Western Europe and the United States of America. This was linked to the ruralness of the region and remoteness from the influence of urban centers. The population was also French Catholic and had relatively low levels of education. Mean marriage to first birth interval/inter-birth interval were determined as 1.22/1.98 years during the pre-transition phase, progressively increasing to 1.41/2.25 in the late transition phase (Dribe et al. 2017). Interbirth-intervals were relatively short, notably also since such were retained at a late stage of the fertility decline (1960-1971). Farmers had relatively high/higher fertility rates during pre-, early and late transition phases.

Stockholm, Sweden: A marked decline in total marital fertility to 3.8 recorded for the late transition phase which was already reached relatively early during (1910-1926; Dribe et al. 2017). Early onset of birth control and more rapid decline of fertility than for the rest of Sweden (forerunner of overall fertility decline in Sweden: op. cit. Dribe et al. 2017). The fertility decline of low/unskilled workers lagged behind higher and skilled socioeconomic groups during the early and late transition phases.

Patterns of fertility decline were similar across populations, with pronounced decreases experienced from early to late transition phases regarding fertility parameters linked to first- and higher order births. Fertility levels were about 30-50 % lower in the late transition phase; with larger decreases in respect of higher order births. Fertility declines in Alghero (1916-1935) and Saguenay (1930-1959) started much later than in Scania (1880-1909), Utah (1880-1919) and Stockholm (1878-1909). Spacing of births is an important part in fertility transitions. Generally, time between marriage and first birth increases and higher-order birth intervals become longer during the transition. Higher occupation families generally tend towards relatively longer birth spacings in

comparison lower socioeconomic groups; with farmers tending to sustain shorter birth spacing.

Families with higher occupations (elite groups, professionals, managers) led the fertility decline in all study populations (Scania, Sweden; Stockholm, Sweden; Utah, USA; Alghero, Sardinia/Italy and Saguenay, Quebec/Canada). Already during the early transition phase higher occupation families experienced the lowest rates of marital fertility (forerunners of the decline). Farmers and unskilled worker families sustained relatively higher fertility rates. From the early to late transition phases, all socioeconomic status groups experienced declining fertility. Thus, higher-occupation families appear early in the transition compared with lower socioeconomic status groups, with converging to lower fertility of lower socioeconomic status as the transition progressed. However, although also having experienced fertility declines over the later transition phases, families headed by farmers and unskilled workers retained relatively higher fertility rates into the post-transition phase (based on higher order births) than other groups (approximately 30 % higher). (**AS: experienced lower levels of procursive impacts and thus lower levels of patho-information-engram accumulations due to uninterrupted transgenerational affluence/population density stress: intra- and transgenerational continuity of resource abundance and progressively higher impacts of urbanization effects: 2.1.2; 2.1.3**). The generally reported or assumed reversal of a fertility advantage of higher socioeconomic status during pre-transition phases to relatively lower fertility in subsequent transition phases is often not detected because such reversal could have occurred further back in time not covered by the available data (Breschi et al. 2017).

Breschi et al. (2014): Breschi et al. (2014) investigated marital fertility patterns for the Sardinian population of Alghero for the period 1866-1935. Pre-transitional fertility variations were linked to cultural and biological factors (breastfeeding, age-related lower coital frequency and temporal sub-fecundity due to nutritional deficits). The total marital fertility rate $TMFR_{24\text{-}29}$ was 7.7, mean age at last birth was rather late (over 39) and birth intervals were comparatively short (less than 2.5 years). For the population of Alghero, as Sardinia in general, marriage behaviours (late marriages or constraining factors in respect of marriage access) rather than reproductive behaviours (such as limiting total number of births) were instrumental in adapting to available resource levels (op. cit. Breschi et al. 2014). Differences in marital fertility according to socio-economic groupings were detected: for the small minority of non-manual workers marital fertility started to decline, especially after 1885. In Alghero, children born to the upper classes experienced substantially lower mortality rates than those of the poorer classes.

Sardinia experienced the slowest and most gradual fertility transition in Italy (Livi bacci 1977, op. cit. Breschi et al. 2014). Initially having relatively low levels compared to other Southern regions, Sardinia had the highest fertility levels in Italy during the 1950s (TFRs: National average: 2.3; Southern regions: 2.3; Sardinia: 4 children per women). Contrasting this, Sardinia currently has the lowest fertility levels in Italy (Santini 2008, op. cit. Breschi et al. 2014). The system of family formation and reproductive behaviour which prevailed in Sardinia differed from the Mediterranean model (low female marriage age and high fertility) by resembling the north-western European model: late marriage and requiring spouses to have accumulated sufficient resources to sustain a self-sufficient household (AS: resembling a more K-selected reproduction strategy). Marital fertility was relatively high around 1861; with first signs of reduction after 1939-1945. From 1862 to 1962, marital fertility only fell by about 15

%, the national level of Italy by 50 % and in northern and central regions by around 70 %. Later age at marriage and restricted marriage rates in response to resource level constraints controlled fertility in Sardinian populations during the 1800s, persisting to about 1950. A moderate decline in marital fertility, but a more pronounced decrease in general fertility was recorded towards the end of this period. Variability in marriage-fertility dynamics in Sardinia is taken to be associated with socioeconomic context factors such as pastoral, mining or coastal activities (op. cit. Breschi et al. 2014). In Alghero, various socioeconomic groupings were represented, including a large presence of farmers and shepherds, thereby providing the opportunity for a differentiated investigation of the unusual progression of the Sardinian fertility transition (Sardinia has become post-industrial without ever being fully industrialised: Bottacci 1999, op. cit. Breschi et al. 2014). Standards of living for lower socioeconomic groups were generally low. Farmers represented a separate socioeconomic group in Alghero due to their numerical relevance and their closer relationship with rural populations of the interior of Sardinia (**AS: with the occurrence of Blue Belt populations as characterised by notable longevity: Table 2.5.1.2b**).

There seems to be general agreement that the relationship of socioeconomic status and fertility changed over the course of the fertility transition (Skirbekk 2008; Cummins 2009, op. cit. Breschi et al. 2014): individuals of higher socioeconomic status had relatively high number of children before the onset of the fertility transition, but then acted as forerunners of declining fertility during the transition. (**AS: LHS-modes PM before the transition and shifting Pm to pM LHS mode realization during the decline phase: lowering fertility towards LHS mode pM↑:4 predominance: Tables 2.3.3j/k**). Over the period 1866-1905, total marital fertility, mean age at marriage and mean age at last birth of five year marriage cohorts remained largely unchanged/stable (representing a natural-type of fertility schedule), resembling a pre-transitional stage. Furthermore, the results of Breschi et al. (2014) revealed that the non-manual group (higher occupations/lower to medium skilled) had the lowest total marital fertility rate averaging at 6.6; average values were higher for lower socioeconic groups (Manual workers: unskilled, low skilled, farmers, skilled), reaching 8.0 for farmers. Associated evidence indicated that some fertility control was operative in the non-manual group. In Alghero, as in the rest of Sardinia, neonatal/infant mortality was notably low compared with the rest of Italy. A link to extended breastfeeding, sometimes lasting over a year, was implicated (op. cit. Breschi et al. 2014).

Large amounts of research on the European fertility transition has as yet not resulted in any consensus regarding precise causes and mechanisms of the underlying demographic processes. According to Carlsson (1966, op. cit. Breschi et al. 2014) fertility control took place when conditions for innovation (emergence of new attitudes triggered by new knowledge) or adaptation (adjustment behaviour to new circumstances) are being realised.

Finland

Following Gillespie et al. (2008), regarding resource-poor landless families in pre-industrial Finland (1709-1815) maternal fitness returns were reduced with increased maternal fecundity (Gillespie et al. 2008). This resulted from the average offspring contribution to maternal fitness declining with increasing maternal fecundity. In

contrast, for land-owning families, recruited offspring fecundity increased with increased maternal fecundity. (**AS: Sustained sufficiency/affluence of resources supported investment in both reproduction and maintenance, thereby making provision for both quantity and quality of offspring due to a more relaxed trade-off between between quantity and quality under conditions of relative affluence (positive association between wealth and fertility in pre-demographic transition era**). Unaffected by socioeconomic status, the proportion of offspring recruited decreased with increasing maternal fecundity. Subsequent offspring fecundity however increased with increasing maternal fecundity in landowning families, but remained constant in landless families; implying a trade-off between offspring quality and quantity in the case of families of lower socioeconomic status (Gillespie et al. 2008).

Rickard et al. (2010) investigated the effect of food availability around the time of birth on the reproductive success of men and women during 1700-1800 in Finland. The population studied was subject to natural mortality and fertility rates typical of many pre-industrial societies. Individuals had differing access to resources due to social stratification. For those born into landless families (low resource availability), marital prospects, probability of reproduction and offspring survival were positively associated with local crop yield during the years of birth. In the case of landless individuals born when crop yields were below median, only 50 % of adult males and 55 % of adult females gained any reproductive success within their lifetimes. No such effects were recorded for individuals belonging to landowning families (Rickard et al. 2010). These results furthermore suggest that maternal investment in pre-natal and early postnatal life has significant implications for the evolutionary fitness of human offspring. Thus, fertility advantages of the wealthier are realized under conditions when the poorer socioeconomic classes are subject to fertility constraints due to inadequate nutrition.

Korpelainen (2000): The life histories of two socio-economic groups (European aristocrats/rural Finns) with birth cohorts from the 1700s and 1800s were investigated. Fertility selection was greater for European aristocrats and mortality selection greater among rural Finns. The life history of the rural Finns involved shorter female life spans, a considerably longer period of reproduction, higher juvenile mortality, a greater total production of offspring and slightly higher individual fitness. Longevity and progeny survival increased from 1700s to the 1800s. Longevity was linked to reproduction and fitness more so than socio-economic status or birth cohort. Demographic transitional reduction in reproduction had not yet reached the levels observed during the past 100

years. Organisms may trade-off a long life span for enhanced reproduction, or *vice versa*.
The birth cohort significantly influenced age at death and offspring survival in both sexes. In both populations (both sexes) the number of all progeny declined from the 1700s to the 1800s, but the number of surviving progeny (percentage progeny survival) increased. Age at death increased in both populations. The mean life span of both groups and sexes increased from the 1700s to the 1800s. The number of all offspring was greater among the rural Finns and the mean number decreased somewhat from 1700s to 1800s. The survival of progeny was significantly higher for the aristocrats and it improved towards the 1800. Both sexes among the rurals continued reproduction longer. Birth intervals shorter among young mothers and increasing among aristocrats by the 1800s; but staying about the same among the rural women. The index of opportunity for selection among aristocrats changed clearly from a very high value of the 1700s to a considerably lower value in the 1800s. The change was only minor among the rural Finns. The fertility component (down: 1700s to 1800s) of selection was greater than the mortality component among the aristocrats; while the situation was reversed among rural Finns (also: mortality component up: 1700s to 1800s). The change was only minor among the rural Finns. Fertility selection was greater among the aristocrats and mortality selection among the rural Finns; reflecting socio-economic differences between the two groups. High birth rates and low offspring survival are typically associated with poorer socio-economic conditions. Individual fitness as measured by $\lambda^{(m)}$ depends on the timing and quantity of reproduction, as well as on survival (McGraw & Caswell 1996). It integrates these components of fitness into a measure that projects the rate at which an individual would be able to propagate copies of itself (genetically) into the future.
The reproductive efficacy and fitness of women increased along with their life span until post-menopausal age. Trade-off between human longevity and reproductive success. Support the disposable soma theory which predicts that investments in reproduction divert resources away from somatic maintenance, resulting in faster ageing. The relationship between high offspring survival and long parental life span indicates a role of the genetic component in human longevity. In the present study, a significant relationship between maternal longevity and offspring survival was detected; in accordance with the role of maternally inherited mitochondrial DNA in ageing (Linnane et al. 1989, op. cit. Korpelainen (2000).

Sweden

Low & Clarke (1992): Analysed wealth and lifetime reproductive success in Swedish parishes 1824-1896. Richer individuals had higher lifetime fertility and children alive at age ten. Wealth thus positively influenced lifetime reproductive success in early phases after the onset of the demographic transition (**AS: Table 2.3.3n**).

Low (1994): In 19th century Sweden, richer men had more children than poorer men. In monogamous societies, with positive wealth-status associations and family wealth dependant on the wealth of men, the status/wealth of men affect fertility patterns. Access to resources (land ownership, higher status, stable occupations) determined the reproductive success of men. Landowners were more likely to marry, married younger women and had more children. Women who married richer men tended to marry earlier and had higher age-specific fertility than poorer women (Low 1994). Sons and daughters to wealthier fathers had higher survival rates, chances of marrying and more than the median number of children than children born to poorer fathers (Low & Clarke

1992). Richer adult men were more likely to father at least the medium number of children and to have at least the medium or a greater number of children who survived to age 10 than poorer men. After one generation, lineage increase through sons and daughters were seemingly greater for rich than poor men (Low & Clarke 1992).
(**AS: Wealth-fertility correlations associated with access to marriage: never marrying/first age at marriage – resource availability gradient: Table 2.3.3n**).
Women experience more conflict between resource acquisition and fertility than men (food gathering, employment). Industrialization (requiring more investment in education and training for competitive offspring; weakened supportive kinship networks by spatial disruption) and women employment: lowered female fertility.

Low (1991): Differences in demographic patterns between 19th century Swedish parishes. Nineteenth century Sweden was largely agricultural, with emerging protoindustrialization (Mendels 1981, op. cit. Low 1991). Population growth was greatest in southern and western Sweden (also Norrland) and lowest in eastern and central areas (1800: 2.3 million; increased by 23 % from 1800-1830; and increased from 1830-1860 by 34 % to a total of 3.9 million vide Jörberg 1975, op. cit. Low 1991). Nedertorneå, the most northern parish, had at all ages the highest age-specific fertility, the highest total fertility rate, but a net reproductive rate comparable to other parishes. The average life completed fertility of all women 15 years and older was the highest of any parish, but since infant mortality was high (attributed to the habit of feeding infants on cow milk rather than breastfeeding them: Brändström 1984, op. cit. Low 1991), the number of children surviving to age ten was little higher than in other parishes.
Nedertorneå was a poor farming parish, with low nutrient, somewhat acidic soils and short summers (**AS: Circumstances supporting LHS-mode PM: Table 2.2.2b**). In northern 'forest' counties (e.g. Västernorrland, which includes Tuna Parish, and Norbotten, which includes Nedertorneå), forestry and ironworks, as well as hunting and fishing, supplemented agriculture; resulting in a diversified economy. In contrast, in many areas in (mainland) southern Sweden single crops (rye and corn) dominated the economy. Corn was particularly labour intensive, affecting broad sectors of the population. In the north, agriculture was more mixed and was consistently supplemented by fishing and forestry. Fertility patterns for women in Locknevi parish (Southern Sweden: high population growth) were similar to those in Tuna parish (Central-northern Sweden: low population growth). (**AS: Irrespective of any factors discussed by Low 1991, interpreting any demographic patterns, it is noted that reproductive performance is seemingly different over the course of the study period for parishes of northern latitudinal location and nutrient-poor forested environments relative to parishes in southern Sweden with nutrient-richer soils and at more southern latitudes: slow-LHS PM mode realization *versus* fast-LHS Pm > pM mode realization: 2.2.2e**). **AS: Diet effects (Table 2.5.1.2e): a high metabolic turnover-boosting nutrient-dense diet underpins increased fast-LHS expression (LHS-mode Pm > Mp: increased fertility-longevity trade-off); whereas a diet of growth-curbed plant items (nutrient-poor, arid, cool temperature growth) favours slower LHS-mode PM (reduced fertility-longevity trade-off constraints: Table 22.2b)**.

Low & Clarke (1991): Actual lifetime fertility (NBC: number of biological children, i.e. children born to the individual). This measure is is analogous to NRR, although based on individual patterns. In addition, the survivorship (S_{10}) and mortality rates of children within each family to age ten, and the resulting number of children alive at age

ten (RS_{10}) is a refection of "net success" of each family, the result of interaction of other measures analysed: survival to maturity, probability of marrying, age at marriage, age at birth of first child, marital fertility rate, and childhood survivorship. It is thus a summary measure reflecting the net success of any family lineage in a given generation, as a function of the fertility and and survivorship particular to that family.
The study period 1820-1900 covered the time period from pre-transition into the first demographic transition. Family size as measured by NBC, declined over the study period. For Locknevi (southern Sweden) NBC declined from 5.2 (RS_{10}: 4.0) in the first generation to 3.8 (RS_{10}: 3.0) in generations 2-4. For Nedertorneá (northern Sweden), NBC and RS_{10} levels were largely sustained over the generations at 6.1/5.4 and 3.3/3.4, respectively.

The above results of Low & Clarke (1991) are here interpreted to indicate that fertility patterns in southern Sweden changed from generations born 1 to 2-4 consistent with shifts from pre-transition into the first demographic transition (LHS-mode PM → LHS-mode Pm > pM:1; Tables 2.3.3e); whereas those of northern Sweden sustained pre-transition fertility patterns into the first phase of the first demographic transition (sustained LHS-mode PM: Tables 2.3.3e).
Circumstances of accentuated fast-slow LHS trade-off constraints (high PIE loadings; lower cold adaptation effects; nutrient-rich envronments; early demographic transition phase), as were applicable in southern Sweden relative to northern Sweden, underpinned LHS-mode Pm > pM(1) realization (2.2.2e: fast LHS-mode expression; declining fertility; heightened fertility-longevity trade-off constraints); whereas under circumstances of attenuated fast P-slow M LHS trade-off constraints (pre-transition low PIE loadings; pronounced cold adaptation effects; nutrient-poor environments: Table 2.2.2b), as were prevalent in northern Sweden, sustained LHS-mode PM realization was supported (2.2.2e: sustained performance, reproduction and health).

Dyson (2011): During c. 1800-2000, countries in Europe (and North America) experienced both industrialization and urbanization at around the same time. ***Economies changed from being largely agricultural and rural to industrial and urban***. The associated decline in fertility and mortality is interpreted in that the mortality decline is considered as the underlying cause of the fertility decline. For Sweden, between 1750 and 1850, urban death and birth rates were relatively high, with death rates being higher than birth rates. Rural death and birth rates were also relatively high, but birth rates exceeding death rates. After 1850, urban death and birth rates declined, with death rates declining sharper than birth rates; resulting in positive population increases of urban areas. The decline of rural death and birth rates was slower, with little changes in rural population sizes. Towards c. 1930, both fertility and mortality rates continued to decline, converging to similar rates in urban and rural areas. Dyson (2011) intimated that declining mortality supported population growth resulting in rural to urban migration, thereby facilitating urbanization (cities as population

surplus sinks). The mortality decline is then considered to be the remote cause of the associated fertility decline.
(AS: According to the interpretation based on LHS trade-off constraints, fitness is maximised through the realisation of maximised use of improving/abundance of resource availability and the translation into numerous progeny: LHS-mode Pm > pM; that is, at the expense of survival-promoting maintenance investment. Thus, the combination of high fertility and mortality).

Germany

McDade (2003): Immune function is a major component of maintenance effort, and subject to resource limitation, trade-off constraints are expected between maintenance and other life history functions such as growth and reproduction. Natural selection favours the optimal allocation of resources across life history functions. Since individuals are not identical in their access to resources or in their resource use efficiencies, such individual variation in resources leads to positive correlations among growth, maintenance and reproduction at the population level, thereby obscuring intra-individual trade-offs. Given the costs of reproduction, increased lifetime reproductive effort is expected to be associated with accelerated immune-senescence and early ageing. Reproduction entails a survival or fertility cost, as reflected in the trade-off between current and future reproduction (Hill & Hurtado 1996, op. cit. McDade 2003). Analyses of historical demographic data from Germany revealed that, after controllung for the duration of marriage, the lifespan of a woman was negatively related to the number of children she gave birth to (Lycett et al. 2000). However, this only applied to poor landless women (again demonstrating the importance of controlling for phenotypic correlations). (**AS: Predominance of fast rather than slow LHS realization in individuals of low socioeconomic status: fertility-longevity trade-off: 2.2.2 b, c, d**).

Lycett et al. (2000): Krummhörn population (northwest Germany; 1720-1870). Analyses using data from aristocratic families unaffected by economic deprivations revealed that, for all social groupings, the duration of marriage was positively associated with both longevity and number of children (to be anticipated as generally found). However, when controlling for the duration of marriage, the expected negative relationship between longevity and number of children was found, and this relationship became stronger with increasing economic deprivation (**AS: Pre-transition: under chronic energy deprivation/famine: accentuated P-M trade-off. Post-transition: chronic feast: accentuated P-M trade-off. LHS-mode PM sustained by feast-famine alternations**). The trade-off between longevity and reproduction is expected to be strongest under constrained conditions of existence. The mean age at death for woman increased from around 1700 onwards (Westendorp & Kirkwood 1998); suggesting an improvement in living conditions. The association between extreme longevity and reduced fertility was most pronounced among the pre-1700 women; with a much reduced effect for post-1700 women. As living conditions improved with time, the differential effect of reproduction on longevity appeared to be reduced. A similar effect was observed over different social classes of Krummhörn. As relative wealth increased, the strength of the association between reproduction and longevity weakened: positive relationship between longevity and number of children for women in the small holder and farmer groups, but a negative relationship in the landless. Thus, for the poorest social group, there is a trade-off between reproduction and longevity. For all social groups the duration of marriage is positively associated with both

longevity and number of children. Those who could support marriage, the trade-off between longevity and fertility appeared to be weak (AS: LHS-mode PM)

Brown & Guinnane (2002): Using district data from Bavaria (1880-1910), Brown & Guinnane (2002) analysed correlates of the fertility decline, confirming the role of religion and secularization, but also revealing crucial effects of economic and structural factors (*inter alia* industrialization and urban/rural differences). The authors state, that for centuries European women regulated fertility by postponing or avoiding marriage (largely depending on resource availability levels). The German state of Bavaria was overwhelmingly Catholic and industrialization occurred relatively late. Its fertility transition was relatively late and modest in comparison with other states of Germany. The steepest fertility declines occurred in urban districts. A sustained fertility decline began only after 1900. Percentages of marital fertility decline (rural/urban): 1880-1895: 1.6/2.8; 1895-1910: 9.7/25.8. The rural/urban fertility divergence began in about 1880. By 1910 urbanization is strongly associated with reduced fertility. Off-farm employment opportunities for women had a strong negative effect on fertility. Specific county comparisons: Friedberg, Schwabach, Wolfstein and Kemnath.
Friedberg. Most urbanised rural district in 1880 and overwhelmingly Catholic. Half of its population in agriculture, farming on small to medium-sized family farms. Real wages for women were below average for rural Bavaria, but even in 1880, its marital fertility was well above the average for rural Bavaria. By 1900 employment in agriculture fell to one third. Over the period 1880-1910 wages of female day workers increased by 60 % and marital fertility declined by 30 %. Substantial urbanization offset the positive effect on fertility associated with Catholicism.
Schwabach. Protestant; with marital fertility just below average. Substantial economic change: agricultural employment fell from 60 to 43 % and increasing employment opportunities for women. Fertility declined more than in other rural districts (by 38 %). The rise in wages of women (which had already been relatively high) was implicated as an important factor in the fertility decline in this area.
Wolfstein. Situated in the uplands known as the Bavarian Forest. Overwhelningly Catholic and least industrialized in 1880. Largest part of the population dependant on agriculture (71 %). In 1880 had about the same fertility rate as Friedberg (marital fertility was well above the average for rural Bavaria). Little economic change from 1880 to 1910. Linked to the absence of economic change and Catholicism, regressions indicate nearly zero reduction in fertility; fertility actually rose from 1880 to 1910.
Kemnath. Situated in a region of low mountains in the Upper Palatinate (Fichtelgebirge). Two thirds of the population in agriculture and 88 % Catholic. Marital fertility in 1880 was lower than in the Protestant and much more urbanized district of Schwabach. Little economic change between 1880 and 1910. Substantial increases in female wages, but wages remained relatively low. Marital fertility registered a small increase between 1880 and 1910.
In areas with the type of economic development providing increased employment opportunities for women experienced the most rapid fertility decline.
The fertility transition in Bavaria occurred relatively late and less pronounced than experienced in Prussia () and other western European regions.

Becker et al. (2010): Investigated the link between education and fertility for a period before the demographic transition in Prussia (part of German Empire founded in 1871). Their results show that differences in education in 1849 predict cross-county variation regarding the fertility transition starting at the end of 19th century, suggesting that a

child quality-quantity trade-off (implying numerous children are at the expense of maternal investment per child, i.e. child quality) becomes apparent during the fertility transition. It is conceivable that the transition itself created demographic conditions/responses supporting the quality-quantity trade-off (reversal of causality).
Fertility and birth rates start to trend downwards from 1880 onwards.
Negative associations between the child-women ratio (child-women ratio = number of children age 0-5 over the number of women aged 15-45) and school enrolment, degree of urbanization and population density were revealed, but a positively association with the proportion of married women and livelihood/income security.
Urbanization is generally associated with lowered fertility (e.g. Galloway et al. 1998, op. cit. Becker et al. 2010). Marital fertility rate (= number of children aged 0-5 over number of married women) was found to be negatively associated with school enrolment and degree of urbanization, but positively with livelihood/income security (County-level data from the Prussian Census 1849). Marital fertility rates (1890-1905) declined with increasing school enrolment, share in industry (taken as index of female employment) and increasing urbanization over the time period 1890-1905.
The analyses indicate a robust negative association between fertility and education already in a pre-transition economy. (The authors state that causal interpretations of coefficients are not permissable). Results corroborate the notion that there is a child quality-quantity trade-off applicable even before the demographic transition (already existed early on during the industrial revolution). In conclusion, Becker et al. (2010) have shown that education levels in 1849 are strong predictors of the strength of the fertility transition between 1880-1905. Counties with high school enrolment levels during 1849 show a steeper fertility decline at the turn of 1900 into the next century.

Gavrilova et al. (2003): Data base on European royal and noble families: aristocrats (a family-linked data base) 1800-1854/1855-1880. Mean age at death 1800-1854 of daughters increased from 65.8 to 69.5 years and of sons from 63.8 to 63.7 years (female/male age differential increased from 2.0-5.8). Mean age at death 1855-1880 of daughters increased from 71.3 to 76.0 years and of sons from 64.1 to 65.8 years (female/male age differential increased from 7.2-10.2). Significant increase in lifespan over the studied period, especially for females; and relatively more so in comparison to males.

Women born during the latter half of the 19th century began to achieve higher mean ages than males (Kemkes-Grottenthaler 2004). As differences in average heights between males and females of different countries increase, so does the difference in life expectancy increase (op. cit. Samaras & Elrick 1999). In study cohorts in Germany, male and female offspring lifespan for the 1650-1699 cohort was notably higher (probably underpinned by LHS-mode PM performance: Table 2.3.3n) than during the period 1700-1900 (LHS Pm > pM expression: Table 2.3.3n). Women born during the latter half of the 19th century began to achieve higher mean ages than males (Kemkes-Grottenthaler 2004). This is interpreted to be due to increasing Pm-type realization in order to utilize resource abundance (1700-1900: increasing food resource abundance).

Increased LHS-mode Pm > pM expression trade-off constraints more so manifesting/pronounced in males.

Voland (2000) provided a review of the relationships between fertility, family formation strategies and the socioecological context during premodern and early modern periods of European history (1600-1900). Strong positive correlations existed between wealth, probability of marriage, younger age at marriage and completed fertility during these historical periods (Voland 2000; Rickard et al. 2001). Highly fertile women tended to have shorter lives (Voland 2000); supporting the notion of a reproduction-longevity trade-off (2.2.2b).

Loss of fitness maximization

Borgerhoff Mulder (1998): As a result of the European demographic transition, which began in the late 1800s in the developed parts of Europe, marital fertility halved in less than 30 years in some countries (Borgerhoff Mulder 1998). Characteristically, well-off families reduced their fertility earlier and often to a greater degree (Livi-Bacci, op. cit. Korpelainen 2000). Borgerhoff Mulder (1998) suggests that reproductive decision-making might be driven by a human psychology (subject to natural selection) geared towards maximizing material wealth. Following from this, mechanisms governing reproduction and parental investment are considered to respond to modern conditions with a fertility level much lower than that maximizing fitness.
Investigating scientists attempting to explain demographic transitions are primarily puzzled by two phenomena: the pronounced decline of the number of offspring in spite of increased availability of resources and that rich (notably aristocratic) families reduced/are reducing their fertility earlier and generally more markedly than the rest of the population; leading to the emergence of negative correlations between wealth and fertility, thereby contrasting the situation in populations preceding the demographic transition when correlations between wealth and fertility were decidedly positive (**AS: Table 2.3.3n**). The reduced fertility levels prevailing at current and advanced stages of the demographic transition can no longer be considered fitness maximizing and since more competent social groupings are disproportionally negatively affected, widespread dysgenic reproductive behaviour patterns seem to prevail in European populations.
Borgeroff Mulder (1998) specifically contrasted two evolutionary hypotheses as possible exlanations for the demographic transition:

1. Lowered fertility rates are optimal because of the competitive environment in which offspring are raised. Under conditions where high levels of parental investment to offspring are costly but increasingly important (offspring competitiveness), parents optimize fitness by producing few children with high levels of investment rather than many with less investment *per capita* (trade-off between offspring quality and quantity).

The central prediction under this hypothesis is that the number of grandchildren would peak at an intermediate level of fertility. However, Kaplan et al. (1995) showed that men with the most children had the highest number of third generation descendants, in

contrast with the observed modal fertility of two children in the population as such. Thus, fitness maximization was not associated with intermediate levels of fertility but rather with investment in having numerous offspring.

2. Lowered fertility rates being a maladaptive by-product of rapid environmental change that has no adaptive value. Changes in social, economic, political and ecological conditions experienced in human societies resulted in evolved mechanisms (psychological or physiological) no longer generate appropriate responses to external conditions and maladaptive levels of fertility are observed.

According to evolutionary theory, organisms (including humans) are designed by natural selection to maximize fitness (variability in fertility levels are particularly exposed to selection), whereas economics does not seem to be causally linked to fitness maximization during the demographic transitional period. Following from evolutionary theory, models can be formulated of how fertility, subject to evolved physiological and psychological mechanisms, is likely to be shaped by extrinsic features of the environment (Kaplan 1996). (AS: Link between economics and fertility broken by accumulated patho-information-engram loading; compromised metabolic functional efficiency and thus reduced instinct-vitality affecting the economically successful disproportionately due to thse being subject to affluence/population density effects more so and trangenerationally earlier).
Two phenomena requiring explanation: Reduced levels of fertility despite material abundance and the breakdown of the link between resources and fertility as characteristic for predemographic transition populations.

Kaplan & Lancaster (2003): In response to conditions as outlined, people no longer maximize fitness through their fertility decisions (Kaplan & Lancaster 2000, op. cit. Kaplan & Lancaster 2003). Observed fertility levels were lower than would be required for fitness maximization (Kaplan et al. 1995; Borgerhoff Mueller 2001). Parental fertility of parents and their offspring of higher educational and economic status is lower; but the lowered earning capacity of children from large families does not decrease their fertility. No fitness reduction was thus observed with lowered parental investment per child (Kaplan et al. 1995). Furthermore, contrasting the situation in pre-industrial societies, where a positive relationship between resource-holding or power and reproductive success was consistenty exhibited, higher-earning adults do not produce more children or produce even less children than lower-earning ones as the demographic transition progresses (Kaplan et al. 1995 + REFS). Education became an increasingly important determinant of wages and increasingly so towards the last third of the 20th century when fertility decreased even more (Kaplan et al. 2002). Education effects on fertility are related to postponement of marriage, a delay from marriage to reproduction and age effects on reproduction, resulting in lowered completed fertility; particularly in parents at the high end of the education continuum (Kaplan et al. 2002).

Hill & Kaplan (1999): People in modern societies in developed countries do no longer maximize fitness through their fertility decisions (op. cit. Hill & Kaplan 1999). Observed fertility behaviour deviates from that which is expected to maximize fitness in two ways: fertility is lower than that expected based on models of fitness maximization and higher-earning adults do not produce more children than less-earning counterparts. Rather, higher parental fertility is associated with lower levels of of educational and economic status. This is in contrast with data on pre-industrial societies which consistently exhibited a positive relationship between resources and

reproductive success (op. cit. Hill & Kaplan 1999; Borgeroff Mulder 1998). Studies of low-fertility societies indicate a breakdown of the positive relationship between fertility and wealth/power. The abrupt change in this wealth-fertility association which occurred at the same time when fertility became reduced historically requires an explanation.

Attempts to understand deviations from fitness maximization:

The historical novelty of effective birth control (Barkow & Burley 1980. op. cit. Hill & Kaplan 1999). The suggestion that humans track cultural success as a proxy for fitness and that the costs of attaining social success rise with modernization (Irons 1983, op. cit. Hill & Kaplan 1999). With modernization the most successful individuals sacrifice their own fertility in order to achieve high levels of social and economic success (Boyd & Richerson 1985, op. cit. Hill & Kaplan 1999). Turke (1989, op. cit. Hill & Kaplan 1999) suggested that the breakdown of extended kin networks lowers fertility since the costs of rearing children are paid directly and fully by the parents.

According to *inter alia* Kaplan (1996) fertility among hunter-gatherers is regulated by a coordinated system by behavioural and physiological systems. Following the importance of skill in the human foraging niche, human psychology evolved to detect the relationship between parental investment and income of offspring as adults. Parental investment towards support and provisioning of offspring (length of support) is adjusted accordingly; but involves costs in terms of maternal nutritional status and fertility. Kaplan & Lancaster (op. cit. Hill & Kaplan 1999) generated a series of predictions regarding parental investment and rates of fertility decline in developed countries: Education has become an important determinant of age at first reproduction during this century; more educated parents invest more per child than less-educated parents; the level of parental investment in children is positively associated with their educational attainments. In respect of explaining the demographic transition, the multigenerational life history model presented by Hill & Kaplan (1999) emphasise that adults not only face a trade-off between quantity and quality of children, but also between investment in own embodied capital and reproduction. Hill & Kaplan 1999 tentatively conclude that the low fertility in modern societies is due to the combined effects of lowered mortality, higher pay-offs in investment in survival and health and in offspring income, a perceived lack of diminishing returns to other forms of consumption, and increasingly effective birth control technologies. They contend that the existence of extra-somatic wealth may have been the critical condition to which our evolved proximate mechanisms are not responding so as to maximize fitness. The commitment to intensive investment in embodied capital, for self and offspring, appears to be related to responses to modernization. AS: Slow LHS expression

Due to developing technologies of production and improved public health, these factors interacted to increase the pay-offs in investments in skill and education, investments in health, longevity and child quality, with greatly reduced fertility. Such priority shifts towards extreme maintenance investment (high to low life history strategy) may be a predictable consequence of our evolutionary heritage, but may not be adaptive of being currently fitness maximising (Hill & Kaplan 1999). The extremely low fertility in modern societies can be seen as a trade-off cost due to investments in extra-somatic wealth and payoffs derived from its use for education-based embodied capital.

Clark & Cummins (2009): It was hypothesized that, in seeking to maximize the chances of at least one surviving child, preindustrial families chose high gross fertility rates. In the case of richer families this also resulted in high rates of net fertility; but due to poorer health, poorer nutrition and lower economic resources, the poor in the

preindustrial era were unable to match the rich in gross fertility (with a larger fraction of the poor dying childless). There were substantial variations in child mortality rates during the preindustrial era, depending mainly on population density. Child mortality rates were very high in large urban centers, such as London, and low in the least densely populated rural environments. Based on this variation, Clark & Cummins (2009) tested the hypothesis of whether high net fertility rates among the rich were a product of high mortality rates. The test however suggests that high preindustrial mortality rates do not explain the positive correlation between wealth and net and gross fertility before 1800. Furthermore, a decline was observed in gross and net fertility rates among the rich in England, starting much earlier than the start of the demographic transition.
In rural areas the children of the rich were significantly more likely to survive to age 25 notably so in low population density rural parishes. In London and the towns the rich did not have any survival advantage. Before 1800 no sign was found that gross fertility was was correlated withchild mortality rates; rather, the lower the mortality risk for children, the higher were both net and gross fertility. Before 1800 the rich always produced more surviving children than the poor. There was no sign of any contraction of fertility in response to lower child mortality for the rich in rural environments before 1800. The rich acted as though the number of children was always a normal good, with more birth the higher the wealth level; whatever the mortality environment. Around 1800, more than 80 years before the general decline in fertility observed in England in the context of the first demographic transition, the fertility of the rich declined. Within one generation, the pattern observed between 1500-1800 of high gross and net fertility rates among the rich compared to the poor, disappeared. Thus, generations before the classic demographic transition the rich in England began to moderate their fertility. The contraction in gross fertility among the rich resulted in their having much lower chances of producing at least one child or grandchild still alive at the time of their death.

Korpelainen (2003): Changes in human reproduction emerged in most developed countries in the late nineteenth century due to economic and industrial growth. The following stages can be identified for this, the first demographic transition: 1) both high birth and death rates; 2) death rates start to decline, but birth rates remain relatively high; 3) death rates level off, but birth rates decline; 4) both death and birth rates are low.
According to the Darwinian theory of evolution all organisms, including humans, are expected to maximize their fitness within relevant socioecological constraints (Voland 2000). Children produced at an early age contribute more to fitness of the female parents than children produced later in life (Stearns 1992, op. cit. Korpelainen 2003). An indicator of fitness, life time reproductive success (LRS) does not take variation in generation length into account. The indicator of fitness λ includes rate measures sensitive to both reproductive quantity (LRS) and timing (parental age of reproductive events): McGraw & Caswell 1996 (op. cit. Korpelainen 2003). Thus the combination of early reproduction and high LRS implies high fitness (λ).

From the first (FDT) to the second demographic transition (SDT)

France

Wrigley (1985b): Nuptiality (Im) measures the degree to which potential fertility is restricted by celibacy/low marriage access and late marriage. Proportion of women reaching the mean age of maternity p (m), p (m) up implies mortality down. The product of Ig x Im x p (m) multiplied by a constant provides an estimate of NRR. Mutual accommodation of three variables to keep NRR close to zero (intrinsic growth rate close to zero) 1871 marked the date ending the quarter of century during which marital fertility had paused in its long descent (1845-1870); control of marital fertility started to conform to the pattern found elsewhere in western Europe (control of fertility within marriage). Low marital fertility and high nuptiality were usually found together; both in association with low mortality (high p m). Combinations: High marital fertility, low nuptiality (fertility control through marriage), high mortality. (**AS: LHS-mode Pm > pM**). Low marital fertility, high nuptiality (fertility control within marriage), low mortality. (**AS: LHS-mode pM > Pm**).
Region 9 (Guyenne: Lot-et-Garonne, Gers):
Low marital fertility, high nuptiality (fertility control within marriage), low mortality. LHS-mode pM > Pm. Marital fertility was already low in 1831 (0.415), low levels only reached in Germany, England and Sweden in 1920. For the south-west corner of France, some work suggests (Henry) Ig values of 0.705 (1740-1769) and 0.663 (1770-1789); a substantial marital fertility decline had thus taken place between 1790 and 1831 (Ig in 1871: 0.396 and 1901: 0.255).
Region 4 (Normandy):
Had the second lowest Ig at 0.451. Marital fertility fell less than anywhere else in France, matched by a slow improvement/decline in mortality. The relative rise in fertility towards 1900 was offset by a relative increase in mortality. Mortality may have been rapidly falling during 1700-1800s; associated with an unusually early fall in marital fertility in Normandy. Low marital fertility, high nuptiality (fertility control within marriage), low mortality. LHS-mode pM > Pm.
Regions 1 and 6 (1: old provinces of Champagne, parts of Orléans and Burgundy; Picardy, parts of Champagne):
1: Marital fertility low at 0.471 (1831, but declining towards 1871 and 1901) population density low; mortality was crippingly high (1806: pm 0.447 = low = mortality high). By 1871 it had become the healtiest region: pm = 0.720 = low mortality. Expectation of life improved by more than 16 years between 1831 and 1871, while in Normandy it did not change at all. As in Region 9 low marital fertility in Region 1 was offset by high nuptiality. The tendency for marital fertility and nuptiality (frequency of marriage: high = fertility control not through marriage, marital fertility low/mortality low; when low = fertility control through marriage = marital fertility high/mortality high) to be linked where the one was high and the other low, was consistent for French regional demography.
6: Ig of 0.464 (1831) similar to 1, subsequent fall less rapid than national average. Part of a long belt running along the northern shores of France where the proportional fall in marital fertility (1831-1901) was less than elsewhere in France between 1831 and 1901.
Regions 3 and 10 (Brittany and southern Massif central/Pyrenean departments)

Brittany. Regions with the highest marital fertility in 1831 (Ig of 0.766). Brittany polar opposition to Region 9 (Guyenne). High marital fertility was at a level as in France a century earlier, or Germany before the fall began after 1880. Ig was still at 0.735 forty years later and even rose slightly in the following decade to 0.753 in 1881, before falling sharply in the last 20 years of the century. Levels of nuptiality very low (control through marriage), actually falling between 1831-1871 and even in 1901 was scarcely above the level found 70 years earlier. Brittany experienced high mortality rates during 1800-1900. Life expectation was the lowest of any region. Thereafter there was a rapid improvement towards 1901. Apart from region 5, with its large industrial population, and Normandy in 1831, Brittany had the highest population density of any of the French regions, and with the exception of region 5 (also with substantial population increase), was the only region to end the century with a bigger population than that of 1831. Regions 1, 4 and 7 actually lost population between the two dates. High marital fertility, low nuptiality (fertility control through marriage), high mortality. (AS: LHS-mode Pm > pM) 1870: LHS-mode shift Pm → pM.

Region 10 (southern Massif central and Pyrenean departments)

High fertility in 1831. No reason to suppose family limitation. In the region as a whole the Ig level was bout the same as in pre-transition England. Thereafter marital fertility fell moderately between 1831 and 1871. Some departments had reached low Ig values by 1901. After 1871 marital fertility began to fall rapidly. Nuptiality was always lower than for France as a whole, but rose somewhat between 1831 to 1871; instead of falling as in Brittany. Region 10 began the century with the second highest expectation of life at birth, but like Normandy, did not achieve any advance until the last 30 years of the century.

Region 5 (Artois and Flandre: Pas-de-Calais and Nord)

Was not an area of agriculture, market towns and administrative centers, but more industrialising. The population density was more than twice the average of the 77 departments in 1831 and approached four times the average in 1901. Particularly the female population rose by more than two-thirds in 70 years in the region overall and even more rapidly in industrial areas where almost all the growth occurred. Marital fertility was relatively high (Ig = 0.620; 0.653 in 1871) and 0.658 in Nord, much more industrialised than Pas-de Calais. Marital fertility then rose over the next 40 years to place the region only behind Brittany in this respect; followed by a fall towards 1901: 0.526. In the predominantly textile-manufacturing (proto-industrialised) Nord the fall was exceptionally steep. Nuptiality in this markedly industrialised area was consistently below average. In 1831 the region had relatively high mortality rates, but these declined thereafter relative to the national average over the last 70 years of the century. High marital fertility, low nuptiality (fertility control through marriage), high mortality. (AS: LHS-mode Pm > pM) LHS-mode shift: Pm > pM → pM > Pm.

Regions 2, 7, 8 and 11

Ig was relatively low in 1831, its fall over the next 40 years was slight; but then falling disproportionately rapidly between 1871 and 1901. Began the century with high prevailing mortality rates; not declining between 1806 and 1871. Divergence in subregions (1831-1901): Low Ig, high nuptiality, low mortality (2) or low Ig, rising nuptiality, declining mortality (8) or high marital fertility, low nuptiality, increasing mortality (7).

Region 11 (Provence/Languedoc). Relatively low marital fertility, high nuptiality, increasing mortality (11). Pattern 5 = 11. In region 11 marital fertility levels remained relatively stable between 1831 and 1870, rapidly falling between 1870 and 1900.

Relatively high mortality rates stable between 1831 and 1870, then declined towards 1900.

General patterns: high marital fertility, high mortality, low nuptiality or low marital fertility, low mortality, high nuptiality associations.
Marital fertility patterns over time: 1931-1861 declining, 1861-1871-1881 increasing or stabilising below 1831 levels, 1871 starting to decline further. An exception to this pattern was represented by Region 5, the industrial north of France, where marital fertility rose from 1831 towards 1871 and then declined (also regiomn 11).
Change in NRR between 1831 and 1871 in France as a whole was slight. Although changes in marital fertility, mortality and nuptiality were substantial, combined effects of these changes on the intrinsic growth rate of the population were minimal. During the first three-quarters of the 1800-1900s, intrinsic population growth rates remained close to zero (with the exception of region 5). Regarding region 5, the period before 1870 is of interest: intrinsic growth rates were broadly similar to elsewhere in Europe and marital fertility rates only started to fall at the same time as elsewhere in western Europe (also had high population densities). Wrigley (1985b) suggested that homeostatic forces were weaker in region 5 due to its industrialised economy, being very different from vast tracts of rural France where traditional constraints remained powerful.

Control of fertility by marriage pre-1870 and within marriage thereafter. After about 1870 marital fertility fell everywhere. Rates of fall higher in higher fertility regions. Pause of fall in marital fertility in the middle decades of century, the renewed fall towards the end of the century (1900) showed novel features. There was a simultaneous decline in mortality, but earlier links with nuptiality had disappeared, and net reproductive rate (formerly stable at around unity) fell steadily to below unity in the early part of the 20th century (1901-2000). With the exception of the industrial north (region 5) there was a notable similarity across French regions to about 1870 in terms of intrinsic growth rate (summation of fertility, nuptiality and mortality rates).
Conrasting patterns between high and low fertility regions before and after the fertility recovery during the Second Empire (1852-1870; economic growth 1852-1859). The five regions with above average Ig in 1881 (3, 5, 7, 10, 11) experienced a fall in marital fertility of 17.2 % between 1881 and 1901; compared with a fall of only 12.9 % in the other remaing 6 regions. Between 1831 and 1871, Ig of the high Ig-group fell by only 5.2 % on average; whilst the low Ig-group experienced a fall of 16.5 % (AS: were in a falling phase from before 1831).

For France, declining fertility is reported to have started as early as 1790 towards 1850, when stabilising somewhat (Wrigley 1985a/b); contrasting the pattern in prominently industrialised countries or regions, such as England and Germany, and the French region 5, where marital fertility slightly increased from a level of above 0.600 in 1831 to 1871, then declined as in other regions and western European countries (Wrigley 1985b). Industrial Revolution: 1760-1840. Daily caloric supply (cal. per capita): 1750-1800 for Great Britain; c. 2200 and France c. 1850; 1850: Great Britain and France both c. 2400 (Fogel 2004).
Lower expectation of life at birth (≈ higher mortality) in France than England and Sweden during 1740 and 1810; Gross reproductive rate (GRR) decreasing in France and increasing in England, then declining towards 1930 in both countries (Wrigley 1985a).

Cummins (2013): In France the transition to declining fertility became widespread towards the end of the 1700-1800s. Before this, fertility was apparently uncontrolled within marriage (Cummins 2013). (**AS: but controlled through marriage access**). The author presents an explanation for the fertility decline in France where he attributes this to decreases in the level of economic inequality after the revolution in 1789, supporting the emergence of social mobility, thereby providing incentives to lower fertility.

(**AS: The Industrial revolution provided for the sustained availability of relative affluence increasingly also for the lower socioeconomic classes, i. e. for most of the population**). Also bringing increased urbanization and female employment.

According to annual estimates of fertility levels for France in 1740-1911, Weir (op. cit. Cummins 2013) determined indices of marital fertility (Ig: fertility relative to an observed maximum, that of an twentieth century religious group, the Hutterites, who married early and prohibited contraception). He found that during the late 1700s, fertility declined from relatively high levels of 80-90 % of the Hutterites to low levels by 1911 (about 31 % of Hutterite levels). This transition was placed to have occurred around 1776, about a century earlier than when such transitions occurred in Western European countries generally. Hadeishi (2003, op. cit. Cummins 2013), regarding the town of Nuits in Burgundy in 1744-1792, recorded a positive relationship between marital fertility and income.

Samples from rural villages (covering 1770-1850): Average children born and surviving to age 10 years, across three increasing wealth terciles: Non-declining/declining villages 4.87/5.50, 5.90/4.88 and 5.93/3.88. Net family size: 3.22/4.34, 3.76/3.78 and 3.97/3.21. Where fertility was relatively higher or unchanging (lower wealth villages), a positive relationship existed between wealth and fertility; whereas for villages (higher wealth villages) with declining fertility this relationship was reversed, i.e. the wealthier had lower fertility than the poorer. (**AS: non-declining villages (lower wealth villages) representing pre-transition conditions, while fertility-declining villages (higher wealth villages) representing the early phase of transition**).

Ferility declining villages had lower rates of child mortality up to the age of 10 years (rates per thousand): Non-declining/declining villages 327/201, 342/211 and 335/167 in the wealthiest tercile. Non-decline villages: no difference in child mortality between the rich and the poor (**AS: Declining villages (wealthier): LHS-mode shift Pm → pM = decreasing mortality; pre-transition: LHS-mode Pm > pM**). Expected fertility, holding non-wealth influences constant, across three increasing wealth terciles for non-declining/declining villages: 6.19/6.39, 7.25/5.85 and 6.86/4.95. According to the interpretation of (Cummins 2013), female age at marriage and length of reproductive span were driving the reproductive advantage of the rich in the non-decline villages. In decline villages the wealthiest had a significantly lower estimated gross fertility (4.95 children) than the poorest (6.39 children). Resource availability no longer explains why fertility declines.

Wrigley (1985a): According to Wrigley (1985a), the fall in marital fertility began about 70 years earlier (by c. 1800) in France than in other European countries (*ca* 1870, levelling out around 1930). Considered and analysed the decline period representing two separate parts: an earlier half, having much in common with traditional European

systems of population control and a second half, resembling in character the changes which had taken place elsewhere in Europe. France experienced relatively low rates of population increases relative to England, Sweden and France during the periods 1700-1800 and 1800-1900. Life expectancy at birth was decidedly lower in France relative to England and Sweden during 1740 and c. 1810 (**AS: LHS-mode Pm>Mp**), converging to similar levels thereafter (1810-1880). Mortality declined between 1780s and 1820s; life expectancy rose from 28 to 39. (1780-1820: **AS: LHS-mode shift Pm>Mp → pM>Pm**). The fall of mortality in a peasant country (peasant economy) like France may reduce fertility commensurately, but may not be parralled in a country like England in the early decades of the Industrial revolution (wage-paying economy).

Gross reproduction rates in France remained similar but slowly declining (2.53-2.00) between 1740 and 1810, then progressively declining towards a level of 1.15 by 1930. Gross reproduction rates in England increased from 2.27 to 3.06 between 1740 to1820, thereafter also progressively declining to 1.14 by 1930. The intrinsic population growth rate for France remained close to zero between 1740 and 1880; both fertility and mortality contributed equally to this. Marriage fertility (Ig) declined rapidly from about 1870 in England Sweden and Germany; whereas in France a moderate decline commenced already from 1740 to about 1850, with an accelerated decline from 1870 onwards, as for England, Sweden and Germany. France: after a long period of steady and rapid fall in marital fertility it slowed down and recovered for about a generation (1840-1870), before the fall was resumed after 1870. Female age at first marriage increased from 1680 to 1780, then declining towards 1880/1900. Percentage never marrying increased after 1680 until c. 1810 (marriage access declined), but declined then towards 1870 (improving marriage access). Considerably higher rates of prenuptial pregnancies (children born/baptised within 8 months of marriage) were found for England (1650-1850; notably for women marrying younger than 25 years of age) than in France (1690-1820; moderately increasing over this period. Somewhat higher levels for women marrying at ages 25 and older than those marrying at ages below 25).

Wrigley (1985a) envisaged the increasing adoption of family limitation in France around 1800 as part of a Malthusian-type system of maintaining equilibrium between populations and resource availabilities. Levels of fertility were determined through marriage rather than within marriage. French net reproductive rates were sustained around 1 from 1740-1880. Changes in French nuptiality, fertility and mortality interacted in a way keeping the net reproductive rate close to unity. Declinig mortality between the 1780 and 1820s; progressing more gradual over the succeding 60 years. Life expectancy at birth improved by an average of 2.75 years per decade between the 1780s and the 1820s, parallelled by a rising proportion of women reaching the mean age at maternity (36 % 1780-1820), followed by a slower rate of improvement of 13 % during the subsequent 60 years. The exceptional early fall in marital fertility in France did not represent similar changes elsewhere post-1870, but involved demographic homeostatic feed-back mechanisms between nuptiality, marital fertility and mortality (from fertility control through marriage to control within marriage).

Marital fertility: France, England, Sweden and Germany: Sweden: High 1801 to 1871-1880 (0.688-0.751), then declining to 0.306 by 1931. Germany: High 1750-1886 (Knodel and Wilson 1981) up to 1883-1887 (Wrigley 1985a), then declining to 0.264 (1931-1935). England/Wales: Declining from 1851 (0.657) 0.292 by 1931. France: High 1740-1790, then declining to 0.478 (1851); stabilising at 0.478 and slightly increasing to 0.494 (1871), then declining again to 0.273 in 1931. Industrialised

region 5 region slightly increased from a level of above 0.600 (Wrigley 1985b) in 1831 to 1871, then declined as other regions and western European countries.
Gross reproductive rates in England increased between 1740-1810/1820, then declined towards 1840/1850, then stabilising and slightly increasing between c. 1850-1870, then finally declining towards 1930. Between 1755 and c. 1790 the GRR of both France and Sweden declined; in France the decline continued towards 1930; whereas Sweden followed a similar pattern to that of England, but phase-shifted. Increasing towards 1825, then decreasing and slightly increasing between 1825 and c. 1875; continued decline thereafter towards 1930.
Marital fertility (Ig) was relatively high between 1740 to c. 1870 (c. 0.700), the declining to between 0.200 and 0.300 towards 1930. Gross reproductive rate in England had been rising since 1680-1690.

Evolving fertility declines

Korpelainen Analysis of life histories of married Finns for the years 1870-1949, reproducing on average at age 30 years, revealed substantial changes during this period. Birth cohorts from 1870 to about 1900 represented the transition from the second to the third stage of the demographic transition, when the death rates are relatively low, while birth rates remain relatively high but are starting to decrease. Birth cohorts 1900-1930 represent the third stage, with considerably decreasing fertility, but only slightly decreasing mortality. Birth cohorts 1930 to 1949 represent the fourth stage at which both birth and death rates are low.
A feature of the demographic transition was that rich families reduced their fertility earlier and often to a greater extent. The earlier Finish cohorts were mainly composed of rural families for which fertility decreases occurred more slowly. The fertility levels of European arisocrats born between 1800-1899 (Korpelainen 2000) were comparable to those of detected in the present study for Finns born between 1870-1900, whereas the fertilities of aristocrats born between 1700-1799 were somewhat higher. However, fertilities of Finns born 1700-1799 or 1800-1899 were considerably higher (mean number of progeny ranging from 5.2 and 6.2: Korpelainen 2000). Such differences in timing of the demographic transition between the Finns and some other European countries are causally attributed to past socioeconomic disparities.

Kaplan et al. (2002): A detectable reduction in fertility rates occurred in Europe, North America, Australia and New Zealand between 1880 and 1920. In France the fertility transition had apparently already started at the beginning of the 19th century (op. cit. Kaplan et al. (2002). Over the last 30 years many countries of the developed nations underwent a further decline in fertility (Lesthaege 2010) towards below-replacement fertility levels (total fertility rates below 2.2).
The hypothesis of Kaplan et al. (2002) involves extra-somatic wealth as the principal novelty to which our evolved psychology responds by desiring less than fitness maximizing fertility. In the past, when there was a positive association between absolute wealth/social standing and fertility, a psychology had developed favouring the notion that the pursuit of relative wealth/social standing supported family-lineage interests. However, as contended by Frank (1985, op. cit. Kaplan et al. 2002), if relative wealth/social standing, rather than absolute wealth/social standing, guide human decisions regarding wealth flows, parental investment and fertility, it is possible that 'run-away' consumption and investment in the education of children result from this psychology and modern education-based labor markets and consumption possibilities.

In the conceptual model presented by Kaplan et al. (2002) the interaction of individual psychology, cumulative cultural knowledge, practices and reproductive physiology determine fertility. Psychology and fertility interact indirectly through psychology adjusting parental investment (productive behaviour, wealth flows) and reproductive physiology translating parental investment decisions into fertility. Maximizing lifetime expected resource production by relevant activities and wealth flows would maximise fitness when all wealth is in the form of food and surplus food translates into higher fertility. Underlying the demographic transition are two new socio-ecological factors: the existence of extra-somatic capital and changes in the pay-offs to embodied capital (especially education). As stated by Kaplan et al. (2002), extra-somatic wealth may then break the link between wealth and fertility, since for wealth held outside the body there is no mechanism ensuring that it is eventually converted into reproduction. Rather the evolved psychological mechanisms sensitive to the effects of behaviour on future wealth may in fact support wealth maximisation at the expense of fertility.
The authors proposed two routes through which social, economic and technological changes resulted in below replacement fertility: changing pay-offs to investment in education progressively having involved the whole population and the escalating work force participation of women and its impact on family formation; against a background of a strengthening relationship between education and income. Education tends to delay entry into marriage and also increases the delay to reproduction within the marriage. Men 35-44 years of age with less than high school had a mean of 2.6 children, whereas those with graduate degrees had an average of 1.5 children. In women, high school dropouts had a mean of 2.77 children, (2.22: high school degrees, 1.95: bachelor degrees) and 1.43 children for graduates.
Most people seem to desire only two children and tend to stop reproduction after the birth of their second child (Coleman 1996, op. cit. Kaplan et al. 2002). As a result of own investment in education, fertility may be delayed enough for target fertilities to be no longer achievable. Below replacement fertility would accordingly largely be the result of the failure to achieve the target fertility because of delayed reproduction interacting with age-related physiological fertility declines.

Skirbekk (2008): The study by Skirbekk (2008) revealed that as fertility declined, a shift from positive to negative/neutral occurred in the status-fertility relationship; i.e. those with high income/wealth/high occupation/social class switch from having relatively many to fewer or equal numbers of children than those of lower status. Education was found to be negatively associated with fertility (1900 onwards). As fertility levels decline, elites are the first in reducing their fertility, resulting in a negative status-fertility relationship. When fertility has declined to be close to replacement level, differences in fertility levels between high and low status groups are generally small, but variable. In such countries as Belgium, Sweden and Germany, a pronounced fertility gap between the high and low educated has been sustained over the past few decades. In general, a status increase from from low to medium and from medium to high was associated with higher fertility until the mid-1700s. From 1750-2006, occupation and social class tended to be negatively related to fertility.
Relative fertility of the high status groups for Europe and North America: variable d = (Fertility high status-fertility low status)/fertility low status.
All status groups: d = 35.8 (< 1750), -8.2 (1750-1899), -15.1 (1900-1924), -17.0 (1925-1949), -15.5 (1950-1974), -5.2 (1975-1989), -9.0 (1990-2006).
Income/wealth: d = 24.3 (< 1750), -45.0 (1750-1899), 6.1 (1900-1924), -12.4 (1925-1949), -13.9 (1950-1974), 2.3 (1975-1989), 6.7 (1990-2006).

Occupation/social class: *d* = 30.9 (< 1750), -4.2 (1750-1899), -22.3 (1900-1924), -45.6 (1925-1949), -6.0 (1950-1974), *na* (1975-1989), -7.9 (1990-2006).
Education: *d* = -35.7 (1900-1924), -25.8 (1925-1949), -21.8 (1950-1974), -24.6 (1975-1989), -17.8 (1990-2006).
Demand for child quality increased at the expense of child quantity. Empirical results consistently confirmed that the upper classes were forerunners in the decrease of family size. According to Dribe et al. (2014) this top-down chronology is suggestive of social diffusion of fertility behaviour as a general pattern). (**AS: Alternatively interpreted as being due to the earlier onset of procursive impacts in the upper classes; being subject earlier to the performance vitality-compromizing effects of patho-information-engram accumulation: 2.2.2j**).

Phases of epidemiological transitions

Omran (2005): The classical (Western) model of epidemiologic transition describes the progressive transition from high mortality and high fertility to low fertility and low mortality accompanying modernization in most European countries. Three successive stages of epidemiologic transition were identified: 1) Age of pestilence and famine (mortality is high and fluctuating, precluding sustained population growth; life expectancy low and variable: 20-40 years); 2) Age of receding pandemics (mortality declines progressively as epidemic peaks are less severe or disappear; average life expectancy at birth increases from c. 30-50 years; sustained and increasing population growth) and 3) Age of degenerative and man-made diseases (mortality continues to decline eventually approaching stability at low levels; life expectancy rises gradually exceeding 50 years). Following the stage of pestilence and famine, prevailing during the pre-modern and early modern periods, mortality started to decline gradually, declining more pronounced progressively towards the turn of the 20th century, by which time fertility had started to decline. The author notes that socioeconomic factors were the primary determinants of this transition; augmented by the sanitary revolution in the late 19th century and medical and public health progress in the 20th century. Degenerative and man-made diseases replaced infections as leading causes of mortality and morbidity in the second and third decades of the 20th century.

During 17th century London c. 55 % of death were related to infectious diseases and diarrhea. A gradual shift in disease patterns involved the steady decline of infectious diseases (including tuberculosis and diarrhea) and the moderate increase in cancer and cardiovascular disease in England and Wales up to1920. The decline in infectious and rise in degenerative diseases becomes more distinct after 1930; with 10 % of deaths being attributable to infectious diseases and c. 50 % to heart diseases and cancer by 1960. The determinants of the transition of infectious to degenerative disease are complex. Three major categories of disease determinants were summarized: 1) ***Ecobiologic determinants*** of mortality relate to a complex interaction between disease agents, their virulence and host resistance. The recession of the plague in most of Europe toward the end of the 17th century and of other pandemics was not related to the progress of medical science (McKeown & Brown 1955, op. cit. Omran 2005). 2) ***Socioeconomic, political and cultural determinants*** relate to standards of living, health habits, hygiene and nutrition. 3) ***Medical and public health determinants*** involve specific preventive and curative measures to combat disease; such as improved public sanitation, immunization and the development of specific therapies. Such medical and public health factors came into play late in the western transition. It thus needs to be pointed out that the reduction in mortality in Europe during the 19th century

according to the classical model of epidemiologic transition was basically determined by ecobiologic and socioeconomic factors.

Second demographic transition

Lesthaege (2010): The second demographic transition involves sustained sub-replacement fertility, a variety of living arrangements other than marriage and the disconnection between marriage and procreation. Gains in longevity at older ages in combination with sub-replacement fertility results in further population ageing. Had it not been for immigration, declining populations in many European countries would already have become evident. Typical features of the SDT include the increased expression of rising rates of divorce, delayed ages at first marriage, increased proportion of singles, rising rates of pre- and postmarital cohabitation, divorce and increasing proportions of births out of wedlock. Investment in the child, as still featuring during the first demographic transition was replace by motivation for adult self-realization. A Maslowian preference drift from the realization of material needs to higher order non-material needs and expressive values took place (*inter alia* freedom of expression, participation and emancipation, self-realization and autonomy, recognition). Associated was a shift in values with tolerance to diversity and respect for individual choice gradually taking over from solitarity and social group adherence and cohesion SDT: started with a multi-facetted revolution: 1. Contraceptive revolution (invention of the pill; re-invention of IUDs); 2. Sexual revolution (sex no longer confined to marriage and linked to procreation); 3. Gender revolution (asserted right of biological autonomy in terms of fertility regulation). All three these revolutions fit into a framework of of a rejection of traditional authority (anti-authoritarian). Pattern of fertility was associated with the SDT is its marked degree of postponement of parenthood, leading to sub-replacement fertility.

Most cohorts of Caucasian national populations born after 1960 are not expected to rebound to a total fertility rate of 2.1 (Council of Europe 2004, op. cit. Lesthaeghe 2010). Fertility levels of 1960 cohorts: Scandinavia, Britain and France (close to replacement fertility); Austria, Germany and Italy (falling below 1.7); Central and Eastern Europe (still reaching two children on average; but not in the Russian Federation, Slovenia and the three Baltic states; Council of Europe 2004, op. cit. Lesthaeghe 2010). In Western and Southern Europe (current total period fertility rates below 1.5). Collective behaviour is no longer guided by a normative structure based on family values, with marriage as the core entity of rearing offspring. From duty to the family unit to primacy of individual rights. The SDT is founded on the rise of higher order needs (vide Maslow 1954, op. cit. Lesthaeghe 2010). Such are centered on self-actualization and an increasing shift away from respect for authority. Behavioral elements of conformity (obedience, order and neatness, thrift, hard work, traditional gender roles, religious faith) and social orientations (loyality, consideration for others) are weakened and gradually replaced by the emphasis on expressive personality traits (self-presentation, independence, autonomy, symmetrical gender relations).
Results of analyses (cited from Lesthaeghe 2010):

- Secular, egalitarian, and anti-authoritarian orientations, expressive values, and values stressing individual autonomy are strong predictors of life courses that include “unconventional” states such as premarital cohabitation and parenthood among cohabitors. These effects are net structural effects linked to education, socioeconomic status, employment, or degree of urbanness.

- Cohabitants without children tend to exhibit the extreme non-conformist values profile, including greater gender symmetry, less intolerance to all types of minorities, greater protest proneness, but also greater tolerance for breaches of civil morality.
- Marriage and parenthood are associated with major readjustments of value orientations in the conventional and conformist direction. Married couples who never cohabited display by far the most conservative attitudes. (Association: marriage/conservative attitues). Any earlier cohabitation experience leaves a more permanent imprint in the non-conformist direction, even after marriage and parenthood have been achieved. (Association: cohabitation/non-conformism). Divorce produces a departure from the stability of conventional opinions held by married parents.

The main explanation for the SDT is based on the association of the fertility decline and the postponement of parenthood and the shifting of fertility to older ages. In some countries, however, as each cohort postpones childbearing for longer than its predecessor, the ultimate fertility remains largely constant due to recuperation at older ages of postponed births. Such recuperation effects have been observed notably for the Netherlands, Scandinavian countries, France and Belgium, but apply only modestly or are absent in Meditteranean and German-speaking countries of Western Europe.

Countries with higher levels of Inglehart postmodernism (Van de Kaa) or higher on the composite index of SDT values (Sobotka) had higher mean ages of women at first birth and an earlier onset of fertility postponement (Lesthaeghe 2010). Eastern European countries tended to have low post materialist scores (10-18) and lower mean ages at childbearing (24.5-28.0): Bulgaria, Belarus, Romania, Russia, Estonia, Hungary, Poland; contrasting the situation in mainly Western and Northern European countries with higher postmaterialist scores (24-33) and higher men ages at childbearing (between 28 and 31 years): Britain, West Germany, Sweden, Spain, Belgium, France, Italy, Switzerland, Netherlands, Finland. Years when the mean age at first birth increased for the first time by two years were negatively associated with SDT index values (Sobotka 2008). Consistent country groupings emerged: postponement leaders (between 1980 and 1988) had also the highest SDT index values and were represented by Sweden, Denmark, Netherlands, Finland, Germany and France. Late starters (between 2002 and 2010) exhibited lower SDT index values were represented by Belarus, Russia, Lithuania, Poland, Latvia, Romania, Estonia, Bulgaria and Slovakia.

For the period 1999-2000 to 2004 some recuperation of total fertility rates has taken place in some of the countries where postponenment had started earlier (TFR: 1.6-2.2): Sweden, Denmark, Netherlands, Finland, Iceland, Luxembourg, United Kingdom, France and Ireland. Cases of lower period total fertility rates (between 1.2-1.5) involve countries where postponement had started later and recuperation (fertility rebounding at older ages) of fertility was weak (German-speaking populations, Southern European and most formerly Communist countries). By 2007, Belgium, Denmark, Finland, Sweden, Norway and the United Kingdom had periodic TFRs above 1.8 (Prioux 2008, op. cit. Lesthaeghe 2010). Recuperation of fertility seems enhanced by factors that facilitate the combining of work and parenthood for both women and men and also by the alleviation of opportunuity costs of parenthood and family building. In countries with enhanced fertility levels due to recuperation, we have factors that alleviate time pressures on parents of young children (better adapted services and longer working hours of facilities for infants and toddlers, for pre-school children in kindergarten and for children in primary shool). It is noteworthy in his context that sub-

replacement fertility and postponement of first childbearing are also applicable to notably industrialised and urbanised Asian countries: Japan, South Korea, Taiwan, Hong Kong and Singapore (TFRs in the range of 1.0-1.25).

Sustained subreplacement fertility levels, as experienced during the second demographic transition has numerous negative implications: accelerated population ageing placing a strain on welfare systems, stimulation of replacement migration to counteract labour force shortages, new living arrangements more unstable and representing less adequate settings for procreation and socialisation (Lesthaeghe 2010).

Van de Kaa (2001): As modernisation progresses, the emphasis on survival and economic achievement will be replaced by an emphasis on the quality of life (Inglehart 1997, op. cit. Van de Kaa 2001): from the disciplined, self-denying and achievement-orientated norms of industrial society to an increasingly broad latitude for individual choice of lifestyles and individual self-expression; that is, involving a shift from "materialist" values (economic and physical security) to "postmaterialist" values (individual self-expression and quality of life). Intergenerational value change is then predicted to be in a postmaterialist direction as standards of living increase and younger cohorts age.

Van de Kaa (2001) advanced that changes in family formation and fertility were linked to socioeconomic development and the process of modernisation (postmaterialism/postmodernism). Countries which had moved farthest in a postmaterialist/postmodernist direction would also be exhibiting greater advancement in features of the demographic transition:

- Declining total fertility and declining higher-order birth rates
- Postponed childbearing within marriage and declining fertility among young women
- Increasing divorce rates
- Increased prevalence of cohabitation, increasingly seen as an alternative to marriage
- Increased age at first marriage and mean age at first birth
- Increased levels of voluntary childnessless
- Total fertility rates tend to stabilise at low levels
- Lower-order birth rates increase at higher ages of childbearing, but not all postponed births can be made up during the remaining childbearing years
- Cohort fertility appears to stabilise at below replacement levels.

Postmaterialists cohabit, and characteristically exhibit postponement of marriage and childbearing (mainly Western and Northern European countries: Netherlands, Ireland, Switzerland, France, Western Germany, Spain, Britain, Ireland, Belgium, Italy and Sweden, Finland, Iceland, Norway). In contrast, Eastern European countries (Bulgaria, Romania, Russia, Hungary, Latvia, Poland, Estonia, Belarus, Slowenia, Lithuania, Czech Republic), generally with lower postmaterialist scores, have smaller percentages of their fertility at ages above 30 years. In many of these Eastern European countries childbirth has always typically occurred earlier than in Western Europe; the aging of fertility has yet to begin. Van de Kaa (2001) attributes the relatively low total fertility of this group of countries to difficult socioeconomic circumstances encountered; which is consistent with relatively low scores for subjective well-being detected for these countries. Subjective well-being is much closer related to fertility and marriage transition than postmaterialist scores.

Postmaterialist/postmodernist: typically characterised by low value placed in religiosity and low respect for authority (fading away of conservative values). Committed to the logic of now and the immediate (Gibbins & Reimer 1995, op. cit. Van de Kaa 2001). Postmodernity is most expressed in Sweden, Finland, West Germany and the Netherlands; lowest in eastern European countries, Iceland and Ireland. Postmodernity is significantly negatively associated with first marriage rate and positively so with mean age at first marriage, the incidence of cohabitation among woman 25-29 years and subjective well-being (also postmaterialist score). Postmodernists do not generally feel that a women needs a child. (AS: Wealthier segments of populations are more subject to procursive influences: inappropriate diet, transgenerational affluence effects, population density stress).

Postmaterialists generally give birth to fewer children than materialists. Postmaterialist women tend to overestimate the number of children they will ultimately have; but reproductive postponement (especially in the more educated) is substantial and actual achievement of the desired number of children seldom realised. Comparative results between number of children considered ideal and actually born reflect this average desired/average born discrepancy (Van de Kaa 2001). Western/Northern European countries have relatively high scores of subjective well-being (here taken to indicate socioeconomic prosperity; absence of harshness/unpredictability) and also higher postmodernity percentages (Inglehart 1997, op. cit. Van de Kaa 2001): Sweden (percent postmodernity: 48.0/well-being score: 86), West Germany (42.8/70), Netherlands (42.6/85), Denmark (30.2/85), Norway (28.1/81), Austria (27.3/59), France (23.1/67), Belgium (22.5/77); with much lower values of both indicators for Eastern European countries: Czech Republic (13.6/32), Lithuania (13.1/13), Slovenia (12.4/23), Bulgaria (10.2/4), Belarus (8.6/-2), Russia (6.8/-1) and Hungary (6.7/28).

From the findings of Van de Kaa (2001) two country groupings are being differentiated: Eastern (low postmaterialist/postmodern scores = here termed conservative) and Western/Northern (high postmaterialist/postmodern scores = here termed liberalistic). The Eastern country-group is subject to relatively low socioeconomic prosperity, but generally less population density stress (lower levels of urbanization). Country-wide low total fertility rates are here interpreted to relate to socioeconomic constraints and higher levels of female employment. The Western/Northern country-group has generally high socioeconomic prosperity, relatively high population density stress apply to the countries involved (also higher degrees of urbanization). The wealth-fertility link no longer held during the period of the second demographic transition. Slightly higher fertility rates (plus/minus 2) are recorded, especially in Northern European countries.

Psychosocial incoherence

Surkyn & Lesthaeghe (2004): The study pursued the tracing of the connection between value orientations and life course choices in respect of living arrangements and family formation (household positions). The existence of such connections are central to the theory of the Second Demographic Transition (SDT). A fundamental transformation had occurred in the pattern of household formation and reproduction during the 1960s in North-Western Europe. Marked shifts in values were associated with demographic changes (linked to accentuation of individual autonomy in ethical, moral and political spheres, concomitant rejection of institutional controls and authority and the rise of expressive values in terms of higher order needs). The age at first marriage rose, premarital and post-marital cohabitation increased soon followed

by procreation in these informal unions. Divorce and separation rates continued to increase among cohabitants. In the late 1960s fertility postponement emerged; followed by partial recuperation of births at later ages. Total fertility rates (TFRs) in western countries reflected levels of fertility postponement (1970s); but reflected differential degrees of fertility recuperation at later ages during the 1990s. Until the 1990s, earlier patterns of marriage and fertility had prevailed in central and Eastern Europe, but after 1990 postponement of marriage and childbearing progressed (excluding the CIS countries such as Armenia, Belarus, Russia, Moldovia), causing a fall of national TFRs to below 1.5/1.3 children. Particularly the younger generations had different priorities than those of the older cohorts with respect to family and childbearing.
Profiles of value orientations covering a variety of dimensions were identified (such as *inter alia* religiosity, ethics, civil morality, family values, social cohesion, expressive values, gender role orientations, trust in institutions, protest proneness, post-materialism and tolerance for minorities). These were analysed (multiple classification analyses) in respect of eight different household positions. For purposes of analyses, four country groups were formed: West (Belgium, France, Germany), Iberia (Portugal, Spain) and Scandinavia (Sweden, Denmark). Similar value profiles according to household position were found for all three sets of countries. Surkyn & Lesthaeghe (2004) note that such pattern robustness is supportive of the contention that ideational/cultural factors represent relevant elements (but not sufficient) for the explanation of demographic changes during the SDT. In conclusion the authors found that associations between value orientations and household types were similar in various regions of of Europe.
Groupings of non-conformist (AS: liberalistic) value items:
I) **Atheist, secular, activist**. Rejection of the basic elements of religion and the importance of God in life. Protest proneness and activism. Weaker family orientation, more libertarian civil morality and a more cosmopolitan outlook.
II) **Non-conformist regarding marriage and family**. Non-conformist in relation to matters of marriage and family. Distrust in the church as institution.
III) **Youthful deviations regarding civil morality, lack of child orientation, distrust in institutions, low social involvement**. Lack of interest in children.
IV) **Self-actualization (expressive work values, tolerance towards ethnic minorities and deviant groups)**. Weaker civil morality, low community involvement and lack of national pride.
V) **Orientation towards companionship and social status; distrusting social environment**. Stressing companionship in marriage and social status aspects of work. Distrust in other people and in the justice system.
VI) **Egalitarian, anti-authoritarian, post-materialist, expressive socialization, adult forms of civil morality deviations acceptable**. Items in four subcategories. Firstly, preference for a more egalitarian partnership (importance of tolerance and understanding, sharing chores, happy sexual relationship). Secondly, anti-authoritarian and and post-materialistic outlook. Thirdly, accentuation of expressive socialization values (independence, imagination). Fourthly, indications of greater acceptability of more adult forms of civil morality deviance (such as tax evasion, tax cheating, social security fraud). Many items are related to a preference for equity in social relations and an aversion for authority.

Tending to **non-conformism (AS: *liberalistic*)**: secular, individual autonomy, weaker civil morality, expressive values, distrust institutions, protest prone, tolerance to minorities, world orientation, postmaterialist:

Coh0 (cohabitating with no children)
FmNu (formerly married or in union, not yet in a new unit)
Coh+ (cohabiting with children)
Single (never married and not in a union)
Respar (resident with parents)
Tending to **conformism (AS: *conservatism***): religious, respect for authority, trust institutions, conservative morality, local or national identification, lower tolerance to minorities, expressive values not stressed:
MarN (married with children, never cohabited)
MarE (married with children, cohabitation at some stage)
Mar0 (married and no children)

Coh0 (cohabitating with no children): Childless cohabitants have the highest non-conformist score of all household positions (in terms of secularization, ethics, civil morality, egalitarianism, anti-authoritarianism, tolerance, worldorientation, etc.). The Scandinavian group has a more distinct preference for segment II items (non-conformist regarding marriage and family); whereas the Western-Iberia grouping has a profile favouring items of segment I (atheist, non-religeous, social activism).
Coh+ (cohabiting with children): Also having a relative surplus of non-conformism; but moves into parenthood or marriage are associated with value adjustments in the conformist direction. Scandinavian cohabitants are linked to segmenet VI items (egalitarian partnership, post-materialism; endorsement of expressive socialisation traits, tolerance for minorities and groups with deviant behaviours). Sandinavian cohabiting parents are more comparable in their value orientations to married individuals than is the case in Western/Iberian countries. Iberian cohabiting parents have stronger preferences for items of segment III (youthful forms of distrust in institutions and tolerance for deviations regarding civil morality). Western cohabiting parents show preference for items in segment II (maintaining non-conformism regarding marriage and family). Western cohabiting parents share similar value preferences with Respar, Single, Coh0 and Coh+ (segments I: secular, activist and II: non-conformism regarding marriage and family).

Single (never married and not in a union): Relative surplus on the non-conformist scale. In Western/Iberia regions preference for value items of segment II (non-conformism regarding marriage and family); and regarding the Scandinavian country group for segment III (youthful deviations regarding civil morality, lack of child orientation, distrust in institutions, low social involvement).

Respar (resident with parents): Compared to their Scandinavian counterparts, residents of Western/Iberian countries have stronger preferences for items in segments I (more secularised) and VI (orientation towards egalitarian and anti-authoritarian value orientations).
MarN (married with children, never cohabited): Married women who never cohabited represent the most conformist group (similar in all three country groups). Small group of non-conformist items relate to segments IV and V: expressive work values, work with prestige and responsibility and emphasis on companionship. Aversion to items of segments I (atheism, activism) and II (non-conformist regarding marriage and family).
MarE (married with chidren, cohabitation at some stage): Married parents with an earlier cohabitation experience have a more non-conformist outlook than those without such an experience. Specific value profiles differ little between MarN and MarE in the Scandinavian countries (routinisation of cohabitation). In Scandinavian countries, both groups are also located in segment V (orientation towards companionship and social

status; distrusting social environment). In Western/Iberian countries, the MarE group is much closer to segment VI (large clusters of items related to anti-authoritarianism and equality). MarE has retained more "new left" and "post-materialist" traits in Western Europe and Iberia (Southwestern Europe) in comparison with Scandinavian countries. Mar0 (married and no children): Childless married Scandinavians have a relative surplus on the overall non-conformist scale and value items are located in segment VI (egalitarian partnership, anti-authoritarian, expressive socialization). In Western/Iberian countries married childless persons have a relative conformist outlook. Small number of non-conformist items are located in segment IV (self-actualisation through the expressive work qualities).
FmNu (formerly married or in union, not yet in a new unit): Currently divorced or separated respondents show value profiles in the direction of segment VI (egalitarian and anti-authoritarian values) and away from segments IV and V (typical for married persons: expressive work values, work with prestige and responsibility and emphasis on companionship). This shift is more pronounced in Scandinavian countries (coupled to more secularization). Other aspects of non-conformity are less pronounced in Scandinavian respondents; whereas in Western/Iberian countries higher overall non-conformist scores are exhibited.
Number of positive net deviations in the non-conformist direction for 80 value items according to household position for three groups of European countries
For the household groupings Respar, Single and Divorced (FmNu): mean for Scandinavia 35.7 and the Western/Iberia grouping 55.5. The highest values applied to cohabitants without children: mean 63.3; with cohabitants with children typically having lower values: mean 47.0 (no significant regional differences for cohabiting households). For married households the values are Scandinavia/Western-Iberia respectively: Married without children 44/32.0; Married with children (no cohabitation) 22/15; Married with children (with some pre-or post marital cohabitation) 35/29.

Non-conformist (liberalistic) scores are interpreted as index values of psycho-social incoherence; based on the similarity of the non-conformist value traits with those exhibited in populations subject to chronic/transgenerational population density stress *vide* Knaul (1985), as associated with accumulated patho-information-engram loadings (2.1.2). Non-conformist scores are accordingly here termed social incoherence scores. From the results of Surkyn & Lesthaeghe (2004), the following patterns can be derived: 1) Childless household types are associated with higher social incoherence scores than corresponding household types with children (the lowest social incoherence scores were reported for married couples without any experience of cohabitation); 2) High social incoherence scores are associated with childless cohabitants, somewhat lower for cohabitants with children (no regional differences); 3) Household types Respar (residence with parents), Single and divorced have relatively high social incoherence scores in Western/Iberia countries and 4) mean social incoherence scores over non-marital household types were 43.8 for Scandinavian and 55.3 for Western/Iberia

countries, respectively. However, mean social incoherence scores for marital households were higher in Scandinavia (33.7) than for Western/Iberia countries (25.3).

In summary, two divergent household groupings, which were relevant to all countries subject to the SDT, were identified:

I) Those tending to non-conformism (AS: *liberalistic*): secular, individual autonomy, weaker civil morality, expressive values, distrust institutions, protest prone, tolerance to minorities, world orientation, postmaterialist) included the household types Coh0 (cohabitating with no children), FmNu (formerly married or in union, not yet in a new unit), Coh+ (cohabiting with children), Single (never married and not in a union) and Respar (resident with parents). Characterized by ***higher*** levels of ***psycho-social incoherence*** and

II) Those tending to conformism (AS: *conservative*): religious, respect for authority, trust institutions, conservative morality, local or national identification, lower tolerance to minorities, expressive values not stressed) included marital household types MarN (married with children, never cohabited), MarE (married with chidren, cohabitation at some stage) and Mar0 (married and no children). Characterized by ***higher*** levels of ***psycho-social coherence*** (***lower*** levels of ***psycho-social incoherence***).

During the SDT progressively more individuals are subject to liberalistic value systems relative to those with conservative value systems, reflecting increasing psychosocial incoherence and an associated shift away from family-based to non-family based childbearing within a context of sustained low fertility rates (below replacement fertility rates).

As population density increases towards environmental carrying capacity, intraspecific competition increases; taking the forms of either scramble (in the context of psychosocial incoherence: LHS-mode M:4) or interference competition (supported by P-vitality: LHS-mode P > M:2; family as a defended breeding territory). Under scramble competition conspecifics have relatively free access to resources which they exploit and convert to growth and reproduction before they are depleted by others. In contrast, under interference or contest competition, conspecifics do not have equal acces to resources due to active interference in the form of aggressive interactions, dominance relationships or territoriality. Territoriality as resource defence mechanism is typically prevalent for populations shaped by K-selection and tends to regulate

population densities in relation to the carrying capacities of the environment (Geist 1978).

Germany

Knodel and Wilson (1981): M as an index of underlying fertility: any circumstances which increased marital fertility rates at younger ages were reflected in increased M values (Pm > pM shift). Marital fertility rate associated with increasing fertility at younger female ages (20-24, and also 25-29; fertility declining > 30 years of age) for marriage cohorts 1800-1900 onwards (AS: LHS-mode Pm > pM) in comparison with 1750-1800 cohorts (Pm ≈ pM). Elevated M (increased fecundity) values for German villages between 1840-1900 (AS: Pm > pM) relative to values during 1751-1825. Shift in birth seasonality of second and higher order births from predominance of winter births in the years 1750-1774 (AS: Pm ≈ pM) progressively towards spring/early summer births during 1875-1900. (AS: Pm > pM). Lerchl et al. (1993) reveals a shift in birth seasonality from births predominantly occurring during the first half of the year (March-June) in 1951-1955 to 1971-1975, towards births occurring predominantly during the last half of the year (July-Septemmber) in 1981-1990 (shift already evident from 1971-1980). (AS: LHS-mode pM↑; SDT)

Hank (2001): During 1995-1997, West German rural districts (Landkreise) had a mean TFR of 1.47 (n = 236) while urban districts (Kreisfreie Städte) had a mean TFR of 1.24 (n = 92). High population density regions, with lower fertility, displayed steeper fertility declines; whereas those with lower population densities changed at a slower and delayed pace. Urban-rural fertility behaviour did not converge over time. Districts with relatively high reproductive rates were characterized by low population densities, low levels of education, and a high share of the population working in agriculture. Geographically, high fertility regions were concentrated in two regions: nothwestern (along the Dutch border) and southern Germany (Bavaria/Baden-Württemberg border zone). Both regions correspond to a cluster of 22 rural districts with a similar family milieu (Nauck 1995, op. ci. Hank 2001) characterized by low divorce rates, high birth rates, young overall population and a high proportion of unemployed and recipients of social assistence. (**AS: According to the LHS explanatory model these syndromes of association can be explained as the causal outcome of regional transgenerationally lower rates of patho-information-engram loading accumulation under conditions of lower levels of affluence/population density stress in regions currently exhibiting relatively high fertility rates, resulting in a compatratievely slower progression of the fertility transition**). Nauck (1993, op. cit. Hanks 2001) showed that educational levels of women in university towns are higher, while the proportion of married women, birth rates and the proportion of children are lower. For the period 1995-1997 (Hank 2001), female school-leavers in high fetility areas had generally achieved lower educational qualifications (e. g. 20 % had achieved

Abitur compared with 36 % in low fertility districts). (**AS: According to the LHS explanatory model, individuals with higher performance competence would have been subjected to transgenerationally sustained conditions of affluence/population density stress and associated higher levels of patho-information-engram loading accumulations; leading to an earlier onset of demographic transition effects, i.e. fertility decline**).

Kemper (1991, op. cit. Hank 2001) pointed out long-standing cultural differences beyond a simple urban-rural dichotomy. Church attendance and proportion of Protestants between the years 1966-1986 were identified as measures of secularization; where church attendance was positively associated with local birth rates, while the reverse association held for the proportion of Protestants and aggregate levels of fertility. Nauck (1995, op. cit. Hank 2001) found evidence for historical stable differences between regions in terms of their sociocultural milieu. Marriage and parenthood are closely connected in southern regions of Western Germany, this not being so in northern parts of Western Germany. Consistent with these findings, Bertram & Dannenbeck (1990, op.cit. Hank 2001) found a clear north-south divide in respect of the desired number of children: the proportion of respondents living in northern rural and urban areas desiring only one child was higher than in southern regions; while the reverse was true for three children. The pattern is one of a greater prevalence of a traditional/conservative sociocultural milieu associated with greater fertility in southern Germany (slower advancement of the demographic transition) and a modern-liberalistic sociocultural milieu and lower fertility rates in northern Germany (advanced progression of the demographic transition).
RE Table 2.3.3b (**AS**: **On the basis of southern Germany having been historically less subject to affluence and population density stress than northern Germany, it can be predicted that the demographic transition to low fertility would have advanced faster/earlier in northern Germany: affluence/population density stress ≈ patho-information-engram accumulation ≈ driving demographic transitions according to the LHS explanatory model**). This is consistent with conservative voting to be associated with regions of less advanced demographic transition progression than in regions with predominantly liberalistic voters in regions of advanced progression of the demographic transition, a pattern also reported over counties of the United States of America (Lesthaeghe and Neidert 2009).

Hank (2002): Analyses showed that regional variation of fertility in Western Germany (Hank 2001) resulted from differences in the spatial distribution of individual characteristics. This was found to apply particularly in respect of the occurrence of first births during the observation period (1995-1997). However, some effect of regional context was revealed regarding the transition to the second child. This is consistent with the findings of Birg et al. (1990, op. cit. Hank 2002) that regional differences have been evident for especially higher parity births. The probability of married women to experience a first birth is many times higher than for the unmarried. Being married also increases the propensity of women to have a second child. Educational activities are associated with post-ponement of childbearing.

Heiland et al. (2008): The decline in actual fertility was paralled by a decline of the average number of children individuals wanted. For West German women completed cohort fertility has fallen from 2.2 to 1.6 children per woman between 1935 and 1956 birth cohorts, wheras the corresponding desired number of children declined from 2.5

to 2.2 (Heiland et al. 2005, op. cit. Heiland et al. 2008). The average number of children wanted has remained above two in most Western European countries, whereas the ideal in Germany and Austria is now below replacement level (op.cit. Heiland et al. 2008). Analyzed longitudinal survey data for West Germany collected during 1988-1994/1995. The importance of background factors are confirmed: positive associations with the number of children desired and growing up with both parents, more siblings and Catholic religious background. These background factors mainly affect the total of children wanted early in life. Women of the same age group who already had one child at the time of the first interview desire larger families throughout. Women who are Catholic change their desired fertility more frequenly than other women. Catholic women are more likely to start with childbearing earlier and have the desire to realize a traditional large family when young, but lower their desired fertility subsequently in response to information regarding the costs and benefits of larger family sizes. Young women raised in a two-parent household were found less likely to change their desired fertility across interviews (positive family experience during childhood: stability of fertility norms). Greater instability of desired fertility was recorded for women with college high school education. Women aged 25-36 years with greater household income displayed more stable desired fertility; unlike those who had experienced divorce or separation. The analyses have supported the hypothesis that childbearing and rearing affects the total number of children wanted (consistent with greater increases in the expected benefits of having a large family among women who start childbearing early). (AS: Note the association between early childbearing and pronatalist attitudes: indicative of prevailing LHS-mode Pm > pM).

Dorbritz et al. (2015): Childnessless has become a mass phenomenon in Germany (*ca* 20-22 %), particularly so in Western Germany. For women of the birth cohort 1950 the equivalent rate was 14 %. The low fertility rate in Germany (and other European countries) is primarily related to increasing childnessless and the low and declining proportion of families/women with three or more children. In higher qualified women rates of childnessless are even higher (*ca* 28 % for the 1970 cohort). For the academically qualified, the proportion of childnessless rose from 25.4 % in 1982 to a possibly asymptotic peak value of 34.5 % (Bujard 2012, op. cit. Dorbritz et al. 2015). However, there is also a trend of childnessless increasing in the less qualified in Western Germany and the higher qualified in the formerly German Democratic Republic; implying that the rise in the country-wide extent of childnessless can be expected to continue for the time being.
Increased childlessness for women of birth cohort (1970-71) according to qualification status 14.7 % (without qualificaton), 20.7 % (apprenticeships), 21.5 % (technicians) and 27.8 % (college/university graduates). Employment status and percentages of childnessless (2012): Both male and female full-time employed (26.4); male full-time, female part-time employed (5.2); male full-time, female non-employed (7.9); male part-time, female full-time employed (23.7), both male and female part-time employed (11.6); male part-time, female non-employed (15.2) and male non-employed, female full-time employed (28.7). For western Germany, when both male and females are fully employed, the proportion of childnessless amounts to 34.2 %. Number of children and partnership status: 1.84 (marriage), 1.09 (non-married partnerships and 0.97 (single parenthood). Childnessless in relation to migrant background (MB) and non-migrant background (NMB): Overall NMB: 21.4, MB: 11.5; Education: high NMB: 29.3, high MB: 20.4, low NMB: 26.6, low MB: 7.6; Parnership status (marrie/non-married): married NMB: 11.0, married MB: 6.9, non-married NMB: 40.2, non-married MB: 22.4.

Declining fertility is the main indicator of an ongoing demographic transformation. Characteristics of this progressively unfolding transformation are outlined by Dorbritz et al. (2015): 1. Increased maternal age at first birth; 2. An increasing proportion of childness women; 3. An increasing proportion of children born out of wedlock, indicating a decoupling of marriage and parenthood and 4. Partnership forms between men, women and children change, with a reduction of the importance of marriage being the central feature of this change.
Progressive disintegration of the traditional family model with gender-specific roles, were men were responsible for provisioning/protection and women focusing on duties of reproduction and rearing of offspring.
Socioeconomic factors: Higher levels of education in women is generally negatively associated with the probability of transition to having a first child (Skirbekk 2008, op. cit Dorbritz et al. 2015). A tertiary qualification has a negative effect on the readiness to establisch a family (Schaeper et al. 2013, op. cit Dorbritz et al. 2015). Insecurity in respect of career/employment has negative effects on the readiness for family establishment (Blossfeld et al. 2005, op. cit Dorbritz et al. 2015). Women in short-term employment have a 20 % lower probability of the rate of moving towards having their first child than permanently employed women (Kreyenfeld 2008, op. cit Dorbritz et al. 2015). Income and career security of the partner (generally the husband) has a positive effect in this contet. A stable career is accordingly also of great importance for moving towards paternity (op. cit Dorbritz et al. 2015).
Partnership dispensations: The first-born rate for married couples is more than double of those for non-married partnership types.
Dorbritz et al. (2015) differentiate between risk-avoiding and autonomy-emphasising childnessless; both basically relating to the reluctance of prospective parents to face the challenges of mastering the conflicts between parenthood and career/self-expression. The majority of Germans in the age group 20-39 consider childnessless as normal. (AS: low instinctual and functionality).
Summary of findings:

- Links to education: Higher qualified women experience a higher degree of childnessless than lesser qualified ones.
- Forms of partnerships: Married couples have lower rates of childnessless than unmarried couples.
- Livelihood security: Highest levels of childlessness are experienced in employment situations characterised by full-time employment of women.
- Migration background: Women without migration background are more often childless than those with a migration background. Substantial differences exist in this regard as to country of origin of migrants.

Fertility across socio-economic strata

Miettinen et al. (2014): After the mid-20th century childnessless has been increasing in most countries. Childnessless is common among highly educated women, but increasingly also in low educated women. In men, childnessless remains to be concentrated in the less-educated groups. The negative association between childnessless and cohort completed fertility has become stronger over generations (suggesting childnessless being a fertility indicator: childnessless as important component of low fertility). Most of the increasing childnessless is unwanted. Proportions ever married in populations are negatively correlated with life time female childnessless, also recorded for younger generatons. Childnessless is relatively

common among well-educated women, but increasingly so also in both men and women of lower socioeconomic strata (lacking socioeconomic resources). Childnessless is higher in countries with high average mean ages at marriage and delayed childbearing; and also in countries with higher levels of individualisation. Increasing rates of involuntary childnessless.

Family formation and childbearing

Frejka et al. (2008): Provided a summarising overview of factors influencing family formation and childbearing during the last 60 years in Europe in relation to political, economic and social changes. During this period profound changes were also observed in values and attitudes regarding family and childbearing, affecting fertility trends. In countries of Northern and Western Europe fertility stabilised at moderately below replacement levels (total fertility rates between 1.7-2.0 per women), whereas fertility continued to decline to low levels in Southern Europe and predominantly German-speaking countries. In the first decade of the 21st century, three-quarters of Europe's population live in countries with total fertility rates of 1.3-1.6 children per women (Southern, Central and Eastern Europe). A pattern of delayed parenthood represented an important factor in these trends of declining fertility. In Western and Northern Europe, delayed births were generally recuperated when women reached their twenties and thirties. Recuperation remained at lower levels in countries of Southern, Central and Eastern Europe. By the end of the 20th century, the two-child family had become the norm, but tended to decline to a greater incidence of one-child families subsequently; especially in Southern, Central and Eastern Europe.

Modern methods of birth control, although giving women greater control over their reproduction (*inter alia* providing tools to appropriately time pregnancies in relation to education, employment, career development and marriage), historically, they only had marginal effects on fertility levels. The basic demographic mechanism underlying declining fertility levels were considered to consist of delayed family formation and childbearing and only partial recuperation of delayed births at higher ages in comparison with older generations. Concomitant with fertility change was a transformation involving the nature of sexuality, family formation and family life; as manifesting in declining rates of marriage, increasing cohabitation and non-marital childbearing, increasing union instability and divorce rates (Frejka et al. 2008). However, relationships between these manifestations and fertility are not straightforward. Interacting factors (late 20th and early 21st century in Europe) include difficulties for young people to establish separate households, to find stable employment and to pursue a career (with Nordic countries as partial exception). An increasing proportion of women have been joining the labour force, placing them in a conflict situation of competing responsibilities of childbearing/rearing and career requirements.

Intimate relationships among un-partnered individuals, acceptance of non-marital arrangements, childnessless and divorce became widely accepted. These changes in norms and values relate to broader economic and social developments associated with the second demographic transition: increasing posterity, rising educational levels and the spread of labour force participation by women. For those with parenthood still a priority (a declining proportion of populations), childbearing results from a planned decision and responsible parenthood places emphasis on the well-being of the children.

According to the classical scenario (Lesthaeghe 2010), the second demographic transition follows along a pathway of cultural and value changes driven by economic

affluence, and are characterised by secular individualism/self-fulfilment leading to changes in family behaviour. However, experiences in Nordic and Western European countries (forerunners in the SDT process) suggest that the demographic transition does not necessarily lead to a long-lasting decline in fertility to sub-replacement levels, as implied by the classical scenario (Frejka et al. 2008).

Substantial migration streams into Northern, Western and Southern Europe occurred after 1990 and this immigration is associated with an increasing proportion of births in Europe being attributed to immigrants (Frejka et al. 2008).

Sobotka (2008): Re-examined the link between shifts in values and attitudes regarding family, reproduction and children, and fertility. For SDT low fertility countries the author identified a strong positive association between fertility and fertility at later childbearing ages. Due to this recuperation effect the transition may not necessarily lead to below-replacement fertility.
Lesthaeghe & Van de Kaa (1986, op. cit. Sobotka 2008) were first to present the idea of the second demographic transition, referring to interrelated changes in fertility, family formation and partnership behaviour which started in the late 1960s in several countries in Western and Northern Europe.During the SDT, in European countries births and marriage were progressively postponed. Cohabitation increasingly emerged as a substitution for marriage, marriage rates declined and the connection between marriage, sexual life, and childbearing was eroded. Increased partnership instability was associated with cohabitation and alternative life styles and increased divorce rates. In a rising number of countries, having a first child within marriage became the experience of a minority. Common directions of changes:

- Tolerance and acceptance of intimate relationships among unmarried and unpartnered individuals (including young adults and teenagers)
- Positive acceptance of cohabitation as a premarital stage and even as an alternative to marriage
- Tolerance and increased acceptance of non-family living arrangements and voluntary childnessless.

Although marriage and childbearing have increasingly become optional, the family has not become an obsolete institution, but in a somewhat transformed state, value is still attached to family and children and a positive attitude still persists towards parenthood. Compared to the era preceding the SDT, the acceptance of voluntary childnessless and non-family living arrangements has increased and although marriage and family life has become increasingly optional, attitudes towards parenthood have remained positive. Parenthood has ceased to be the main goal in the lives of both men and women. Having children is no longer considered a precondition for self-fulfilment. West German respondents most frequently express the intention to remain childness. Non-marital childbearing is more prevalent in younger people and residents of big cities. The SDT is associated with a pronounced postponement of parenthood, a rise in the proportion of non-marital births (cohabitation, union instability), and leading to structural long-term subreplacemeny fertility. ***Falling fertility rates are first associated with a reduction in higher-order fertility and later by the postponement of parenthood.*** The onset of long-standing fertility postponement marks the onset of the SDT. The SDT2 index was found to be correlated with the timing of the onset of fertility postponement, mean age at first birth and negatively so with fertility rates

below age 25. ***Some fertility recuperation of women who had postponed births by having children later in life was evident; but this was generally not sufficient to bring fertility back to replacement fertility (Van de Kaa 2002, op. cit. Sobotka 2008)***. The onset of fertility postponement, the central characteristic of the second demographic transition, as indicated by when the mean age at first birth had increased by two years, took place between 1983-1987 in Finland, Sweden, Germany, the Netherlands, France and Denmark; between 1990-1995 in Spain, Italy, the United Kingdom and Greece; between 1995-2000 in Croatia, Austria, Slovenia, Portugal, Hungary, Ireland and Czech Republic; between 2002-2005 in Slovakia, Bulgaria, Estonia, Poland, Romania and Latvia; and between 2006-2008 in Lithuania, Russia and Belarus (from Sobotka 2008). Values and attitudes emerged during the second demographic transition which were notably negatively correlated with fertility rates of women below age 25, but not for women above age 35 (recuperation component). Low and very low fertility rates in contempory Europe relate to fertility postponement, structural and institutional constraints exerting negative influences on fertility decisions and also shifts in family-size norms towards subreplacement fertility (e.g. childnessless). Voluntary childnessless in Europe has reached the highest level in western Germany, especially in respect of higher-educated women (Dorbritz 2008).

Behavioural changes typical of the SDT, having started well before 1990, accelerated thereafter: postponement of first births and first marriages (less so in Eastern and Southeastern Europe, but more so in Central Europe and in Baltic countries), falling fertility levels, increasing percentages of non-marital births, falling marriage rates and high/increasing divorce rates. For Romania, Rotariu (2006) reported that the fertility behavioural change, as manifested by falling fertility rates, fertility postponement and rising proportions of non-marital births, preceded the "shift in the system of values and attitudes toward family and children". This pattern also applied in other eastern European countries. The absence of ideational change preceding or being associated with fertility decline has been noted for a number of eastern European countries: Rumania (Rotariu 2006), Poland (Kotowska et al. 2008, op. cit. Sobotka 2008) and Russia (Gerber & Cottrell 2006, op. cit. Sobotka 2008). Implying cause-effect relationships between falling fertility rates and ideational changes are therefore problematic/not substantiated.

For eastern European countries, Sobotka (2008) considers that long-lasting changes in both family-related values and fertility-linked behaviour are mutually reinforcing. As in Western countries, a consistent relationship in changes in family behaviour and value orientations seems to apply. Direct fertility responses to changing economic conditions are not observed; rather continued low fertility with improvements of living conditions in 1999. Transformation in values in respect of family and children and the spread of individualism is being observed for the whole region, especially among the younger, more educated, urban population. Extramarital childbearing (also cohabitation) represents a typical feature of the second demographic transition, spreading from the lowest-educated part of the population to the more affluent and higher-educated social groups. Some behaviours associated with the SDT first spread as a reaction/accommodation to socioeconomic constraints rather than as an alternative lifestyle of highly educated individuals. Postponement of births and marriage was widespread. Marriage rates had plummeted and the link between marriage, sexual life and childbearing has been eroded. Increased partnership instability, as linked to the spread of cohabitation and high/increasing divorce rates, is prevailing. The occurrence of postponement of marriage and fertility and childnessless was/is prominent in higher-educated women, while lower-educated individuals can

more often be associated with unstable living arrangements and non-marital fertility. However, higher-educated people resist longest the erosion of the traditional, middle class family concept, especially when childrearing becomes relevant. Despite all the negative effects playing out in this phase, the continuing strength of the family and associated positive attitude towards parenthood may partly explain the persistence of fertility levels (although at low levels) and relatively sustained childbearing intentions in contemporary Europe.
Sobotka (2008) identifies two pathways of behavioural and value changes during towards and during the second demographic transition:

- Cultural and value changes are driven by economic affluence and characterised by secular individualism, orientation towards personal self-fulfillment as preconditions to changes in family behaviour. These behavioural changes prevail in the more educated and socially privileged who adopt new preferences regarding childbearing in relation to education, employment
- In primarily disadvantaged strata, new behaviour patterns (such as cohabitation, non-marital childbearing) constitute a reaction to adverse life circumstances (socioeconomic stress; anomy). Spreading to other socioeconomic strata by diffusion. This pathway seemed to have prevailed in Central-Eastern Europe.

Eastern Europe

Zakharov (2008): In Russia, during the 1970-1980s some features of the traditional pattern were preserved: obligatory marriage, link between sexual and matrimonial behaviour, a high tempo of family formation at young ages, voluntary childnessless largely absent and little regulation of the timing of first births. There were transitional features associated with modernization (two-child family ideal). The pattern was not based on economic rationality. Coping with every day life for a family with children was difficult, since the income of a young family was often inadequate; requiring additional support from extended family or the state. Young couples responded by the creation of a family and the birth of a child, favouring a situation of sustained poverty. (WN: under economic rationality: first tried to achieve economic independance)

Signs of the second demographic transition in Russia since the mid-1990s ("a quiet revolution in family formation"). In Russia, the fertility of women under the age of 20 has halved within the last ten years, suggesting that a profound change in the behaviour of young people has been taking place (towards fertility aging since 1995). The mean age at first marriage is also increasing. One third of the total number of births over the last 15 years were non-marital births. Non-marital childbearing has become more socially acceptable. Preference of Russian women did not shift in the direction of one child or childnessless. Desired and expected mean number of children are lower in the city of Moscow than for Russia as a whole. Marital status remains to be a significant advantage with regard to number of children born. The incidence of informal partnership unions is increasing.
Period total fertility rates: (Urban/rural) 1979-1980: (1.70/2.50); 1994: (1.24/1.91); 2004: (1.25/1.67). Completed cohort fertility (2002) by educational levels (Higher professional/general professional/full secondary/general and lower): Birth cohort 1948-1952 (1.57/1.78/1.91/2.40); 1953-1957: (1.60/1.83/1.99/2.45); 1963-1976: (1.47/1.72/1.94/2.20). (AS: Interaction: more educated people tend to aggregate in urban environments).

For Russian female birth cohorts 1841-1875, an average of 7.0 children (6.8-7.2) were born alive, with a mean survival proportion to age 20 of 0.44 (0.44-0.46). For birth cohorts 1876-1905, an average of 5.6 children (4.6-6.8) were born alive, with a mean survival proportion to age 20 of 0.50 (0.48-0.53). For birth cohorts 1906-1930, an average of 2.9 children (2.2-3.7) were born alive, with a mean survival proportion to age 20 of 0.72 (0.57-0.89). For birth cohorts 1931-1970, an average of 1.9 children (1.5-2.1) were born alive, with a mean survival proportion to age 20 of 0.95 (0.92-0.96).

1.6 children per women (as for birth cohort of 1980-1981) are considered to represent contemporary expectations.The ageing of fertility is progressing at a slower pace than in Western countries, and even slower than in other eastern/Baltic counties. Russia not expected to arrive at the age profile of fertility experienced in Western countries within the next 10-15 years. For generations born in the 1970s, the proportion of childless women was estimated at 10 %; and is not expected to exceed 15 % in the medium-term future.

Gavrilova & Gavrilov (2009): Declining fertility rates have the greatest impact in causing population ageing. Particularly fast population ageing is anticipated for Eastern Europe and Russia after 2010 (mainly as aresult of fewer children being born after the post-war birth peak). Population ageing results from declining fertility making recent cohorts smaller than preceding ones (tilting the age distribution towards the accumulation of older ages). After 1989 a transformation of childbearing patterns involved a rapid decline in fertility rates, postponement of childbearing and increased proportions of extramarital births (Sobotka 2003, op. cit. Gavrilova & Gavrilov 2009). An increase in life expectancy involves two components with opposing effects on ageing: firstly, a mortality decline among infants, children and people younger than the mean age of the population (acting against population ageing by concentrating mortality decline in the youger age groups, having the same effect as increased fertility: Preston et al.2001, op. cit. Gavrilova & Gavrilov 2009) and secondly, an accelerated decrease in mortality among the elderly (mortality decline concentrated in the older age groups). Such a trend in mortality decline emerged in the 1950s in developed countries. This second component of mortality decline, as concentrated in older age groups, is considered an important determinant of population ageing (more so for women) in industrialzed countries (**AS: LHS-mode pM↑: 2.2.2e**). This component, in contrast, has not played a significant role with regard to population ageing in Russia and Eastern European populations. In none of these countries significant increases in life expectancy were experienced during the last decades; life expectancy even decreased in some countries (Russia, Belarus, Ukraine) after 1990. (**AS: consistent with LHS-mode Pm↑: combination of relatively retained Pm vitality and anomy**).
Generally, in the context the demographic transition where societies move from high rates of fertility and mortality to low rates of both. Initially, infant and childhood mortality declines, but as fertility declines, population ageing sets in. Then population ageing is accelerated further as late-life mortality also starts to decline.
In the 2000s poverty became a problem for people of working ages and their children in Russia (Gustafsson & Nivorozhkina 2004, op. cit. Gavrilova & Gavrilov (2009). Fertility rates in Russia are now among the lowest in the world; with substantial regional variation (highest in North Caucasus; lowest in big cities: Moscow, St. Petersburg; DaVanzo & Krammich 2001). The Russian population remains relatively young in comparison with other European countries (**AS: according to expectation of**

the LHS-mode Pm↑: 2.2.2e). Feminization of population ageing. Generally females have lower mortality than males in respect of age groups and for most causes of death; resulting in the 'feminization' of population aging (being particularly acute in Russia, Ukraine and Belarus). Russia and most countries of Eastern Europe lag behind Western Europe as to the extent of population ageing.

Sweden

Hoem & Hoem (1996): The Swedish TFR dropped from about 2.5 in the mid-1960s to c. 1.7 (1980), then increased to above replacement level by 1990, followed by a decline to below 1.7 in the subsequent six years. Interpretations: 1965-1980 – Fertility decline attributed to attitudinal changes with women taking control of their childbearing (contraception, abortion). Childbearing was temporarily postponed or curtailed. 1980s – Fertility increase included all birth orders and women of all ages. Economic trends were favourable, resulting in increased wealth of the population. Massive public policy investments towards family with children bearing fruit. Optimism regarding increasing benefits from family policies. 1990s – Reduced economic prosperity (unemployment, job insecurity, recession with public sector cutbacks of benefits and family-policy generosity). Slacking of incomes and pessimistic expectations favouring a rational response to postpone a first birth or forego higher-order births. In summary, most of fertility variation concerns the age at which children are born (tempo of childbearing, not the quantum). The values of how many children are desired (fertility quantum) have been relatively stable for the cohorts studied, but fertility swings moved in concert with economic and political conditions. Births have been delayed substantially over the past 25 years. As fertility declines with age for progressive birth orders, the final sibship size is unlikely to be sustainable at its current level (considering that a third of women at age 30 were childless in 1995).

Trade-off constraints between socio-economic/cultural achievement and fertility

Voland (2000): The term demographic transition is used for the complex historic transformation from traditional populations with high fertility and mortality to modern populations with low fertility and mortality. Analyses have shown that the decline in mortality cannot be causally related to this transformation (Coale and Watkins 1986, op. cit. Voland 2000). Two different potentially explanatory scenarios for this historic transformation have been discussed (Borgeroff Mulder 1998, op. cit. Voland 2000). According to the first scenario modernization of the nineteenth century stimulated parents to invest in competitiveness of their children through, for example, education and legacies. Under such circumstances of modernisation as associated with highly competitive conditions, and subject to quantity-quality trade-off constraints, parents may have considered socioeconomic competiveness (offspring quality) of greater importance than number of children (offspring quantity). (**AS: Quantity-quality trade-off constraints: 2.2.2b; 2.2.2d**).
Secondly, economic opportunities are increasingly more highly rated than generative opportunities. Since the availability of resources for raising offspring were often in short supply in the past, psychological mechanisms attaching higher priority to the accumulation of resources rather than to the repeated birth of children were expectedly selected for due to latent resource shortages for the raising of children and parental survival being more regularly in jeopardy than childbearing. Voland (2000) surmised

that the preference for economic opportunity in preference to generative activity might be a phylogenetically fixed psychological preference adapted to former conditions of latent resource shortages. This preference no longer automatically contributes to the maximisation of genetic fitness under the changed constraints of modern society (*vide* Turke 1989, op. cit. Voland 2000).

Voland (1998): The requirements of increasing offspring competitiveness (education/wealth) in industrialized, modernised societies with their new economic opportunities may have resulted in parents limiting the number of their offspring in favour of greater per capita investment; which can only occur at the expense of the number of offspring (quantity/quality trade-off). It is unclear whether this approach can support genetic fitness under conditions of industrial societies. Secondly, the pursuit of economic opportunities at the expense of generative activity according to a psychological preference, adaptive under Pleistocene conditions of latent resource shortages, as also expressed in modern societies is unlikely to contribute to the maximization of genetic fitness as a result of associated changed socioecological conditions.

(AS: The capability of survival during times of crisis is expectedly central to differential lineage survival and thus in shaping human reproductive strategies. Both the accumulation of resources/wealth in order to buffer the risk of extinction during a crisis and as well as the realisation of producing and raising numerous offspring in accordance with available wealth are central to fitness maximisation. Life history strategies with sufficient plasticity allowing for both fast and slow life history traits may cater for an optimal balance on the fast-to-slow life history gradient; subject to applicable trade-off relationships (reproductive/performance rates/offspring quantity/current reproduction *versus* maintenance/offspring quality/future reproduction: 2.2.2b; 2.2.2d).

Newson (2009): For developed countries, a trade-off is posulated between socio-economic cultural achievements (social rewards: educational qualifications, prestigeous career, acquisition of prestige goods) and reproductive success. If human reproductive decision making is the result evolved psychological mechanisms monitoring the availability of physical resources, then family size should increase with economic development. If individuals montor their social environment to determine the consensus on when a new baby will be welcome, the link between economic development and family limitation is less puzzling. During human evolutionary history, social groupings were smaller, more stable and more kin-based than those of developed societies. Social interactions between kin are expected promote fitness maximising decisions, while in more open communities consensus as to the desirability of high fertility would tend to be uncertain. Evidence suggests that social interactions between non-kin is less likely to encourage fitness-maximizing reproductive behaviour.

Kalmijn (2007) showed that the proportion of women in paid employed was associated with lower marriage rates, higher divorce rates and higher levels of cohabitation (higher levels of anomy). Policies thus (notably applied in Nordic countries) which reduce the incompatibility of work and childbearing were found conducive to for the recuperation of fertility at later childbearing ages, especially among more educated women (Sobotka 2008; refer also to D'Addio & d'Ercole 2005).

Women employment has negative effects on fertility particularly in respect of second and third-order childbearing (Brewster & Rindfuss 2000). The relationship between female labour force participation and fertility at the individual level is negative, but this has changed to positive at the national level. Women in all countries face challenges in balancing their work and family responsibilities, but coordinating these responsibilities is easier in some countries than others. Considerable evidence indicates that the degree of conflict experienced between work and fertility varies across advanced industrialized countries; as do family benefits, maternal or paternal leave policies and childcare availability. Such aggregate characteristics however did not turn out to be good predictors of national fertility levels.

Closely following D'Addio, A. C. & d'Ercole, M. M. (2005), the results of their report (*OECD Social, Employment and Migration Working Papers*) can be summarised as follows:

- Feritility rates have declined substantially in all OECD countries over the past decades (pace of decline and levels achieved varied between countries). Cohort indicators of fertility indicated in spite of postponement of first childbirth, recuperation at higher ages is only partial. Completed fertility is accordingly unlikely to return to replacement levels in most countries. Postponement of childbearing is furthermore associated with an increased proportion of children without siblings, a higher frequency of childnessless among women in their 30s and 40s and greater risks of certain health problems for mothers and their children. The gap between desired and observed fertility rates is increasing.
- Two factors have been contributing to current fertility trends: higher education and employment of women, associated with changes in patterns of family formation; shifting values of younger women towards a less

traditional role of women within family and society. Women in paid employment, with higher educationand who are not married have lower births than other women. As these trends progress total fertility rates are being further reduced; and partly explained by shifts in the values of individuals regarding family and gender roles.

- Cross-country comparisons revealed that total fertility rates are relatively higher in countries with wider childcare availability, lower direct costs of children, higher part-time availability and longer leaves. Provisions that allow mothers to better cope with family and career responsibilities help to remove obstacles to childbearing. Policies relaxing some of the constraints to childbearing may raise total fertility rates (and thus population and labour force sizes).

Brewster & Rindfuss (2000): The negative association between fertility and female labour force participation reflects on the incompatibility between caring for children and economically productive work in industrial societies. Increasingly women in advanced industrial societies choose to take on both work and child rearing, with the result that fertility levels are below self-repacemment in most countries. While this role incompatibility was evident in the past, countries that now have the lowest fertility are those with relatively low female labour force participation (cross-country macro-level: refer also to Kohler et al. 2006). At the individual level (micro-level), the negative association between fertility and female labour participation remains to hold. Over the long-term/lifespan, labour force participation and participation plans inhibit fertility (op. cit. Brewster & Rindfuss 2000). Labour force participation increases the costs of childbearing in terms of foregone wages; time spent in market work reduces time and energy for child rearing; as well as leisure time (important for parental stress alleviation). For women pursuing careers, time spent out of the labour force negatively occupational advancement. This translates into women in paid labour force having fertility levels of about one-half to one child lower (post-ponement of childbearing, reduced incidence of second and third order births) than women who are not labour force participants.

Continuing fertility declines?

Myrskylä et al. (2011): A change in the fertility-development relationship has occurred in highly developed countries (1975-2008), suggesting an association between further socioeconomic development and a reversal of the fertility declining trend. The underlying mechanism of this fertility reversal was investigated by analyzing the links between development and age of cohort fertility patterns, as well as the role of gender equality. The results indicate that the reversal exists in respect of both period and cohort fertility and is largely driven by ***increasing older reproductive age fertility***. Fertility above age 30 is key to the reversal of the development fertility

relationship (from negative to positive). Regarding fertility below age 30, cross-sectional and longitudinal analyses showed a continuous fertility decline (continued negative fertility-development association). ***Recuperation of fertility at higher ages is apparently essential for reaching increased levels of fertility in advanced societies***.
Gender equality is crucial for achieving these increased fertilities (conducive to policy environments improving the compatibility between career and childbearing; allowing couples to realize their fertility intentions). The positive impact of development on fertility in high-development countries is conditional on gender equality. High-development countries characterized by good health status, income and education, but low in gender equality, show continued fertility declines (**AS: Causality can however not be inferred between gender equality and fertility advantages from the positive correlations between fertility, late age fertility and gender equality experienced under conditions of higher human development indices. Refer to 2.3.5b for an explanation of these patterns according to LHS trade-off constraints**).

Myrskylä et al. (2013): Results of this study counter concerns about a continued decline of birth rates in the developed world (Lutz et al. 2006). Forecasted cohort fertility (estimates of the average number of children women have over their lifetimes) was often not much different from 2 children per woman, even in some countries where period fertility rates had fallen below 1.3. These results suggest that long-term fertility decline in the developed world is flattening or reversing in many low fertility countries. Although numerically small, the new cohort fertility forecasts, showing recent rises in cohort fertility, do have significant impacts on future population sizes and ageing.
Actual and forecasted cohort fertility1970/1979: Western Europe – United Kingdom: 1.91/2.03; Belgium: 1.82/1.91; Netherlands: 1.76/1.85; France: 2.00/2.08; Germany (West): 1.52/1.57; Ireland: 2.13/2.17; Switzerland: 1.66/1.69; Denmark: 1.98/1.96; Austria: 1.61/1.59. **(WE: 1.82/1.87)**. Northern Europe – Iceland: 2.34/3.39; Norway: 2.06/2.09; Sweden: 2.00/2.02; Finland: 1.90/1.92. **(NE: 2.07/2.35)**. Eastern Europe – Lithuania: 1.76/1.86; Russia: 1.61/1.69; Slovenia: 1.69/1.73; Estonia: 1.86/1.90; Bulgaria: 1.68/1.70; Romania: 1.62/1.54; Czech Republic: 1.89/1.75; Poland: 1.85/1.57; Slovakia: 1.93/1.64; Hungary: 1.88/1.57. **(EE: 1.78/1.69)**. Southern Europe – Italy: 1.48/1.49; Greece: 1.64/1.65; Spain: 1.50/1.40; Portugal: 1.69/1.46. **(SE: 1.58/1.50)**. Myrskylä et al. (2013) interpret these results as implying a trend of increasing cohort fertility in some countries of Western Europe; a noteworthy stability for Nordic and Baltic countries; and that after decades of decline in Eastern Europe and Mediterranean countries, declines are apparently coming to an end. Overall, the results suggest that the long-term fertility decline of the developed world may have come to an end or has stalled.
Recent research similarly found signs of higher cohort fertility for Europe. For women born in 1935 and later Anderson et al. (2009, op.cit. Myrskylä et al. 2013) found that cumulated and completed cohort fertility patterns by education in Nordic countries (Denmark, Finland, Norway, Sweden) showed a high degree of similarity in terms of postponement and recuperation patterns across countries and that completed cohort fertility the 1960s cohorts in the Nordic countries may already have stabilized at a level close to 2 children per woman. Sobotka et al. (2011, op. cit. Myrskylä et. al. 2013) synthesized a benchmark model and the relational model of Lesthaeghe (2001, op. cit. Myrskylä et. al. 2013) involving three postponement indices – initial fertility level, absolute fertility decline at younger ages, and the relative degree of fertility recuperation at older ages. Estimated projected completed fertility level suggested

stabilization in Netherlands at 1.8, in Austria at 1.6, and an increase to 1.9 for the Czech Republic.

Lutz (2006): History has shown that fertility declines have not stopped at replacement levels, but continued to decline (shifting attitudes and norms from quantity to quality to childnessless). The effectiveness of fertility-enhancing public policies is unclear. Germany and Austria are high spenders on family support, but fertility rates in both countries are about a third below replacement level. Refers to Foster (2000) who argued that a genetic predisposion towards nurturing would sustain the wish of men and women to have children (desire to love and nurture a child and to create a family; the desire to have a stake in the future by passing on parental genes to be represented in the future; the desire to find non-material purpose in life).
Lutz (2006) discusses factors which would likely result in further fertility decline:

- Trend towards individualism. As part of modernization a transition has occurred from community (*Gemeinschaft*) to society (*Gesellschaft*) where community refers to a lasting and complete living together under a relatively stable structure, society merely represents the proximity of persons who are independent of one another living under relatively open structures. The family no longer accepted as mainstream model for future living patterns (lower marriage propensities, higher instability of unions, increases in extramarital fertility and lower total fertility). (AS: The body of the people (Volkskörper), now essentially of urban constitution, dissolves into formless masses. The fourth class: 'masses' (anorganic and cosmopolitan) *vide* Spengler 1923).
- Increasing independence of women. Increasing economic independence of women might result in the choice of smaller families. This has not been confirmed to be the case in certain countries (e. g. Nordic countries).
- Instability of partnerships. Universal decline in marital stability in industrialised countries, partly linked to increased economic independence of women.
- Consumerism and use of time. Materialist preference for investing in pleasure for themselves than in children. Opportunity costs of children considered high in relation to leisure time.
- Fertility declines through better contraception
- Decreasing ideal family size. New surveys have found that the personal ideal family size is falling. For example, in German-speaking parts of Europe a new decline in ideal family size has been observed, resulting in stated ideals as low as 1.7 children per women on average.
- Density, pollution and biomedical factors. Evidence that human fertility declines with higher population densities (Lutz & Qiang 2002).
- Competitiveness associated with globalization. Increasing globalization is arguably associated with increased levels of competitiveness at many levels (increased investments in education, increased mobility, more overtime work). Modern economic conditions tend to be structurally unfriendly to establish a family. The forces of increasing competitiveness are expected to become even stronger as drivers towards even lower fertility in the future.

In terms of its age structure, Europe has entered a period of negative population momentum and this negative momentum will enhance further population shrinking and population ageing independent of the level of future fertility.

Lutz et al. (2006): Describe potential self-reinforcing mechanisms that could result in the continued decrease in the number of births in affected countries. Three components:

(1) the negative population growth momentum (fewer potential mothers in the future resulting in fewer births); (2) declining ideal family size for younger cohorts (as a consequence of the actual lower fertility they observe in previous cohorts) and (3) based on the relative income hypothesis implying that fertility results from the combination of aspiration and expected income (if aspirations of young adults are increasing while expected income declines, fertility is plausably depressed). All three factors may contribute towards further downward spiralling of fertility in the future (low fertility trap hypothesis).

Largely following **Kohler et al. (2006)**, sustained below-replacement fertility has become the predominant pattern for developed countries and Europe leading the trend to low and very low fertility levels. The notion that fertility levels may stabilise at replacement levels (2.1 children per woman) has as yet not come to be manifested. Rather, total fertility rates per woman (TFR) for Europe over the last 15 years was at or below 1.3 children per woman. Kohler et al. (2002) has termed such fertility levels *lowest-low* in order to emphasise the dramatic implications of these: persistence of such low fertility levels in the long-term imply an annual reduction in the number of births by 50 % and a halving of the population size within 45 years. The median total fertility rate, i. e. the TFR level below which 50 % of the populations in Europe live is currently 1.31. Divergent fertility trends of European countries: ranging between countries that stabilised at moderately below-replacement fertility levels to lowest-low fertility countries with TFR declines below 1.3. Countries with sustained below-replacement fertility during late 1960s and early 1970s had relatively increased fertility levels during the last decade (2002; TFR c. 1.7: Netherlands, Denmark, France, United Kingdom). This is/was contrasted by pervasive TFR declines in Southern, Central and Eastern Europe to levels below 1.3. Low birth rates in Europe have induced the generation of negative population momentum, expected to result in population shrinkage over the coming decades due to the fact that past below replacement fertility will result in declining numbers of potential parents (Lutz 2006; Lutz et al. 2006). Continuation of such trends will exacerbate ageing and shrinkage of populations. According to Kohler et al. (2006) the central driver towards low fertility is postponement of childbearing due to socioeconomic changes and institutional settings resulting in low quantum fertility, notably more so in Southern, Central and Eastern European countries.

From family-based fertility to exra-marital fertility: across country analyses. In 1975 total first marriage rate and high fertility were still positively associated but within the 1990s (2002) this association no longer existed. While higher levels of divorce were

still associated with lower fertility; this correlation reversed by 2001-2002: countries with higher divorce levels exhibited higher fertility levels. The relationship between extramarital childbearing and fertility also reversed along with the decline in the importance of marriage between 1975 and 2002, when total fertility and extra-marital births were positively correlated. (AS: WN 1975-1990s-2002:
Pm < pM shifting to pM↑; E Pm > pM shiting to Pm↑). (Table 2.3.3n) High P/M realizatiom ratio by Pm-types (family/fertility) in certain countries 1975: higher fertility determined by Pm-types (LHS-mode Pm > pM:1). 1990s-2002: slow LHS-mode pM↑:4 predominance: lowered fertility, but positive correlation between total fertility and extra-marital births. Shaped by predominance of Mp-types (Table 2.3.3n).

In cross-country analyses (macrolevel), marriage formation and dissolution (divorce) are no longer predictors of national fertility levels during the late 1990s. Fertility and female labour force participation over OECD countries changed from a negative association (1975) to a positive relationship during the mid-1980s/early 1990s (1996). Changes in fertility levels rather than female employment levels were prevalent between 1975-2002. Kohler et al. (2006) recognized three transition processes towards lowest-low fertility in Europe: the first demographic transition leading to parity-specific stopping behaviour within marriage, the second demographic transition resulting in ideational changes and the rise of non-marital family forms and the postponement transition where the timing of fertility shifted to late childbearing.

Coleman & Rowthorn (2011): The last generations to completely replace themselves in Western Europe were those born in the 1950s (Sobotka 2008). Declining populations are notably represented by Germany and Eastern European countries. Regarding some Eastern European countries, declining of populations was linked to emigration (Haug 2005, op. cit. Coleman & Rowthorn 2011), very low fertility and high levels of mortality (Cawla et al. 2007, op. cit. Coleman & Rowthorn 2011; Vladov 2007, op. cit. Coleman & Rowthorn 2011). (**AS**: **low levels of well-being; anomy. LHS-mode Pm > pM → Pm↑:3**). Subreplacement fertility results in populations becoming older for about two generations, after which a new structure is established at an older, but stable age-distribution; with population sizes tending towards extinction over time. Small reductions in fertility have an increasingly large effect on population size. Perceived negative consequences of lowered population sizes of countries: population ageing, negative effects in respect of economic growth/prosperity, relatively lowered military security, decreasing strategic impact of smaller populations on the international level.

Compromized fitness maximization

Given the low fertility in Europe under conditions of an abundance of resources represents a challenge to evolutionary biologists (*inter alia* Korpelainen 2003). The prevailing resource abundance would potentially allow for higher fertilities than observed and the voluntarily lowered fertility requires an explanation. Some authors suggested that the deviation from fitness maximization in terms of reproductive success is driven by an evolved psychology which responds to cues of the modern environment giving preference to higher parental investment in children and selection to maximize material wealth (Kaplan 1996; Borgerhoff Mulder 1998; Hill & Kaplan 1999; Voland 2000; Kaplan et al. 2002). Since the value of juvenile investment needs to be realized later in life, juvenile investment period and adult reproductive lifespan should coevolve (Hill & Kaplan 1999). Emphasis on education and material wealth leads to a delay in the onset of reproduction, which results in the production of fewer children than desired as fecundity declines with age (Kaplan et al. 2002). Data regarding pre-industrial societies consistently show a positive relationship between resources/power and reproductive success (Hill & Kaplan 1999). Currently we have a phenomenon contradictory to fitness maximization through reproductive decisions in modern societies: higher parental fertility is associated with lower educational and and economic status; and lower income of children from large families does not decrease their fertility and fitness (Downey 1995, op. cit. Korpelainen 2003).

Mason (1997): Under the classic demographic transition theory (*inter alia* Notestein 1953, op. cit. Mason 1997) fertility decline is attributed to changes in social life caused by industrialization and urbanization. These changes are taken to bring about a decline in mortality, setting the stage for fertility decline as the survival of children and family sizes increase (rearing more than a few children becomes increasingly more expensive). The ideational theory of demographic transition (Cleland 1985 and Cleland & Wilson 1987, op. cit. Mason 1997) attributes the timing of the fertility transition to the diffusion of information and new social norms about birth control. Coale (1973, op. cit. Mason 1997) concluded that fertility would decline when three preconditions were met: 1) when fertility was within the realm of conscious calculation of most individuals; 2) when most of them new about some method to limit fertility; and 3) when they perceived some advantage in limiting fertility. Ideas about industrialization, urbanization and other forms of modernization were discredited. Freedman (1979, op.cit. Mason 1979) emphasised that fertility transitions required combinations of causes which provide sufficient impetus for the widespread adoption of fertility limitation within marriage. For populations where only moderate or relatively small numbers of surviving children per family are considered optimal due to a variety of reasons (AS: certainly for populations subject to K-selection), increases in family size are likely to prove economically stressful.

Mason (1997) emphasises some pertinent facts about fertility transitions: 1) Fertility transitions occur when combinations of conditions (institutional, cultural, environmental) are sufficient to motivate/enable a substantial proportion of the population to adopt birth control measures on a parity-specific basis. 2) Mortality decline is usually a necessary condition for fertility decline, but in itself not normally a sufficient condition for that decline. 3) Parents will resort to some form of offspring control as and when the number of surviving children exceeds the capacity of the family to accommodate them. 4) The number of surviving children that families could accommodate also varied across pretransitional populations.

Haaga (2001): A central paradox for economic demography was the finding that people who apparently could afford to have more children than their parents wanted, have fewer children and maintain that they can only afford fewer children. They work as hard as ever for incomes that would allow them to raise numerous children. Frank & Cook (1995, op.cit. Haaga 2001) pointed out that we can never have enough if what we really need is more status than the next person has. If people have evolved to respond to cues about social position in relation to the people we know about, then the widening of their social worlds makes life more stressful. Humans appear to be sensitive to threats to their social position; and quickly respond to opportunities to improve their social status as a matter of greater importance than pronatal fertility decisions.

The LHS-mode pM↑:4, as the predominant LHS-mode during the SDT, implies low performance vitality; suggesting an insufficiency of the vitality status in combining fertility and competitiveness; competitive anxiety in win-lose competition mode, especially in the context of increased population density stress. Lutz & Qiang 2002 – population density).

Pritchett & Viarengo (2012) find it puzzling that many people across Europe are chosing to have fewer children than required for demographic stability. Demography is destiny and current fertility patterns seemingly represents “demographic suicide”. Fertility patterns differ across European contries, *inter alia*, in respect of total first marriage rate and the proportion of extramarital births. Significant changes in both these indicators have occurred since 1960: median first marriage rate has virtually halved by 2003 and extramarital births rose from 6 % in 1960 to 20 % in 2003 (Council of Europe, Pritchett & Viarengo 2012; OECD, Pritchett & Viarengo 2012). This indicates that marriage as an institution and expected part of the life cycle, and that the association between formal marriage and childbearing, are no longer social norms. In cross-country comparison, those with the highest TFRs tend to be those with the highest extramarital childbearing. Countries with TFRs above 1.7 (Sweden, UK, France, Norway, Iceland, Finland, Denmark) have proportions of extramarital births above 40 %. Although marriage is considered outdated, having children is not.

According to Billari & Kohler (2004), positive relationships between fertility and marriage rates disappeared in Europe during the 1990s. Declining marriage rates were

associated with an increase in informal unions, such as cohabitation (Kohler et al. 2006). Alternative models of household formation and parenting had emerged: where childbearing is disconnected from marriage but persists (Nordic model) and where marriage remains as the main form of union formation, but fertility has reached very low levels (Southern model). For most Eastern European countries the association of high rates of marriage, low proportions of extramarital births and low fertility rates were evident. Associated with the declining incidence of marriage/stable conjugal unions and moderate fertility rates in some Northern countries, high levels of childnessless are observed. Whereas in Eastern and Southern Europe there are low levels of cumulative fertility, low rates of childnessless are experienced; contrasting the situation in Northern and Western Europe where similar or even higher fertility rates are associated with lifetime rates of childnessless approaching 20 %.

Lesthaeghe & Neels (2002): Innovation behaviour, in order emerge, must yield benefits that outweigh the costs or associated disadvantages, be culturally (ethically/morally) acceptable and implementable.
Innovating regions in respect of the FDT coincided with those with more innovation during the SDT (e.g. Belgium: Lesthaeghe & Neels 2000, op. cit. Lesthaeghe & Neels 2002). Current maps of cohabitation and nonmarital fertility for Austria replicate the maps near the end of the 19th century (Kytir 1993, op. cit. Lesthaeghe & Neels 2002). After an initial decline in illegitimacy, the original spatial pattern of these areas was restored during the SDT. Similar patterns of spatiotemporal restoration were evidenced in Sweden and Norway where cohabitation during the 1960s spread from the northern areas to which the custom had been pushed back about half a century earlier (Coale & Treadway 1986, op. cit. Lesthaeghe & Neels 2002). (**AS: Pushed back during initial phase of the first demographic transition when LHS-mode Pm > pM had been predominant: Table 2.3.3n**). Marriage patterns progressively weakened over the course of the FDT. Premarital cohabitation and procreation outside of wedlock, which had persisted in certain areas came under siege during the FDT. (**AS: especially during the initial phase of the FDT *when male family protectionism*, underpinned by the LHS-mode Pm > pM, had been predominant: Table 2.3.3n**). Earlier pockets of high cohabitation and or illegitimacy had disappeared by the 1950s. Emergence of both cohabitation and extramarital fertility then occurred during the SDT: these practices were largely restored in areas where they had survived during the 19th century and also spread to areas without such historical precedents. These developments were supported by associated societal developments (secularisation, modernist/postmodernist value orientations, female economic autonomy). (**AS: and underpinned by the LHS-mode pM↑(4): 2.3.3e**). During the FDT fertility is increasingly confined to marriage, within which permanent childnessless is low, mean ages at parenthood decline and contraception affects fertility mainly at higher ages. (**AS: This is consistent with early life performance as underpinned by the LHS-mode Pm > pM: Table 2.3.3n**). Earlier marriage was rising with the growth of industrial labour and was also associated with the presence of wage labour in capitalist rather than peasantry type of agricultural systems. This partially accounts for erlier marriage in French regions in which the

nuptiality transition preceded any industrialization by half a century. The SDT starts with a triple revolution in Western European countries: a sexual (rebellion of the youngest generations against sexual mores - traditional customs – of the older generations), a contraceptive (women wanting to be free from the fatalites of nature, seeking biological autonomy; abortion) and a political revolution (rebellion against all forms of authority: parents, teachers, church, army and the political system as such; feminists against "patriarchs"). Fertility postponement has lead to a generalisation of below-replacement fertility in Europe. Without sufficient catching up of fertility at older ages (recuperation after age 30 years) long-term sub-replacement fertility is anticipated. (**AS: Postponement is in alignment with the applicable LHS-mode pM↑(4), which supports later life performance: 2.2.2e; 2.3.3e**).
Main conclusions: 1) Regions of France, Belgium and Switzerland which were in the forefront of innovation in respect of the first demographic transition were also more advanced with respect to the second demographic transition. 2) Socio-economic and cultural correlates of the FDT and the SDT spatial demographic differences are basically the same as those that had emerged at the time of the FDT. 3) In all three countries the link between the FDT and its ideational covariates was prolonged but equally applicable to the SDT. The secularisation dimension as it had emerged in the 18th and 19th centuries, maintained its spatial features until about the 1960s, when further ideational orientations related to individual autonomy and rejection of traditional forms of authority were superimposed on the secularisation dimension during the SDT. Thus, FDT and SDT indicators remained spatially correlated and also to the historical structural and cultural covariates. However, the strengthening of the social cohesion during the FDT changed to a weakening thereof in the SDT. (**AS: Regional divergence of where the FDT to SDT sequence occurred, and where not, can explain the congruence of FDT-SDT spatiotemporal patterns**).

Cohabitation and procreation within cohabitation has increased faster in regions of several European countries with a longer history of tolerance for such forms of of family formation; often rural areas, e.g. northern Scandinavia, Austrian alpine regions. Data ex Coale & Treadway (1986, op. cit. Surkyn & Lesthaeghe (2004) indicated that procreation within consensual unions was widespread by 1900 in mainly rural areas of Austria, Germany, Hungary, Portugal, Spain and Sweden: LHS-mode PM circumstances (2.2.2e): Table 2.2.2b and 2.3.3i.

Balbo et al. (2013): The study of Balbo et al. (2013) reviewed existing fertility research:
1) Human fertility involves two components, *tempo* (timing of childbirth) and *quantum* (total number of children). For European contries a rising mean age at first birth has been recorded since the 1970s, associated with an increasing proportion of births at advanced ages (postponement of childbearing; Kohler et al. 2002). Some interaction applies between tempo and quantum, since postponement or earlier birth affects the childbearing age span of mothers.
2) Theory developed in order to interpret the demographic changes in industrialized societies, the second demographic transition (SDT), was initially developed by Lesthaeghe and Van de Kaa (1986, op. cit. Balbo et al. 2013). According to this framework ideational changes, consisting of rejection of institutional control,

emphasizing individual autonomy and the rise of self-realization needs were considered the driving forces of new family arrangements and behaviour (fertility postponement, reduced number of children, childnessless) that have developed during the 1960s. The SDT framework is/has been been used as an alternative to economic cycle effects.

3) ***Changes in partnership dynamics***. An increasing number of studies have shown a tendency of delayed union formation and postponement of parenthood (e.g. Corijn & Klijzing 2001, op. cit. Balbo et al. 2013); an increased frequency to have several partners before the first child (Wu & Schimmele 2005, op. cit. Balbo et al. 2013); a rise in unmarried cohabitation often associated with later ages of entering into marriage (Bumpass et al. 1991, op. cit. Balbo et al. 2013; Mills 2004, op. cit. Balbo et al. 2013); or even retreat from marriage (Gibson-Davis et al. 2005, op. cit. Balbo et al. 2013). Nevertheless, partnership status remained a strong predictor, with those not in a stable relationship having a reduced chance of having a child (e.g. Philipov et al 2006; Testa 2007). Coupled with an upward trend in non-marital childbearing, a decoupling of first births from marriage is evidenced (Buchmann & Kriesi 2011, op. cit. Balbo et al. 2013).

4) ***Relationship quality and childbearing***. Some studies find a negative relationship between instability of partnerships and childbearing (e.g. Myers 1997, op. cit. Balbo et al. 2013). However, under certain circumstances union instability may lead to earlier childbearing, with children as a measure of uncertainty reduction, enhancing marital solidarity (Friedman et al. 1994, op. cit. Balbo et al. 2013). Rijken & Liefbroer (2009, op. cit. Balbo et al. 2013) investigated the impact of partnership quality and timing of childbearing and found a) that a high quality relationship represents a favourable environment for raising children, and b) that having a child may be a means of revitalizing the relationship.

5) ***Childbearing versus female labour force participation***. Women feeling overburdened at home respond by having fewer children (Matthews 1999, op. cit. Balbo et al. 2013). Begall & Mills (2011, op. cit. Balbo et al. 2013) also demonstrated that the degree of work-family conflict is important for women in many European countries, to the effect that the prevalence of part-time work and higher perceived control over work predicts the intention to become a mother. Overall, family-orientated women tend to be more fertile than work-orientated women, which have fewer children or remain childless (Vitali et al. 2009, op. cit. Balbo et al. 2013).

6) ***Gender equity***. Miller Short & Torr (2004, op. cit. Balbo et al. 2013) found a U-shaped relationship between gender equity within couples and fertility: the probability of having a second child was higher in familes with either very low or very high gender equality. Oláh (2003, op. cit. Balbo et al. 2013), in a comparison between Sweden and Hungary, found that a more equal gender division of household tasks promoted the transition to a second child; specific policies seemed to supported such transitions in Sweden.

7) ***Income, education and fertility***. In respect of the negative relationship between income and fertility, a quantity-quality trade-off (**2.2.2b/d**) is implicated, where an increase in income may lead to fewer children; this being attributed to parents with a higher income placing higher value on children quality (with associated higher costs of raising and having children) rather than quantity; potentially reducing fertility levels (Becker & Lewis 1973, op. cit. Balbo et al. 2013; Becker et al. 1990, op. cit. Balbo et al. 2013). According to this model, as income increases, lower fertility is associated with increased expenditure in the human capital of children (Lee & Mason 2010, op. cit. Balbo et al. 2013). Other interpretive approaches focus on the opportunity costs of having children, especially affecting women. Raising children places demands on parental (especially maternal) time and fertility is more costly for higher-income

mothers (higher opportunity costs), who are thus expected to have fewer children (motherhood wage penalty). Postponement accordingly provides earning benefits, particularly in the case of higher educated women and those in professional occupations (Van Bavel 2010, op. cit. Balbo et al. 2013; Begall & Mills 2012, op. cit. Balbo et al. 2013; Miller 2010, op. cit. Balbo et al. 2013). Career planning by women was found to be the main explanation for postponement of childbearing (Gustafsson 2001, 2002, 2005, and others, op. cit. Balbo et al. 2013). Higher educated women have their first child later than their lower educated counterparts, but are more likely to recuperate any postponement effects on fertility at a later age (e.g. Sobotka 2004, op. cit. Balbo et al. 2013). (AS: as underpinned by slow LHSs).

8) ***Economic uncertainty***. During historical periods of general economic uncertainty and rising unemployment, marriage rates decline and postponement of parenthood is experienced (consistent with the theory of economic deprivation *vide* Easterlin 1976, op. cit. Balbo et al. 2013). Mills & Blossfeld (2005, op. cit. Balbo et al. 2013) found that under conditions of economic uncertainty (economic precariousness/ unempoyment) young people deferred long-term commitments requiring a secure economic basis, notably parenthood requiring a secure economic basis (Oppenheimer 1988, op. cit. Balbo et al. 2013; Rindfuss & Vandenheuvel 1990, op. cit. Balbo et al. 2013). The response to economic uncertainty in terms of postponement is apparently mediated by level of education: lower educated mothers respond to economic uncertainty by adopting the role of mothers (**AS: fast LHS P-HMT specialism: Table 2.3.3o**), whereas their more educated counterparts postpone childbearing (**AS: fast-LHS M-LMT specialism: Table 2.3.3o**).

9) ***Intergenerational transmission of values and behaviour***. Similarities of fertility histories across successive generations have been evidenced: positive correlations between number of siblings and number of own children (e.g. Axinn et al. 1994, op. cit. Balbo et al. 2013; Murphy & Wang 2001, op. cit. Balbo et al. 2013), and between ages at first birth of parents and that of their children (Rijken & Liefbroer 2009, op. cit. Balbo et al. 2013). Such intergenerational transmission of behaviour was linked to intra-familial socialization processes occurring during childhood and adolescence (e.g. Axinn et al. 1994, op. cit. Balbo et al. 2013; Murphy & Wang 2001, op. cit. Balbo et al. 2013). However, Rijken & Liefbroer (2009, op. cit. Balbo et al. 2013) showed that this transmission effect is fully mediated by religiosity; in that the religiosity of the parents is positively associated with the fertility of their children. It thus seems that intergenerationally transmitted knowledge, values and characteristics are individual characteristics that have a long-term effect in the same way that genetic heritage is transmitted from parents to children (Balbo et al. 2013). (**AS: rather on the basis of epigenetic inheritance: Section 2.1.3.1**). Next to socialization mechanisms, also biological and genetic factors have been used to explain intergenerational similarities in fertility behaviour affecting fertility outcomes (Kohler & Rodgers 2003; and other contributions in Wachter & Bulatao 2003). Using Danish twin data Kohler et al. (1999, op. cit. Balbo et al. 2013) found that genetic influences apparently were overriding previous shared social/familial environments in the case of youger cohorts. Growing evidence indicates that genetic variance changes over time and across educational levels, implying that the importance of social norms and individual decision-making also change across time (Kohler & Rodgers 2003).

10) ***Rural or urban residence***. Differences in desired family size explain fertility differences between small towns and rural areas and between the latter two and urban areas (Kulu 2011, op. cit. Balbo et al. 2013). Within urban areas, higher fertility levels were found in suburbs (Kulu et al. 2009, op. cit. Balbo et al. 2013); higher fertility

typically associated with single family households (Kulu & Vikat 2007, op. cit. Balbo et al. 2013). Differences between urban and rural fertility quantum levels were found to persist over time (Kulu et al. 2009, op. cit. Balbo et al. 2013). Differences in fertility timing had only emerged recently, with postponement being more pronounced in larger than smaller settlements.

11) ***Fertility trend reversal?*** During the late 2000s, signs of a reversal of the fertility decline in many advanced countries has received attention (Myrskylä et al. 2011; Myrskylä et al. 2013).

12) ***Proximate associatons and ultimate causality***. Choices are often interpreted to represent rational responses to uncertainty or in conformity with prescribed life course events. For research based on this premise, a problem is the challenge to establish causality (the ability to determine whether any life course factors are actually determinants of fertility or whether certain life course factors/fertility behaviours are being simultaneously affected by other potential determinants). According to the theory of planned behaviour (TPB: Ajzen 1991, op. cit. Balbo et al. 2013), intentions are the cumulation of a combination of three antecedents: I) attitudes (perceived costs and benefits); II) subjective norms (influence of close friends and relatives); and III) perceived control over behaviour (extent to which behaviour is perceived as subject to control by the individual).

Morgan & Bachrach (2011, op. cit. Balbo et al. 2013) introduced an alternative model to explain human fertility, the theory of conjunctural action (TCA). According to this theory, fertility behaviour results from the interaction between a unique state of social circumstances (normative expectations and structural factors) and ***schemas***. ***The latter represent mental structures that the human brain uses to represent the surrounding world and to process information. This theory acknowledges that fertility behaviour may not only be the result of reasoned rational deliberation, but also of automatic processing at the subconscious level.***

At the proximate level various factors are implicated as shaping fertility behaviour; often the one proximate factor as the cause of another. These proximate factors may howvever be subject to an influencing/driving ultimate factor at the subconscious level. According to the life history strategy (LHS) explanatory model, specific relevant LHS-modes are considered to represent such ultimate influencing factors (Sections 2.2.2e and 2.3.3e).

Billari & Kohler (2004): Cross-country correlations in Europe between total fertility with total first marriage rate (p-n), proportion of extramarital births (n-p) and female labour force participation (n-p) have reversed during the period 1975 and 1999. At the end of the 1990s, a negative association between divorce and fertility levels was no longer evidenced. Netherlands: TFR declined to c. 1.6 (1975), then declining further until c. 1985, then showing an increasing tendency. Mean age at first birth progressively increased since c. 1975. Eastern European pattern (Hungary, Czech Republic, Bulgaria): TFR started to decline after 1975-1990, continuing to decline more rapidly during the 1990s. Mean age at first birth remained at relatively low levels (22-23 years), but started to increase during the early 1990s. The postponement of childbearing in Central and East European countries, representing a relatively recent phenomenon, followed a prolonged period of early fertility. Across cohorts born

between 1935 and 1962 in Hungary, the Czech Republic and Bulgaria, completed cohort fertilty remained relatively stable (within the range 1.87-2.13 children). In comparison, Dutch fertility had declined in all cohorts born after 1935 from a level at c. 2.5, then stabilizing at a level around 1.9 for cohorts born after 1950. The cohorts born (Czech Republic) 1955-1970 have slightly higher fertility than the 1950 reference cohort, but fall behind the reference cohort only at ages from the mid to late twenties onwards (suggesting incomplete recuperation). In comparison, cohort fertility trends in the Netherlands are characterized by substantial delays in childbearing (postponement) without marked declines in cohort fertility levels (recuperation). Growing fertility deficit during early adulthood compensated by successful recuperation of delayed births; thus sustaining quantum fertility, the number of children born during the life-course (**AS:** ***earlier impact of the LHS-mode pM↑***).
The relation between marriage and fertility has changed fundamentally in recent decades (between mid 1970s and the end of the 1990s). By the end of the 1990s, countries with relatively higher fertility levels exhibited lower marriage propensities. In 1975, higher levels of divorce in European countries was associated with lower levels of fertility in cross-country comparison. This relationship becomes weak or even reverses in 1999. For European countries in 1975, a negative correlation between proportions of extra-marital births and total fertility rate applied. This relationship had changed to positive by 1999. Unlike 20 years earlier, when a strong positive relationship between union formation and fertility (negative regarding divorce) had prevailed; such interrelationships had become rather indeterminate during the late 1990s. A high prevalence of marriage and institutionalized long-term parnerships were no longer associated with higher fertility in cross-country comparisons by 1999. The postponement of fertility (especially of first births) emerged as crucial factor as fertility determinant.
At the end of the 1990s (during the second demographic transition) a clustering of European countries had emerged:
1) Northern and many Western European countries: moderately high fertility levels; continued postponement of childbearing; increased incidence of cohabitation and extramarital childbearing, relatively high divorce rates.
2) Southern European countries (including foremost Italy and Spain): low fertility rates, latest home-leaving behaviour, low proportion of extramarital births, relatively low female work force participation, marked postponement of first births and lower recuperation of fertility at higher ages.
3) Central/Eastern European countries (represented by Bulgaria, Czech Republic and Hungary): low fertility rates, relatively early household independence and union formation, relatively high non-marital fertility and divorce rates, but first births taking place relatively early.

Billari & Kohler (2004) ***conclude that, regarding causality, the patterns described may either be part of a complex web of causation where fertility and fertility-associated factors influence each other, or they may indicate that other general factors simultaneously drive changes in fertility and proximate fertility-associated behaviour***.

According to the LHS explanatory framework, external resource conditions and endogenous vitality status cue relevant LHS-modes, which from the subconscious level, direct, influence/co-determine rational decision-making affecting fertility behaviour in alignment with metabolic energy allocation patterns embodied in particular relevant LHS-modes: 2.3.3e).

b) Analyses of cross-country associations of potentially fertility-affecting factors

Summary Box 2.3.3b
1) Differential fertility across European countries (north-western *versus* eastern country groups; north to south differences in fertility patterns)
2) Aassve et al. (2013) developed a ***family attitude index***: Liberalistic *versus* conservative family perspectives (psycho-social incoherence)
3) *State Antiquity Index* vide Aassve et al. (2013): State antiquity correlates positively with economic development and associated modernist attitudes in respect of fertility behaviour (children no longer central to parental achievement; high rates of cohabitation, high extramarital childbearing, high divorce rates, high levels of female empowerment and emancipation).
4) Ancestral genetic footprints of post-glacial recolonization (Table 2.3.3b): Dispersal (D-phenotypes) and maintenance (H-phenotypes) differentiation: Life history strategy plasticity *versus* resilience (Latitudinal cold-adaptation)
5) Population density stress: High **s**ensitivity of fertility to population density stress in populations subject to the periarctic metabolic performance mode (K-Selection reproduction strategy). Plasticity of fast-slow LHS adaptability, but associated plasticity costs involving a vulnerability to negative impacts of population density stress on fertility).
6) Divergence of life history strategy expression according to subhaplogroup LHS settings (Table 2.3.3e): Life history strategy expression of divergent subhaplogroup types along west-east and north-south geographic gradients in Europe, as related to Northwestern, Central-Northern, Southern and Eastern European marriage and family patterns.
7) European marriage patterns. Two main European family household formation systems are differentiated: the northwestern and eastern European marriage systems.

1) Differential fertility across European countries (north-western vs eastern country groups; north to south differences in fertility patterns).

Cross-country analyses involving 27 European countries revealed significant positive associations (Table 2.3.3a) of urbanization, subjective well-being scores, postmodernism scores and cancer incidence with fertility postponement (correlations

being positive for age at marriage and negative with the proportion of birth by women younger than 20 years). Urbanization as factor was positively associated with population density, subjective well-being, the incidence of cancer and two variables of childnessless. High population densities of countries is associated with elevated levels of childnessless and low completed cohort fertilities (1960-1961).

The study of fertility determinants has largely been focusing on social, economic and cultural factors influencing reproductive behaviour; whereas ecological factors (such as population density) have received relatively little attention. However, as Lutz & Qiang (2002) note, perceived population density may be an important psychological determinant of fertility. For example, Yasuba (1962, op. cit. Lutz & Qiang 2002) had analysed fertility ratios of states in the USA for the period 1800-1860 and found that the most important factor associated with fertility differences and trends was population density (the higher the density, the lower the fertility). The analyses by Lutz & Qiang (2002) for 187 countries (1960-1990) revealed consistent negative relationships between fertility and female literacy, population density and urban proportion of population. Lutz & Qiang (2002) furthermore note that, with respect to contempory European fertility levels, the low density regions of northern Scandinavia have significantly higher fertility than the high density areas of central and southern Europe.

Table 2.3.3a Correlation coefficients for selected fertility-linked factors over 27 European countries

(Western: Austria, Belgium, United Kingdom, Denmark, France, Western Germany, Ireland, Netherlands, Switzerland; Northern: Finland, Iceland, Norway, Sweden; Eastern: Belarus, Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Russia, Slovenia; and Southern European countries: Italy, Portugal, Spain)

	URB	POPD	WellB	PM	W-C	C-B	PB-20	Cancer	AgeM
URB		0.39	**0.64**	0.40			**-0.55**	**0.53**	**0.56**
POPD	**0.43**		0.34					0.40	0.39
WellB	**0.64**	0.34		**0.53**	**-0.83**	0.42	**-0.89**	**0.61**	**0.82**
PM	0.42		**0.55**		**-0.53**		**-0.56**		**0.44**
W-C			**-0.83**	**-0.61**			**0.73**		**-0.67**
C-B			0.42						**0.56**

PB-20	**-0.55**	-0.38	**-0.89**	**-0.56**	**0.73**			**-0.60**	**-0.72**
Cancer	**0.53**	0.40	**0.61**				**-0.60**		**0.62**
AgeM	**0.56**	0.39	**0.82**	**0.44**	**-0.67**	**0.56**	**-0.72**	**0.62**	
AvCLESS	**0.46**	**0.47**	**0.54**				**-0.58**	0.40	
CNBM10	**-0.50**		**-0.75**				**0.70**	-0.41	**-0.55**
CCoFert60		**-0.49**					**-0.54**		
CHL60	**0.56**	**0.58**	**0.52**				**-0.54**	0.42	

r in bold: P < 0.05 or lower, others listed P < 0.10

URB: Urban population in percentage of total in 1960 (World Bank Data)
POPD: Population density per km^2 (Worldatlas)
WellB: Subjective well-being score (ex Inglehart 1997, op. cit. Van de Kaa 2001)
PM: Percent post-modern (Van de Kaa 2001: World Values Surveys)
W-C: Agree that women need a child, Postmodern (Van de Kaa 2001: World Values Surveys, 1990s)
C-B: Average number of children born, of women aged 45+, Postmodern (Van de Kaa 2001: World Values Surveys)
PB-20: Percentage of births to women aged ≤ 20 years (1990)
Cancer: Age-standardised rates of all cancers per 100000 diagnsed in 2012 (World Cancer Research Funds)
AgeM2014: Age at first marriage of women (Worldatlas)
AvCLESS: Average childnessless-females of 1940-1944 and 1960-1969 cohorts. Data source op. cit. Miettinen et al. (2014)
CNBM10: Children important for marriage 1990. Data source op. cit. Miettinen et al. (2014)
CCoFert60: Completed cohort fertility 1960-1961. Data source op. cit. Zakharov (2008)
CHL60: Cohort childnessless-females 1960-1969 Data source op. cit. Miettinen et al. (2014)

Analyses over country groups (Western: Austria, Belgium, United Kingdom, Denmark, France, Western Germany, Ireland, Netherlands; SwitzerlandNorthern: Finland, Iceland, Norway, Sweden; Eastern: Belarus, Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Russia, Slovenia; and Southern European countries: Italy, Portugal, Spain):

- Differences in urbanization over country-groups were found significant (P < 0.007), with Western and Northern countries being subject to higher degrees of urbanization than Eastern and Southern countries (P < 0.08).
- Population density (P < 0.001): W > N (P < 0.003); W > E (P < 0.03); S < W (P < 0.05)
- Subjective well-being (P < 0.000001): W > E (P < 0.0002); E < W, N (P < 0.0002), S (P < 0.0002); W ≈ N

- Postmodernist score ($P < 0.005$): E < W ($P < 0.07$); E < N ($P < 0.008$)
- A woman needs to have a child/children ($P < 0.0004$): E > W ($P < 0.002$); E > N ($P < 0.0004$); E > S ($P < 0.004$)
- Children born 45+ postmodern ($P = 0.243$)
- Percentage of births to woman aged ≤ 20 years relative to the total number of births ($P < 0.000001$): E > W ($P < 0.0003$); E > N ($P < 0.0005$); E > S ($P < 0.0008$)
- Cancer incidence ($P < 0.015$): E < W ($P = 0.082$); W > S ($P = 0.084$)
- Age at first marriage in 2014 ($P < 0.0.000003$): E < W ($P < 0.007$); E < N ($P < 0.0002$); E < S ($P < 0.0004$)
- Average childnessless ($P = 0.011$): E 9.5 < W 15.5 ($P < 0.08$)
- Children important in/for marriage 1990 ($P < 0.00004$): E > W ($P < 0.0007$) > N ($P < 0.01$) > S ($P < 0.05$).
- Children important in/for marriage 2010 ($P < 0.0001$): E > W ($P < 0.004$) > N ($P < 0.002$) > S ($P < 0.04$).
- Completed cohort fertility 1960 (ns): E (1.97) ≈ W (1.82) ≈ N (2.02) ≈ S (1.75).
- Contribution of mothers under 26 to the completed fertility (%). Data source op. cit. Zakharov (2008) ($P < 0.0001$): E > W ($P < 0.0002$) > N ($P < 0.0002$) > S ($P < 0.0003$).
- Female employment 1970 (Data source op. cit. Miettinen et al. 2014) ($P < 0.03$): E (69.7), W (43.0), N (53.6), S (23.7).
- Female employment 1990 (Data source op. cit. Miettinen et al. 2014) ($P < 0.0001$); E (88.4) > W (67.0); $P < 0.01$, E ≈ N (86.0), E > S (58.7): $P < 0.001$.

Two divergent main European country groupings are revealed: W (Western) and E (Eastern). In the East we have lower subjective wellbeing and lower postmodernist scores, but higher scores for the perceptions that women need to have children and that children are important in/for marriage (1990/2010). Furthermore, in the East, lower ages at first marriage (2014) and accordingly higher contributions of mothers under the age of 26 to the completed fertility (%) and higher percentages of births to woman aged ≤ 20 years relative to the total number of births, were found. Countries with high subjective well-being scores tend to exhibit higher rates of urbanization, higher

postmodernism scores, more childnessless and cancer incidence rates (Table 2.3.3a). Countries with elevated cancer incidence rates exhibit higher degrees of urbanization, higher subjective well-being scores and higher degrees of fertility postponement. Cancer incidence rates are being identified as markers for the extent of accumulated patho-information-engram loadings (2.3.3c).

2) Family attitude index.

Aassve et al. (2013) developed a ***family attitude index*** derived on the basis of the following questions:

- Approve if person chooses never to have children?
- Approve if person lives with partner not married?
- Approve if person has child with partner not married to?
- Approve if person has full-time job while children < 3 years?
- Approve if person gets divorced while children aged < 12years?

Items were evaluated on a scale of 1 (strongly disapprove) to 5 (strongly approved) and the family attitude index is derived using these factor scores. **High values** reflect a **liberalistic** predisposition (more modern attitude), whereas **low** values reflect a **conservative** predisposition (less modern attitudes). High levels of approval were found for Scandinavian countries, lower levels in Mediterranean countries and the lowest levels in Eastern European countries (Aassve et al. 2013). Higher education scores, women in paid work and social capital were positively correlated with liberalistic family attitude scores (liberalistic perspectives: modern attitudes to demographic behavior), whereas church attendance, number of children and being in a partnership were negatively correlated with this index (therewith representing conservative perspectives). Strong evidence indicates that economic development is positively correlated with the acceptance of modern demographic attitudes and norms (e.g. Inglehart & Baker 2000, op. cit. Aassve et al. 2013). Liberalistic family attitudes during the SDT are reflective of psycho-social incoherence (Table 2.3.3m).

3) State antiquity index.

A ***State Antiquity Index*** was constructed by Aassve et al. (2013) to test whether present-day countries which were sited on preceeding nation-states, kingdoms or empires over longer time spans of history had achieved more rapid economic

development in recent decades (e.g. Putterman 2000, op. cit. Aassve et al. 2013). The state antiquity index was found to be positively correlated with GDP per capita (2006), the corruption perception index (2006) and the gender empowerment ratio (2005) and also tended to be positively correlated with the family attitude index; implicating liberalistic perspectives. These results support the contention that differences in current attitudes to demographic behaviour stem from differences in characteristics of economic and institutional development exhibited before modern times (Aassve et al. 2013). State antiquity correlates positively with economic development and associated modernist attitudes in respect of fertility behaviour (high rates of cohabitation, high extramarital childbearing, high divorce rates, high levels of female empowerment and emancipation). Children lost their centrality, being no longer perceived as essential for parental achievement of personal satisfaction and realization (Aassve et al. 2013).
(**AS: Elevated values of the Antiquity index imply that procursive impacts took effect already over longer periods back in time due to circumstances of relative affluence and population density impacts over the past towards present times**: **2.1.3**).

The LHS-mode PM, as supported by a good health status due to low PIE load accumulations prevalent under feast-famine conditions, imply only weak P versus M trade-off constraints; i.e. both P vitality and efficient M functionality occur in combination and fast-slow LHS trade-off constraints minimized. Reproductive performance and longevity are positively related and the combination of both early and late life fertility realization support maximum inclusive fitness (2.2.2e; Korpelainen 2003).

4) Ancestral genetic footprints of post-glacial recolonization and climate adaptational gradients differentially affecting LHS-mode responses across Europe.

Inherent genomic predispositions affecting life history strategy expression along west-east and north-south geographic gradients in Europe are being outlined here; as summarized in Table 2.3.3b. North-south gradients of inherent LHS-affecting predispositions are linked to gradients in heterozygosity and cold-adaptations. West-east differentiation of genomic LHS predispositions relates to dispersal-maintenance phenotype (*sensu* Geist 1978) divergence related to post-glacial resettlement of Europe

by Mesolithic hunter-gatherers) and Neolithic expansion (of pottery-making cultures) from the East European Plain refugium, respectively.

Achilli et al. (2004): Sequencing of mitochondrial DNAs belonging to (or very closely related to) haplogroup H revealed that this mtDNA haplogroup is subdivided into numerous subhaplogroups identifiable by characteristic mutations. Haplogoups H1 and H3 show frequency peaks centered in Iberia and surrounding areas; with a pattern similar to that previously reported for mtDNAhaplogroup V; with these haplogroups also sharing coalescence ages (~ 11 000 years ago). Theses findings confirm that the Franco-Cantabrian refuge area was the source of late-glacial expansions of hunter-gatherers that repopulated much of central and northern Europe from ~ 15 000 years ago. During the Last Glacial Maximum (~ 20 000 years ago) early Paleolithic populations had become extinct or retreated to the south. Gradual repopulation from southern refuge areas (Franco-Cantabrian) then occurred when climatic conditions had improved from ~ 15 000 years ago onwards. Such a scenario is also supported by evidence involving mtDNA haplogroup V (Torroni et al. 1998) and Y-chromosome haplogroups R1b and I1b2 (Semino et al. 2000, op.cit. Achilli et al. 2004; Cinnioglu et al. 2004, op.cit. Achilli et al. 2004; Rootsi et al. 2004).

Torroni et al. (1998): We show that a population living in the Iberia peninsula/southern France before the Younger Dryas contributed substantially to the gene pool of all modern populations of central-northern Europe. This Late Paleolithic population expansion from southwestern to northeastern Europe is supported not only by mtDNA data, but also by Y-chromosome and autosomal data, as well as archaeological records. The Second Pleniglacial was associated with extreme cold and dry climate conditions by 18 000 years ago and resulted in an almost complete retreat of people from the central plains of Europe. Southern France and the Iberian peninsula, in western Europe, and southern Ukraine in eastern Europe served as refuge areas. The western and eastern refugia were isolated from each other (Otte 199, op. cit. Torroni et al. 1998). During the Bölling/Alleröd period (warm period c. 12 200-13 000 years ago), people returned to the northern areas, and Upper Magdalenian industries similar to those of southwestern France began to diffuse into northern France, Belgium, the Rhine region, the Swiss and Swebian plateaus, Bavaria, Thuringia, Bohemia, Moravia and lower Poland; reflecting a major post-glacial expansion from from southwestern to central Europe (Otte 199, op. cit. Torroni et al. 1998). This is in agreement with the population distribution of haplogroup V, its coalescence time, and its diversity in different geographical regions. These data indicate that haplogroup V originated in a population of the Iberian peninsula/southern France and expanded into central-northern Europe after the end of the Second Pleniglacial.

Dolukhanov et al. (2009): Early pottery-making communities in the steppe and boreal areas of eastern Europe started spreading at an early date; coinciding with increased precipitation throughout the forest-steppe area (East European Plain). In most cases, the subsistence pattern remained essentially Mesolithic, with little or no evidence of farmining or stock-breeding. The appearance of pottery-making signalled the appearance of attributes of complex societies, such as sedentism, increased population density, intensive food procurement, technological innovations, development of exchange networks, social differentiation and territorial control. The evidence here

reported confirm the pteviously formulated model of Davidson et al. (2007, op. cit. Dolukhanov et al. 2009) according to which the spread of the Neolithic involved at least two waves from distinct centers. The western center stemming from the Near East, and an eastern one, spreading through the east via the 'steppe corridor'; thereby representing an eastern version of the Neolithic in Europe.

Mielnik-Sikorska et al. (2013): The formation of several H5 subbranches of putative Slavic origin coincides with the time and place of origin of previously described haplogroup U4a2, which is predominantly found in central and eastern Europe and dates to ~ 6-7 000 years ago. Data from complete mitochondrial genomes seem to indicate that the ancestors of Slavs (Poles, Czechs, Slovaks, Ukrainians and Russians) were autochthonous people of central and eastern Europe.

Pala et al. (2012): Human populations contracted into a number of refuge areas at the height of the last Ice Age. European populations are believed to be the descendants of the inhabitants of these refugia. Extant mtDNA linages can be traced to refugia in Franco-Cantabria (haplogroups H1, H3, V and U5b1), the Italian Peninsula (U5b3), and the East European Plain (U4 and U5a). Parts of the Near East were also continuously inhabited throughout the Last Glacial Maximum. On the basis of an enlarged whole-genome mitochondrial database, a substantial signal from mitochondrial haplogroups J and T is reported. These haplogroups were previously thought to have spread primarily from the Near East into Europe with the Neolithic populations, but based on results from this study are implicated to reflect dispersals during the Late Glacial period, ~ 19-12 thousand years ago. Dolukhanov (1993, 1996, op. cit. Pala et al. 2012) proposed two major European refugia, one centered on the southwest and one on the northeast. The Franco-Cantabrian 'Mediterranean province' provided refuge for the 'biotidal, zone of Atlantic Europe (Gamble 2009, op. cit. Pala et al. 2012); connected to less well defined regions along the Mediterranean. The 'Periglacial province' was on the East European Plain, providing for a favourable refugium for Upper Paleolithic communities of central and eastern Europe. It appears that the Near East had been overlooked as a refugium for Europeans because of the emphasis placed on its role as a reservoir for subsequrent Neolithic dispersals, which first reached southeastern Europe ~ 9000 years ago. Haplogroups J and T started to spread from the Near East (here now recognized as a peri-glacial refugium) into Europe after the peak of the last glaciation, ~ 19 thousand years ago; with major expansions in Europe in the Late Glacial period, ~ 16-12 thousand years ago. The distribution of diversity in the whole-sequence tree suggests that such expansions began in Europe and spread to the Near East, central Asia, and North Africa. Thus, several lineages previously thought to have spread to Europe during the Neolithic period can now be seen as having arrived during the Late Glacial period and subsequently dispersed. In summary, the results of this study show that both T and J lineages first entered Europe from the Near East prior to the Neolithic period, and that by implication many of the Neolithic expansions from southeastern Europe into central Europe and the Mediterranean actually represented indigenous dispersals of these lineages. Accordingly, it is implicated that post-Glacial recolonization of Europe took place by originally European lineages from periglacial refugia of Franco-Iberia, the Eastern European Plain and the Near East.

Rootsi et al. (2004): Analyzed haplogroup I (Hg I), the only major clade of the Y chromosome phylogeny that is widespread over Europe, but virtually absent elsewhere.

Hg I accounts for more than one-third of paternal lineages in two distinct regions of Europe: among Scandinavian populations and in the northwestern Balkans. Relatively high frequencies are also characteristic of some French regions (Low Normandy; Corsica). A lower frequency of Hg I distinguished the Baltic-speaking Latvians (7.1 %) from their northern neighbours, the Finnic-speaking Estonians (18.6). Southern Slavic-speaking populations and their adjacent neighbours: Slovenians (38.2) versus northern Italians (4.6).
Subhaplogroup I1a is mostly found in northern Europe, with its highest frequencies in Scandinavian populations (accounting for 88-100 % of Norwegian, Swedish and Saami/Laplander lineages). The Scandinavian Peninsula was completely depopulated during the last glacial maximum and either of the two main European refugia, the Iberian Peninsula and the Ukraine/Central Russian Plain (Dolukhanov 2000, op. cit. Rootsi et al. 2004) could be considered as possible source regions of Scandinavian I1a chromosomes. In France, I1a is the leading subclade, with Hg I being more frequent in Low Normandy and southern France; with much lower occurrence in the Poitier and Lyon interior regions.
The most represented eastern European I1b* subclade is virtually absent in Scandinavia, and together with the higher I1a microsattelite diversity background, point to western Europe as the source of Scandinavian I1a chromosomes (Rootsi et al. 2004). Subhaplogroup I1b* is the most frequent clade in eastern Europe and the Balkans. Its chromosomes dissipate rapidly west of the Balkans; being vitually absent among Germans, French and Swiss, but extend eastward at raised frequencies among Slavic-speaking populations. I1b* which extends from the eastern Adriatic to eastern Europe, declines toward the southern Balkans and abruptly so toward the periphery of northern Italy. I1b* taken to have expanded from the glacial refuge area located in eastern Europe or the Balkans.
The divergent distributions of I1b2 and I1b* suggest that their separation occurred before the LGM (last glacial maximum). The exceptional high incidence of I1b2 in the archaic zone of Sardinia (Cappello et al. 1996, op. cit. Rootsi et al. 2004; Zei et al. 2003, op. cit. Rootsi et al. 2004) can be explained by the presence of I1b2 chromosomes among the first humans who colonized the island ~ 9000 years ago (followed by isolation and genetic drift). The extremely low frequency of I1b2 in the Scandinavian Peninsula (where the 'western European' I1a Y chromosomes account for the large majority of Hg I) suggests that that the ancestral western European populations probably played a minor role in the colonization of that region.
High STR diversity of I1b* lineages (Bosnia) supports the view that this haplogroup might have been present in the Balkan area before the LGM (refer also to Semino et al. 2000, op. cit. Rootsi et al. 2004). Subhaplogroup I1c covers a wide range of Europe, with the highest frequencies in northwesten Europe. I1a and I1c harbour an identical compound haplotype, indicating that I1a and I1c may be part of a single monophylitic clade, probably sharing a common history of expansion; a scenario also supported by the high positive correlation between the geographic distributions of I1a and I1c when Fennoscandia is excluded.
Haplogroup I originated from a pool of European pre-LGM, middle Upper Paleolithic Y chromosomes (Semino et al. 2000, op. cit. Rootsi et al. 2004). It appears that I1a, I1b and I1c all diverged from I* in the Late Upper Paleolithic/Mesolithic period, possibly during the recolonization of Europe after the LGM. The expansion phase of I1a and I1b, displaying contrasting phylogeographies, seems to have occurred later, around the early Holocene. Haplogroup I provides an exceptional record of European-specific paternal heritage, including pre-LGM differentiation followed by contraction, isolation

and subsequent post-LGM expansion and spread. The I1a data in Scandinavia are consistent with a post-LGM recolonization of northwestern Europe from Franco-Cantabria. On the other hand, the expansion of I1b* in in the east Adriatic-North Pontic continuum (eastern Europe) probably reflects demographic processes that had begun in a refuge area located in that region.

Myres et al. (2011): The complex pattern of European Y-chromosome diversity has been attributed to dispersals of anatomically modern humans, incorporating the combined heritage of initial upper Paleolithic colonization, secondary post-glacial Mesolithic re-expansions and the Neilithic era demic diffusion of agriculturalistsfrom the Near East (Barbujani & Bertorelle 2001). Phylogenetic relationships support a West Asian origin of haplogroup R1b. Its initial differentiation there was followed by a rapid spread of one of its subclades carrying the M269 mutation to Europe. Phylogeographically resolved data for M269-derived Y-chromosomes from West Asian and European populations, assessed for the M412 SNP, seperating the majority of Central and Western European R1b lineages from those observed in Eastern Europe, the Circum-Uralic region, the Near East, the Caucasus and Pakistan, are presented. In Europe, basically all haplogroup R associates belong to its sub-clade R defined by M173. R1a-420 varieties are most frequent in the East and the R1b-M343 sub-clade is more common in the West (Kayser et al. 2005, op. cit. Myres et al. 2011). Another sub-clade R1b-M269 is the most common Y-chromosome haplogroup throughout Western Europe (Underhill 2003, Alonso et al. 2005, op. cit. Myres et al. 2011). Haplogroup R1b frequency in Europe is clinal with increasing frequencies observed in Northwest Europe, a pattern attributed to the persistence of Paleolithic Y chromosomes in Europe after a Neolithic demic diffusion from the Near East (Rosser et al. 2000, op. cit. Myres et al. 2011; Semino et al. 2000, op. cit. Myres et al. 2011). The enhanced resolution of M412-related lineages allowed for a finer-grained assessment of the view that R1b-M269coincides with the arrival and spread of farming into Europe. High-resolution SNP genotype results show that the majority of Central and Western European haplogroups relate to common M412 founders whose sub-clades display phylogeographic and temporal patterns consistent with allele surfing at the periphery of expansions (Klopfstein et al. 2006, op. cit. Myres et al. 2011). Accordingly, invoking a pronounced transformation of the pre-Neolithic European gene pool by intrusive pioneer farmers from the Near East must be viewed with caution, especially when such a perspective is based on just a single incompletely resolved haplogroup.

Lazaridis et al. (2014): Show that most present Europeans derive from at least three clearly differentiated populations: West European Hunter-Gatherers (WHG), contributing ancestry to all Europeans, but not to Near Easterners; the Ancient North Eurasians (ANE) related to Upper Paleolothic Siberians, who contributed to both Europeans and Near Easterners; and Early European Farmers (EEF), who were mainly of Near Eastern origin, but also harboured WHG-related ancestry. It is furthermore shown that EEF had ~ 44 % ancestry from a 'Basal Eurasian' population that split prior to the diversification of other non-African lineages.

Currat & Excoffier (2005): Extensive and realistic simulations of the colonization process of Europe by Neolithic farmers and their potential admixture with local Palaeolithic hunter-gatherers, were performed. Two opposing scenarios are invoked to account for the spread of agriculyure in Europe. According to the demic diffusion model (DD), the Neolithic transition diffused in Europe from the Middle East by an

important movement of population (Ammerman & Cavalli-Sforza 1984, op. cit. Currat & Excoffier 2005), without substantial contact with local Plaeolithic populations. The cultural diffusion model, on the other hand, assumes that the Neolithic transition occurred mainly through the transmission of agricultural techniques (Zvelebil & Zvelebil 1988, op. cit. Currat & Excoffier 2005). Under the CD model, the current genetic pool should mainly result from hunter-gatherer lineages, while the Near East Neolithic lineages should be prevalent in the European genetic pool under the DD model. The pattern of mitochondrial (mt) DNA diversity in European populations has been shown to be compatible with an old Palaeolithic spatial expansion (Ray et al. 2003, op. cit. Currat & Excoffier 2005; Excoffier 2004, op. cit. Currat & Excoffier 2005), while contradictory for Ychromosome data. The nature of the founders of a population is important to determine its final genetic composition (Heyer 1995, op. cit. Currat & Excoffier 2005; Milinkovitch et al. 2004, op. cit. Currat & Excoffier 2005), since the majority of individuals present at equilibrium are descendants from the first colonists (Currat & Excoffier 2004, op. cit. Currat & Excoffier 2005; Edmonds et al. 2004, op. cit. Currat & Excoffier 2005). Simulations show that a very small initial Palaeolithic contribution in each deme is enough to lead to a situation where most of the current gene pool can be traced to the Palaeolithic. In keeping with a Palaeolithic expansion, dating of demographic expansion for European populations pointed towards 40 000 years ago or more (Comas et al. 1996, op. cit. Currat & Excoffier 2005; Excoffier & Schneider 1999, op. cit. Currat & Excoffier 2005).

Barbujani & Bertorelle (2001): Three large-scale phenomena were inferred from European archeological record: I) In the Upper Paleolithic, c. 40 000 years ago, anatomically modern humans, having moved in from the Levant, replaced the Neanderthal people as they settled in many areas of the continent (Mellars 1992, op. cit. Barbujani & Bertorelle 2001); II) At the last glacial maximum c. 18000 years ago, Northern and Central Europe were largely covered with glaciers, and human preence became restricted to the warmest regions, the glacial refugia from which post-glacial re-settlement of Europe took place during the Mesolithic period; III) The first evidence of food production (farming and animal breeding) dates at around 10 000 years ago in the Levant (Ammerman & Cavalli-Sforza 1984, op. cit. Barbujani & Bertorelle 2001; Renfrew 1987, op. cit. Barbujani & Bertorelle 2001). Gradually, Neolithic artifacts spread westwards and northwards mainly along the same routes followed by the first Paleolithic colonization.
Accordingly, the overall pattern of European genetic diversity could reflect the effects of the first Paleolithic colonization, or of Mesolithic re-expansions (Torroni et al. 1998; Sykes 1999, op. cit. Barbujani & Bertorelle 2001) or of the Neolithic demic diffusion (Ammerman & Cavalli-Sforza 1984, op. cit. Barbujani & Bertorelle 2001; Rendine et al. 1986, op. cit. Barbujani & Bertorelle 2001; Barbujani et al. 1995, op. cit. Barbujani & Bertorelle 2001). In summary, the clinal distributions of nuclear DNA and protein markers suggest that a directional expansion from the Levant, corresponding to the direction of both the initial Paleolithic colonization and the Neolithic demic diffusion, is the main process reflected in the current genetic diversity. Conversely, most mtDNA haplogroups coalesce in pre-Neolithic times, and this has been interpreted to confirm existence of Mesolithic expansions from glacial refugia.

Following Achilli et al. (2004), Torroni et al. (1998), Pala et al. (2012) and Rootsi et al. (2004), a pattern emerges of post-glacial resettlement of northwestern Europe by

Mesolithic hunter-gatherers from southwestern refugia and a Neolithic expansion of Mesolithic pottery-making cultures of the East European Plain refugium in eastern Europe (Dolukhanov et al. 2009; Mielnik-Sikorska et al. 2013). Genomic imprinting underpinning dispersal phenotypes *sensu* Geist (1978) are implicated for country groupings with ancestral involvement in post-glacial resettlement of southwestern, northern-central and northern Europe; as delineated by subhaplogroups I1b2, Hg I1c /Hg I1a) and Hg I1a respectively (Rootsi et al. 2004; Table).

Dispersal phenotypes are required for colonization (Geist 1978; D-phenotypes: Table 2.3.3b). Plasticity of the dispersal phenotype allows for continued adjustments to competition and other environmental contingencies when dealing with uncertainties of colonization of an area previously unexploited by its genome (Geist 1978).

For Slavic population groups (Hg I1b*: Rootsi et al. 2004; Table 2.3.3b) ancestral genomic imprinting was shaped by conditions prevalent for Mesolithic pottery-making cultures of the East European Plain refugium. These early pottery-making cultures had attributes of complex societies, such as sedentism, increased population density, intensive food procurement, technological innovations, social differentiation and territorial control (Dolukhanov et al. (2009). Under such conditions genomic imprinting supporting maintenance phenotypes *sensu* Geist (1978) is applicable.

As outlined by Geist (1978), maintenance phenotypes represent the holding phase of a population (here designated H-phenotypes in Table 2.3.3b). Competitive abilities are refined by specializing in exploiting resources; i.e. competitive abilities to compete for resources needed for reproduction in *in situ* densely packed communities are maximized (resource use specialism; resilient specialists). Endogamy in densely packed communities is expected to lead to the isolation of genetic pools adapted to local situations and the maintenance phenotypes of relatively densely packed communities will form communities of specialists (as differentiated to dispersal phenotypes distinguished by phenotypic plasticity and generalism).

Following Geist (1978), genetic systems apparently act on clues from the environment and alter phenotypic development adaptively. Once fixed, genes enhance their security by way of epigenetic mechanisms, and by adaptively enhancing the range of responses of the epigenetic mechanism, increased plasticity is gained, supporting effective responses to a greater range of environments. For dispersal phenotypes, thus, under conditions of superabundance of resources, normally only encountered by individuals

colonizing a vacant or new habitat, it is adaptive to prepare individuals for a relatively greater diversity of situations, as well as to make them opportunistic with plasticity of behavioural options. Plasticity of phenotypic development is gained at the expense of phenotypic redundancy (canalization), and vice versa. Under conditions of spatiotemporally stable environments, phenotypic redundancy or canalization would be adaptive and maintenance phenotypes realize higher reproductive fitness. Canalization is a measure of the ability of a genotype to produce the same genotype regardless of variability of its environment; implicating phenotypic robustness/resilience (Hermisson & Wagner 2004). In summary, dispersal phenotypes (D-phenotypes) are characterised by generalist plasticity, whereas maintenance/holding phenotypes (H-phenotypes) are typified by specialization and resilience (Table 2.3.3b). This underlies divergent life history strategy and associated demographic responses (Table 2.3.3b).

European countries are grouped in four subhaplogroups I (Rootsi et al. 2004) sharing characteristics of significance for life history strategy expression (Table 2.3.3b).
A haplotype is defined as a combination/group of genes within an organism that was inherited from a single parent. Certain combinations of alleles occur on HLA (human leukocyte antigen) haplotypes within the population at a higher frequency than expected; due to the phenomenon of non-random gametic association: genetic linkage disequilibrium.

Table 2.3.3b Inherent genomic predispositions affecting life history strategy expression along west-east and north-south geographic gradients in Europe				
	Nordic Europe Northwestern Europe	Central-Northern Europe	Southwestern Europe	Eastern-Central Eastern Europe
Countries	Norway Sweden Estonia Finland Iceland Denmark Netherlands Belgium UK northeastern France	Germany Austria Switzerland (UK northeastern France)	Italy Spain southwestern France	Latvia Lithuania Belarus Czech Republic Slovakia Slovenia Hungary Bulgaria Romania Russia Poland Ukraine
Subhaplogroups I (Rootsi et al. 2004)	Hg I1a	Hg I1c (Hg I1a)	Hg I1b2	Hg I1b*
Post-glacial dispersal and diffusion of maintenance types from refugia within the region (Rootsi et al. 2004)	Post-LGM recolonization of north-western Europe from the Iberia-southern France refugium	France as source region for an early spread from the Iberia/southern France refugium	Post-glacial expansion from southern France/Iberia refugium sion (similar to other subclades)	Neolithic maintenance phenotypes expanding from Eastern refugia
Phenotypes *vide* Geist (1978): dispersal (D) or maintenance-holding (H)	D-phenotypes	D-phenotypes	D-phenotypes	H-phenotypes
Plasticity/resilience	**Plasticity**	**Plasticity**	**Plasticity**	**Resilience**
Plasticity scope LHS-mode plasticity/resilience	High Prevalence for M > P (slow)	Intermediate Prevalence for P > M (fast)	Low Prevalence for P > M (fast)	Inherently low Prevalence of P (fast)
Heterozygosity				
Heterozygosity **Lao et al. (2008): Groupings L (low), I (intermediate) and H (high) levels of heterozygosity** **(Reflecting genetic subclustering along a north-south gradient: Seldin et al. 2006)**	Norway L Sweden L Finland L Estonia L Iceland Denmark L Netherlands L Belgium L UK I north-central France I	Northern Germany L Central- southern Germany I Austria I Switzerland I northeastern France L	Italy H Spain H southwestern France H	Latvia L Lithuania L Belarus L Poland L Ukraine I Czech Rep I Slovakia I Slovenia H Hungary H Bulgaria H (I) Romania H Russia
Subhaplogroup LHS-PM settings	N-M(P): LH	C-PM: HL	S-PM: H↑L	E-P(M): H
Heterozygosity rating	L(I)	I(L)	H	L-I-H
Fast-P > slow-M LHS predisposition	**Reduced (L)**	**Intermediate (I)**	**High (H)**	**Accentuated (H) > (I) > (L)**
Inherent metabolic turnover settings: predisposition of HMT > LMT	N-Low (Table 2.5.1.2e)	C-Low (Intermediate) (Table 2.5.1.2e)	S-High (Table 2.5.1.2e)	E-High (variant) (Table 2.5.1.2e)

Inherent temperature-linked proclivity to faster LHS realization	Low	Low	Higher	Low
Cold-adaptation (Wallace 2005)				
For populations living in the colder temperate and arctic zones the ability to uncouple mitochondrial OXPHOS was required. Mutations which partially uncoupled OXPHOS decreased work efficiency, but provided essential heat for surviving chronic cold (requiring high basal metabolic rates).				
Uncoupled mitochondria underpin sustained performance realization under the cold adaptation syndrome (resource-level buffered metabolic performance; wide functional tolerance breadths/broad resource-level optima: Table 2.5.1.1a).				
Plasticity gains (plasticity scope embracing both fast-P and slow-M capacities) with minimum plasticity costs (attenuated fast-P and slow-M trade-off constraints) as *inter alia* associated with cold adaptation (LHS-mode PM realization: Table 2.2.2b).				
Subhaplogroup LHS-PM settings	N-M(P): LH	C-PM: HL	S-PM: H↑L	E-P(M): H
Inherent degree of plasticity gains at low plasticity costs	High	Substantial	Restricted	Substantial
Prevalence of inherent slow-M or fast-P LHS predisposition	Slow-M > fast-P LHS	Fast-P ≥ slow-M LHS	Fast-P > slow-M	Fast-P > slow-M
Prevalence of early to late life performance	Low	Low	High	High

Dispersal (D-phenotypes) and maintenance (H-phenotypes) differentiation. On the basis of ancestral migration patterns two divergent phenotype dispositions were derived: D-conditioned phenotypes shaped under conditions of dispersal and H-conditioned (territory-holding) phenotypes having arisen in sedentary, more densely packed populations. The former pertaining to western, central and northern European populations and the latter to eastern European (Slavic) populations; characteristically associated with inherent predispositions of plasticity/generalism supporting abilities to cope with diverse contingencies and robustness/resilience/specialism in coping with competition under conditions of population density pressure; respectively (as outlined above and summarized in Table 2.3.3b).

Heterozygosity. **Lao et al. (2008)**: Investigated relevant genotype data for 23 subpopulations widely spread over Europe (involving 2514 individuals). Existing differences were characterized by a strong continent-wide correlation between geographic and genetic distance. Mean heterozygosity was larger and mean linkage disequilibrium smaller, in southern compared to northern Europe. Linkage disequilibrium as a measure of adaptation to local conditions. Genetic drift can create linkage disequilibrium between closely linked loci. Inbreeding causes LD for the same reason as population subdivision
(Lewontin 1988).

Pronounced homozygosity has been reported to favour male longevity (Poulain et al. 2011). Mechanisms relating to the predominance of slow life history strategy-mode expression (**LMT-predisposition associated with high life expectancy variants:**

Tables 2.5.1.2e), indicative of slower rates of ageing, seem to be involved. Slow-LHS expression typically manifests in late female reproductive behaviour, slow somatic aging and longevity. Similarities observed between the spatial patterns of late fertility and longevity seem to be related to higher endogamy/consanguinity, i.e. homozygosity (Montesanto et al. 2008; Poulain et al. 2011; Lisa et al. 2015). High heterozygosity levels reflect an underlying inherent predisposition towards increased HMT-P-fast versus LMT-M-slow LHS-mode expression (Fast-LHS-mode realization: early life fertility realization, fast ageing); as increasingly more prevalent in southern European populations. Low heterozygosity, i.e. homozygosity, underpins an inherent predisposition for slower LHS-mode realization (later life fertility realization, slower ageing); as more prevalent in northern European populations (Table 2.3.3b).

Latitudinal cold-adaptation. Cold adaptation (*vide* Wallace 2005) is an integral part of the peri-Arctic metabolic performance syndrome (Section 2.5.1.1; Table 2.5.1.1a). Of importance in this context is that in cold-adapted uncoupled mtDNA variants, fast-slow LHS trade-off constraints are attenuated, particularly so when assocated with endogenous energetic efficiency (low levels of patho-information engram loads) as manifesting in LHS-mode PM (2.2.2e), characterized by combined P performance vitality and M capacities (health and longevity); based on reduced P-M trade-off constraints (Doblhammer & Oeppen 2003).

Wallace (2005): The efficiency with which dietary calories are converted to ATP (adenosine triphosphate) is determind by the coupling efficiency of OXPHOS (oxidative phosphorylation). When tightly coupled ATP synthesis is highly efficient generating the maximum ATP and the minimum heat per calorie consumed. Contrastingly, if the efficiency of proton pumping is reduced and/or more protons are required to make ATP by ATP synthase, then each calorie burned will yield less ATP but more heat. Such mitochondria are then considered loosely coupled. The coupling efficiency therefore determines the proportion of calories utilized by the mitochondrion to perform work as against those used for the maintenance of body temperature (**AS: plasticity of and attenuated fast-P versus slow-M LHS trade-off expression under cold-adaptation**). For populations living in the colder temperate and arctic zones the ability to uncouple mitochondrial OXPHOS was required. However, adaptive mtDNA mutation are subject to trade-offs. In the tropics, tightly coupled mitochondria maximize the efficiency of physical work and minimize heat production (**AS: low basal metabolic rates as associated with the tropical metabolic performance syndrome; Table 2.5.1.1a; 2.5.1.1**). Mutations which partially uncoupled OXPHOS decreased work efficiency, but provided essential heat for surviving chronic cold (**AS: high basal metabolic rates underpinning the peri-Arctic metabolic performance syndrome; Table 2.5.1.1a; 2.5.1.1**).

Thus, whereas tightly coupled mitochondria underpin maximized performance capacity (peak performance specialism: resource responsive high performance rates; narrow performance breadths/narrow resource-level optima: Table 2.5.1.1a) under tropical conditions; uncoupled mitochondria underpin sustained performance realization under the cold adaptation syndrome (resource-level buffered metabolic performance; stress tolerance, wide functional tolerance breadths/broad resource-level optima: Table 2.5.1.1a).

This interpretation is supported by a positive association of mitochondrial uncoupling with higher rates of metabolism (P-HMT functionality) and lifespan (M-LMT functionality), as revealed by Speakman et al. (2004); representing associations contingent with the peri-Arctic metabolic performance syndrome (2.5.1.1); with metabolic performance with high plasticity gains (reduced trade-off constraints: resource-level buffered metabolic performance; wide functional tolerance breadths), but also with associated plasticity costs (high BMRs: Table 2.5.1.1a). Plasticity gains (plasticity scope embracing both fast-P and slow-M capacities) with minimum plasticity costs (attenuated fast-P and slow-M trade-off constraints) as *inter alia* associated with cold adaptation (LHS-mode PM realization: Table 2.2.2b).

Implications re P vs M, fast-slow, HMT-LMT under RUE vs RUR

Links to cold adaptation as related to inherent LHS-PM predispositions subject to the RUE-metabolic energy use mode

Fast-slow slow Pt > Pr tolerance generalist predisposition rather than P performance specialism

P-M Reduced P-M trade-off constraints: wide functional tolerance breadths/tolerance generalists

NCS E HMT-LMT LE

HMT-predispositions/typology inversely indexed by haplotype inherent LE Inherent HMT-predispositions: N-Low, C-Low-Intermediate, S-High; related to positive temperature responsivity () and inversely related to degree of cold adaptation.

Sort out plasticity gains and costs, N vs S, re homozygosity/cold adaptation
PIE up: M demands go up, shift towards slow-M LHS expression/requirements; P down, little PM capacity; f-P/s-M trade-off (reduced combination scope). Initially f-P > M. then s-M > P as DT unfolds. Unerpinning LHS with minimum P-M trade-off and the roles homozygosity, cold adaptation, autophagy/fasting and dietary factors.
Associations: Fast-P-LHS capacity/expression and heterozygosity with reduced plasticity gains and costs; and, slow-M LHS expression with homozygosity and cold adaptation with increased plasticity gains relative to plasticity costs (relaxed trade-off constraints; especially associated with LHS-mode PM).
S-EU Relying on early fast-P fertility. P capacity heterozygosity-based. PIE up, weakening P (shifting to slower-M LHS expression; intensified f-P vs s-M trade-off), but little capacity for fertilityreplacement at later ages.

FROM P 431 In the peri-Arctic metabolic performance syndrome (as associated with peri-artic/temperate-type conditions), the combined tolerance capacity for both P (Production processes: growth and reproduction) and S metabolic performance (Survival: body size, energy storage, thermogenesis, metabolic maintenance) comes at the cost of comparatively high supporting BMR-settings. Conversely, at the cost of being constrained to narrow metabolic amplitudes, as linked to metabolic functionality strictly in relation and sensitive to resource levels (narrow optimality: resource level tracking) and with high-temperature performance settings with low maintenance costs/low BMRs, the tropical metabolic performance mode combines resource-level responsive metabolic performance (capacity for peak performance under resource surplus conditions) with stress resistance. The partial resource-level independence of the peri-arctic metabolic performance mode is based on on a higher physiological capacity of adjustability (plasticity: wide metabolic amplitude and broad resource optimality). This involves sustainability of performance over time when coping with fluctuating resource and temperature levels. The associated enhanced stress tolerance (sustained resource use efficiency at variable and also relatively low temperatures) however incurs costs due to relatively higher levels of maintenance respiration (high basal metabolic rates). Thus, the underpinning phenotypic/metabolic plasticity is energetically costly (DeWitt et al. 1998).

In cold-adaptive mtDNA variants harbouring uncoupling adaptations, plasticity benefits are realized to a greater extent, involving a wider range of Pm versus Mp realization due to attenuated fast-slow LHS trade-off constraints. Wider adaptability amplitudes associated with reduced/attenuated LHS trade-off constraints (attenuated fast-slow LHS trade-off) have plasticity costs, particularly so as and when these trade-

off constraints are intensified as a result of lowered vitality of functional energetic efficiency (due to PIE accumulation associated with uninterrupted food abundance and population density stress). The greater the extent of cold-adaptation (partially uncoupled OXPHOS mtDNA mutations re Wallace 2005), as required in increasingly colder, more northern regions, (a) the higher the predominance of slower LHS-mode expression and also (b) the lower any fast-slow LHS trade-off constraints (Table 2.3.3b), particularly in healthy individuals (low PIE loadings; LHS-mode PM). However, as PIE loadings accumulated during the course of the demographic transition, fast-slow LHS trade-off constraints (LHS-mode pM↑:4) are intensified, more so in individuals of countries subject to inherently faster LHS-modes towards the south/south-west of Europe; but less so in more cold-adapted northern European countries (more relaxed fast-slow LHS trade-off constraints).

5) Population density stress and fertility.

Sensitivity of fertility to population density stress is highest in populations subject to the periarctic metabolic performance mode (Table 2.5.1.1a; 2.5.1.1b: K-Selection reproduction strategy).

Perceived population density density is pervasively an important psychological determinant of fertility (Lutz & Qiang 2002; Knaul 1985: Table 1.2a). For example, Yasuba (1962, op. cit. Lutz & Qiang 2002) had analysed fertility ratios of states in the USA for the period 1800-1860 and found that the most important factor associated with fertility differences and trends was population density (the higher the density, the lower the fertility). The analyses by Lutz & Qiang (2002) for 187 countries (1960-1990) revealed consistent negative relationships between fertility and female literacy, population density and urban proportion of population. Lutz & Qiang (2002) furthermore note that, with respect to contempory European fertility levels, low density regions of northern Scandinavia have relatively higher fertility levels and high density areas of central and southern Europe have relatively low fertility.

Allostasis (2.1.2a; Table 2.1.2b) is a fundamental process through which organisms actively adjust to predictable and unpredictable events; and allostatic load refers to the cumulative costs of allostasis (responses to procursive impacts) to the body when ineffectively managed by the body. Allostatic overload represents a state in which serious pathophysiology can occur (McEwen & Wingfield 2003). Two types of

allostatic overload are defined with reference to prevailing conditions of energy balance.

Type 1 allostatic overload occurs when energy demand exceeds supply (**fasting conditions, supportive of healing through recursive processes; 2.1.2**), resulting in the activation of the emergency life stage (**RUE functionality; autophagy**); establishing a survival mode which decreases allostatic load and positive energy balance is regained on the basis of RUE functionality.

Type 2 allostatic overload results when there is sufficient or excess energy consumption (**RUR functionality; autophagy blocked**), accompanied by social conflict and other types of social dysfunction (McEwen & Wingfield 2003). (**AS: feast conditions: maximum opportunistic utilization of surplus food availability for reproductive and competitive performance subject to the RUR metabolic energy use mode: fast-LHS expression; 2.2.2e**). In all cases, secretion of glucocorticosteroids and activity of other mediators of allostasis (autonomic nervous system, CNS neurotransmitters, inflammatory cytokines) wax and wane with allostatic load. Pathologies develop when allostatic load is chronically high (allostatic overload: McEwen & Wingfield 2003). (**AS: high intensity of procursive impacts arising from uninterrupted overabundance of food resources and population density stress; resulting in progressive patho-information-engram uploading/allostatic overload**). Accordingly, allostasis and allostatic states apply to all situations involving physiological and behavioural responses to challenge and associated cumulative costs to the organism depend on the balance between energy supplies and demands and factors involving social competition. (**AS: dependent on the magnitude of procursive impacts associated with uninterrupted utilization of food resource surplus conditions and population density stress: 2.3.3e**). Type 1 overload relates to overabundance of energy-food availability resulting in poor health outcomes and type 2 overload relates to space as a resource, the deficit of which is associated with increased stress-related disease states; compromising fertility. Thus, as space as a resource diminishes, fertility declines.

Life history strategy (LHS) responses to resource availability levels entail trade-offs (2.2.2a). Under the **adaptive resource re-allocation hypothesis** such trade-off constraints are postulated to be pronounced (2.2.2f). Since the stress tolerance capacity (plasticity) of the periartic metabolic performance mode is relatively resource-costly

(relatively high BMRs) in respect of both energy and space availability, reproduction is only possible above a relatively high level of resource availability (relatively high reproduction-resource level threshold; high RRT; Table 2.5.1.1a: Reproduction and various levels of resource availability). Reproduction is thus characteristically resource-level sensitive in K-selected populations (relatively high nutritional and space requirements for successful reproduction). The adaptive resource re-allocation explanatory framework is accordingly taken to apply in conjunction with the periarctic metabolic performance mode (2.2.2f).

However (2.2.2f), Adler & Buriansky (2014) presented an alternative, evolutionary more plausible hypothesis, i. e. that of a highly conserved physiological response to DR (dietary restriction) where the up-regulation of autophagy and apoptosis represents a **nutrient-recycling, efficient resource use mode** that enables organisms to maximize immediate reproductive output under conditions of resource scarcity (amounting to a relaxation of the production *versus* survival trade-off under resource constraints). The **nutrient-recycling, efficient resource use mode** involves lower reproduction-resource level thresholds (RRT low), implying that reproduction is relatively resource level insensitive (successful reproduction can be sustained with comparatively **low nutritional and space resource requirements**). The **adaptive resource re-allocation resource use mode**, on the other hand, involves high reproduction-resource level thresholds (RRT high), which implicates relatively high resource level sensitivity of reproduction and successful reproduction can be sustained only with relatively **high nutritional and space resource requirements**).

The **nutrient-recycling, efficient resource use mode** thus involves RUE (resource use efficient) functionality, both in respect of energy and space use; and is associated with lower reproduction-resource level thresholds (RRT low), implying that reproduction is relatively resource level insensitive (successful reproduction can be sustained at comparatively low nutritional and space resource availability levels). Under the RUE functionality mode LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated (reduced P-M trade-off constraints). The **adaptive resource re-allocation resource use mode** represents a RUR (resource use reactive) functionality mode involves comparatively high reproduction-resource level thresholds (RRT high); implicating relatively high resource level sensitivity of reproduction and successful reproduction can be sustained

only with comparatively high nutritional and space resource availability levels). Increased P-M trade-off constraints are associated with the RUR functionality mode.

Based on the insights presented above, two types energy-processing metabolic modes are differentiated (refer also to 2.5.1.4e): I) a balanced resource use efficient (RUE) EUE-LHS-PM supporting metabolic mode (minimized P-M trade-off constraints underpinning a high performance and health/longevity combination) and a II) resource use reactive (RUR) EUR-LHS-P>M energy use metabolic mode (fast LHS extremized, high metabolic turnover expression regarding early life metabolic performance and P-type coping performance in the face of sociospatial density stress; trading off against functional breadth of maintenance realization, including later life performance capacity/longevity, health and fertility). Autophagy as component of the metabolic mode is either present (RUE-EUE-PM metabolic mode) or absent (RER-EUR: P-M traded off metabolic mode; induced under persistent 'feast' conditions both in terms of the overabundance of energy resources and typically associated with increased population density stress impacts).

Depending on circumstances, relating to environmental resource availabilities favouring either LHS-mode PM (Table 2.2.2b), as opposed to LHS-modes P>M(1), M>P(2) and M↑:4, subject to increased plasticity trade-off constraints, the **differential nutrient-recycling efficient resource use** mode or the **adaptive resource re-allocation feast-responsive resource use** mode may apply within the realm of the peri-arctic metabolic performance mode. P performance competitive capacity is required to cope under sociospatial density stress. Such capacity is supported by fast LHS-HMT expression enhancing P-capacity assertion. Under circumstances where and when the **adaptive resource re-allocation feast-responsive resource use** strategy is engaged, as during phases when pursuit of population size increases (maximum utilization of resources) becomes adaptive (as during demographic transitions), the energy use reactive EUR (RUR)-P > M metabolic mode (fast LHS extremized, high metabolic turnover HMT-mode: LHS P > M) applies, and sequentially also in respect of fast-LHS-modes M > P and M↑4 during the demographic transition (Table 2.3.3o). Reproduction output then becomes relatively resource-level sensitive both in respect of nutrition (positively) and space availability (negatively at limiting space availability); reproductive success then being sensitive to population density stress. Adequacy of reproduction of K-selected populations is dependant upon some plenitude of resource

reserves (Table 2.5.1.1a), both nutritionally and regarding space as a psychological resource (conditions and spaces of low psychosocial stress); underscoring sensitivity of reproduction to negative feedback effects of population density stress.

6) Divergence of life history strategy expression according to subhaplogroup LHS settings

Cummins (2014): Longevity began increasing long before 1800 and the Industrial Revolution (for example, Voigtländer & Voth 2013), with marked increases around 1400 and again around 1650. The areas of North-West Europe which later witnessed the Industrial Revolution achieved greater longevity than the rest of Europe even by 1000 AD. Spatial patterns of lifespans of Europe's nobility were revealed which suggest that a particular European mortality pattern has existed since 1000 AD. The parts of Europe that later experience the Industrial Revolution first the (North-West) have higher lifespans than those who later lag behind (the South-East).
The emergence of modern economic growth during the Industrial Revolution was accompanied by an explosion in Europe's population.

Net expected lifespan at average latitude (c. 50) and longitude (c. 0) varied between about 47-53 years during 800-1400, 52-55 during1400-1600 and 55-58 during 1700-1800.

Time trends of noble lifespans over the millennium between 800 and 1800 were estimated. The nobility are forerunners of Europes mortality transition (refer also to David et al. 2010, op. cit Cummins 2014). The rising lifespans predate modern medicine or any public health measures. It also predates the Industrial Revoltion. It is also striking how the post 1600 rise is weaker in central/eastern Europe and southern Europe. Significant oscillations were detected, most importantly the sharp Europe-wide rise in lifespan after 1400. The rise is stronger over the 1400-1600 interval in Ireland, Scotland, and England and Wales.
Why did noble lifespan increase so much after 1400? This change coincides with Voigtländer and Voth's dating of the origin of the European Marriage Pattern (2013). There was something about the North-West of Europe long before 1348 (Black Death) that led to nobles living longer lives. These results suggest that the 'Rise of the West' does not solely originate in institutional innovations of the 17th century (Acemoglu & Robinson 2012, op. cit Cummins 2014) nor in social reactions to the Black Death (Voigtländer & Voth 2013, op. cit Cummins 2014). Western excepionalism exist in individual behaviour differences that are present since the first millennium AD.

Table 2.3.3c Net expected lifespan (years), as estimated from European nobility data for 800-1800 (Cummins 2014)			
	800-1400	1400-1600	1700-1800
Northern Europe	47-50	51-53	55-58
Ireland	46-48	48-54	55-60
England/Wales	47-50	50-55	55-59
	46-50	**48-55**	**55-60**
France	44-47	50-51	50-55
Southern Europe	44-46	48-50	50-54
	44-47	**48-51**	**50-55**
Central Eastern Europe	**47-49**	**47-50**	**50-54**

A fundamental inverse relationship exists between lifespan/longevity, associated with the capacity for low metabolic turnover (LMT) functionality (intraspecific later life metabolic performance) and functionality at high metabolic turnover (HMT) rate settings; usually associated with early life metabolic performance intraspecifically (Table 2.5.1.2e). Four main country groupings have been differentiated on the basis of life expectancy (Table 2.3.3c)/age at death (Table 2.3.3d): Northern (N), Central (C), Southern (S) and Eastern Europe (E). These groupings are congruent with and reflect associated countrygroup-specific subhaplogroup-based variants of LHS-PM settings (Table 2.3.3e). The Northern European variant N-M(P): LH reflects a predisposition for LMT ≥ HMT functionality, the Central European variant C-PM: HL for HMT ≥ LMT functionality, the Southern European variant S-PM: H↑L for HMT↑≥ ≥ LMT functionality and the Eastern European variant E-P(M): H exhibiting resilient prominence of HMT functionality. These inherent countrygroup-specific predispositions have implications in underpinning divergent demographic patterns and processes, notably so also during demographic transitions.

Geographic effect on age at death (Cummins 2014): higher geographic effect indices (latitude or longitude) indicate higher ages at death (Table 2.3.3d):

Table 2.3.3d Geographic effects (latitude/longitude) on age at death (as determined for the European nobility 1400-1800): Cummins 2014) and life expectancy at birth (2006-2010: WHO Europe 2012)		
	Latitude and longitude: Effects on age at death (Cummins 2014)	Life expectancy at birth (years)

					(2006-2010) [b]	
			Geographic effect indices [a]			
	Latitude	Longitude	Latitude effect	Longitude effect		AveFM (Gap)
North-West					F 81-84	83.1
	64.9	-19.0	2		M 72-80	77.4
Iceland	60.5	8.5	2			(5.7)
Norway	60.1	18.6	2			
Sweden	56.3	9.5	2			
Denmark	55.4	3.4				
UK						
	50.5	4.5	0		F 83	83
Belgium	52.1	5.3	0		M 77-78	77.5
Netherlands						(5.5)
Central						
Germany	51.2	10.4	0		F 83-84	83.3
Switzerland	46.8	8.2	0		M 78-79	78.3
Austria	47.5	14.5				(5.0)
France	46.2	2.2			F 85	85
					M 78	78
						(7.0)
Southern						
Italy	41.9	12.6	-2		F 83-85	83.7
Spain	40.5	3.7	-2		M 77-79	78.0
Greece	38.0	23.7				(5.7)
Portugal	38.7	9.0				
Central-Northeast					F 78-83	80.0
					M71-76	73.0
Poland	51.9	19.1		-2		(7.0)
Czechia	49.8	15.5		-2		
Croatia	45.1	15.2		-2		
Hungary	47.2	19.5		-2		
Slovenia	46.1	15.0		-2		
Slovakia	48.7	19.7		-2		
North-East						
Estonia	58.6	25.0		-2/4	F 78-81	79.3
Latvia	56.9	24.6		-2/4	M 67-69	68.0
Lithuania	55.2	23.9		-2/4		(11.3)
Eastern					F 77-78	77.7
Serbia	44.0	21.0		-2/4	M 70-	70.7
Romania	45.9	24.5		-2/4	72	(7.0)
Bulgaria	42.7	25.5		-2/4		
Belarus	53.7	27.9		-2/4	F 74-78	75.8
Russia	55.7	37.5+			M 63-	65.0
Ukraine	48.4	31.2		-2/4	69	(10.8)
Georgia	41.7	44.9		-2/4		
Moldova	47.4	28.4				

[a] Cummins 2014: Geographic effect indices: higher geographic effect indices (latitude or longitude) indicate higher ages at death. [b] WHO-Europe 2012 (World Health Organization)

Geist (1978): Maximizing reproductive fitness involves inter alia the following: 1) Minimize expenditures on maintenance so as to save a maximum of resources for reproduction, 2) Maintain physiological homeostasis, i.e. keep healthy and unharmed, 3) Support individuals with similar gene compositions in relation to their relatedness and 4) Mate with individuals equal or superior to itself in maximizing reproductive fitness.
The maintenance type characterizes the holding phase of a population. It is designed to preclude any opportunity for interspecific competition (resource opportunities for competitors) by removal of all resources within its ecological niche. This is best achieved by maximizing the number of individuals per unit of exploitable resource so as to maximize coverage of the landscape. This can be done by reducing individuals to the smallest possible body sizes; and to diversify ensuring that all possible resources are indeed utilized. Also, it may pay the maintenance phenoptype to select against genetically distant individuals in mate choice. This would reduce heterosis. Heterosis is bioenergetically expensive, and such a cost may be charged against of reproduction of offspring, lowering reproductive fitness. Under conditions of resource scarcity such as under conditions with a maximum number of individuals at carrying capacity, heterosis may be diasadvantageous as it raises the cost of maintenance and reduces resources available for reproduction, without necessarily giving an individual a significant competitive advantage. This must be true particularly for demes of kin-selected individuals in which selection favours a maximum number of adult defenders per unit of defendable resource.

As outlined by Geist (1978), maintenance phenotypes represent the holding phase of a population (here designated H-phenotypes in Table 2.3.3b). Competitive abilities are refined by specializing in exploiting resources; i.e. competitive abilities to compete for resources needed for reproduction in *in situ* densely packed communities are maximized (resource use specialism; resilient specialists). Endogamy in densely packed communities is expected to lead to the isolation of genetic pools adapted to local situations and the maintenance phenotypes of relatively densely packed communities will form communities of specialists (as differentiated to dispersal phenotypes distinguished by phenotypic plasticity and generalism). Dispersal phenotypes (D-phenotypes) are characterised by generalist plasticity, whereas maintenance/holding phenotypes (H-phenotypes) are typified by specialization and resilience (Table 2.3.3b). This underlies divergent life history strategy and associated demographic responses (Table 2.3.3b). Reproductive fitness as driving force of evolution defines the biological/evolutionary success of individuals. In order to

maximize reproductive fitness individuals must maximize the proportion of individuals carrying their own genes in succeeding generations. Inclusive fitness arises as an individual contributes to the success of other individuals in proportion to their genetic relatedness (Geist 1978). To maximize reproductive fitness an individual (groups of related individuals) should minimize expenditure on maintenance in order to conserve maximum resources for reproduction, maintain physiological homeostasis (health) and provide for access to and defence of scarce resources essential for reproduction (Geist 1978).

Table 2.3.3e Life history strategy expression of divergent subhaplogroup types along west-east and north-south geographic gradients in Europe as related to Northwestern, Central-Northern, Southern and Eastern European marriage and family patterns

Subhaplogroup types (Table 2.3.3b)	Nordic Europe Northwestern Europe	Central-Northern Europe	Southwestern Europe	Eastern-Central Eastern Europe
	Northwestern-central (NWC)		**Southern (S)**	**Eastern (E)**
Countries	Norway Sweden Estonia Finland Iceland Denmark Netherlands Belgium UK northeastern France	Germany Austria Switzerland (UK northeastern France)	Italy Spain southwestern France	Latvia Lithuania Belarus Czech Republic Slovakia Slovenia Hungary Bulgaria Romania Russia Poland Ukraine
Subhaplogroups I (Rootsi et al. 2004)	Hg I1a	Hg I1c (Hg I1a)	Hg I1b2	Hg I1b*
Subhaplogroup regions	N : Northern	C: Central	S: Southern	E: Eastern
Haplotype groupings	**Northwestern-central (NW)**		**Southern (S)**	**Eastern (E)**
Post-glacial dispersal and diffusion of maintenance types from refugia within the region (2.3.3b:4)	Post-LGM recolonization of north-western Europe from the Iberia-southern France refugium	France as source region for an early spread from the Iberia/southern France refugium	Post-glacial expansion from southern France/Iberia refugium sion (similar to other subclades)	Neolithic maintenance phenotypes expanding from Eastern refugia
Warm-cold adaptation gradients				
Heterozygosity: 2.3.3b(6)/Table 2.3.3b				
Heterozygosity Lao et al. (2008): Groupings L (low), I (intermediate) and H (high) levels of heterozygosity (Table 2.3.3b)	Predominantly Low	Low to Intermediate	High	Low (E-N) to Intermediate (E-C) to High (E-S)
Fast > slow LHS predisposition	**Reduced (L)**	**Intermediate (I)**	**High (H)**	**Accentuated (H) > (I) > (L)**

Climate-linked (warm-cold gradient) proclivity to fast-LHS realization	Low	Low	Higher	Low
Cold-adaptation (Wallace 2005): 2.3.3b:6/Table 2.3.3b				
Prevalence of inherent slow > fast LHS predisposition	Relatively high	Intermediate	Low	Relatively unaffected (resilience)
Fast-P/slow M LHS trait expression trade-off relaxation by cold adaptation (reduced P-M trade-off constraints)	Relaxation by cold adaptation	Some relaxation by cold adaptation	Inherently low relaxation by cold adaptation	Restricted relaxation by cold adaptation due to LHS-mode resilience
Phenotypes *vide* Geist (1978): dispersal (D) or maintenance-holding (H)	D-phenotypes Dispersal	D-phenotypes Dispersal	D-phenotypes Dispersal	H-phenotypes Maintenance
Plasticity/resilience	**Plasticity**	**Plasticity**	**Plasticity**	**Resilience**
Plasticity scope LHS-mode plasticity/resilience	High Prevalence for M > P (slow)	Intermediate Prevalence for P > M (fast)	Low Prevalence for P > M (fast)	Inherently low. Prevalence of P (fast)
Inherent baseline LHS-PM settings	M(P)	PM	PM	P(M)
Inherent metabolic turnover settings (Table 2.5.1.2e)	LMT > HMT	HMT ≥ LMT	HMT > LMT	HMT > LMT
Life expectancy group type ranking (Table 2.3.3d)	2	0	-2	-2/4
Subhaplogroup regions	N : Northern	C: Central	S: Southern	E: Eastern
Adaptive LHS settings at population equilibrium carrying capacity (K-selection)				
Subhaplogroup LHS settings (Table 2.3.3b)	N-M(P): LH	C-PM: HL	S-PM: H↑L	E-P(M): H
Inherent predispositions for metabolic settings: High life expectancy-low metabolic turnover-M performance (HLE-LMT-M) and Low life expectancy-P performance (LLE-HMT-P)				
Inherent predispositions for metabolic settings: HLE-LMT-M LLE-HMT-P	**HLE-LMT-M > LLE-HMT-P**	**HLE-LMT-M ≥ LLE-HMT-P**	**LLE-HMT-P ≥ HLE-LMT-M**	**LLE-HMT-P > HLE-LMT-M**
Characteristics of subhaplogroup-based variants of LHS-PM settings **HMT/LMT: high and low metabolic turnover respectively** (Table 2.2.2b)	N-M(P): LH Prevalence of M-LMT functional capacity (cold adaptation; slow metabolic turnover environments)	C-PM: HL Plasticity of combined P-HMT and M-LMT functional capacity, with some preva-lence of P-HMT functionality	S-PM: H↑L Prevalence of P-HMT functional capacity (temperature-linked high metabolic turnover responses)	E-P(M): H Resilience in sustaining prevalence of P-HMT functionality under LHS-PM promoting-conditions
Propensity of early *versus* late fertility realization	Low	Low	High	High
Rates of ageing and adult mortality	Low	Low	High	High

Fertility at/towards carrying capacity	Controlled	Controlled	Unrestrained	Unrestrained
Traditional family household type (2.3.3b:7)	Nuclear family households (father, mother and their children) or extended family households, usually including at least three generations (grand parents, their married offspring and grandchildren)			Joint family (sets of male siblings/spouses and children)
EMP: Traditional European marriage patterns (2.3.3b:7)	Northwestern EMP		Southern EMP	Eastern EMP
	Later age of marriage-childbearing Nuclear family		Early age of marriage-childbearing Joint family	

European marriage patterns in alignment with subhaplogroup-based variants of LHS-PM settings (Table 2.3.3e).

North-Western European marriage pattern (2.3.3b:7). Late and non-universal marriage; marriage restricted under conditions of resource limitations, often associated with lower socioeconomic status (SES). The life phase of women from menarche (generally reached at the age of 14 years or about 12 years in elite women: Hajnal 1965) to the birth of the first child was relatively long, averaging ten years (Seccombe 1992). Wealthier couples (*inter alia* noblewomen/gentlewomen) were likely to marry earlier. Moderate rates of fertility, mortality and marriage were tied to economic conditions. Under economically favourable conditions, early marriage and having more children were affordable, whereas under economically limiting conditions, delaying of marriage or non-marriage resulted in fewer children being born. Western EMP typically associated with conditions at carrying capacity (population stability) and underpinned by LHS PM setting, whereas conditions of resource surplus allow for increased population increase rates underpinned by LHS mode P>M (early age fertility realization; more prominent in higher SES, resulting in them realizing higher fertility rates than in lower SES. Reversal of this pattern as the demographic transition progresses. Resource limitations at carrying capacity/population equilibrium associated with low fertility (late age of marriage/increased incidence of non-marriage).

Nuclear family households (father, mother and their children), associated with a propensity for later fertility realization, low rates of ageing and controlled fertility at population equilibrium carrying capacity (Table 2.3.3e). Underpinned by the relevant subhaplogroup LHS-PM variants N-M(P): LH and C-PM: HL (compatible HMT and LMT functionality in both).

South-Western European marriage pattern (2.3.3b:7).

Southern Europe: The distinguishing Northwest European features were not evidenced during the 17th and 18th centuries in parts of southern France and in Italy, where earlier ages of women at first marriage were experienced. In the 15th century, the marriable age was 19 years, and easily 97 percent of women were married by the age of 25 years (De Moor & Van Zanden 2009). Early marriage for both sexes was universal and high fertility was counteracted by high mortality (Kertzer & Barbagli 2001).

Extended family households, usually including at least three generations (grand parents, their married offspring and grandchildren), associated with a propensity for early fertility realization, faster rates of ageing and uncontrolled fertility towards population equilibrium at carrying capacity (Table 2.3.3e). Underpinned by the relevant subhaplogroup LHS-PM variant S-PM: H↑L (prevalence of P-HMT functional capacity: temperature-linked high metabolic turnover responses).

Eastern European marriage pattern (2.3.3b:7). Early marriage for both sexes universal and high fertility was counteracted by high mortality (Kertzer & Barbagli 2001). High fertility even under resource shortages/competition for resources under sociospatial and economic density stress, but associated with higher mortality/reduced longevity. Sustained early life performance (resilience).

The Eastern European marriage pattern invoves the 'Joint family' (sets of male siblings/spouses and children), associated with a propensity for early fertility realization, faster rates of ageing and uncontrolled fertility towards population equilibrium at carrying capacity (Table 2.3.3e). Underpinned by the relevant subhaplogroup LHS-PM variant E-P(M): H (resilience in sustaining prevalence of P-HMT functionality under LHS-PM promoting-conditions).

1)Inherent baseline LHS PM settings/subhaplogroup LHS settings

E maintenance , Geist, kinship, EUE. Population density sensitive in non-PM state.

Temperature adaptation. Warm to low (cold-adaptation). S-C-N

S warm T P_{max} performance, subject to plasticity costs (accentuated P-M trade-off), high P_{max} performance (early fertility) versus M (later life performance/longevity)

C

N Cold T performance PM tolerance; weak P-M trade-off, but energetically costly. When subject to insufficiency of endogenous energy status re PIE accumulation; P-M trade-off constraints accentuated, as M demands rise, P performance vitality declines (fertility down, longevity up).

INVOLVE Wallace (2005) and heterozygosity

Inherent settings NCS (generalist plasticity; LMT-M/HMT-P dispersal-type performance breadth/flexibility) vs E (specialist resilience; HMT-P performance maintenance-type specialism)

Plasticity allows for both P and M performance with little/no P-M trade-off-costs under PM; but with increased P-M trade-off posts under P > M, M > P and M4.

Three LHS-haplogroups:

NW-C Dispersal types, plasticity, later life performance, cold-adaptation, homozygosity. M(P)

N Population carrying capacity equilibrium mode M(P) LMT > HMT (plasticity): relatively low - later fertility and comparatively low mortality. High LE mode (Table 2.3.3c and *Table 2.3.3d*). M(P) vitality; longevity and later age performance.

C Population carrying capacity equilibrium mode PM: HMT ↔ LMT (plasticity): early to late fertility and low mortality. Comparatively high/intermediate LE modus.

S Dispersal types, plasticity, temperature responsive, heterozygosity.

Population carrying capacity equilibrium mode PM HMT > LMT (plasticity): intermediate LE mode. But high plasticity scope; high P-M trade-off constraints (heterozygosity): early fertility up, M up, LE down; later fertility down, mortality down (pronounced: Table 2.3.3d).

E Maintenance types, resilience, cold-adaptation, homozygosity.

Population carrying capacity equilibrium mode P(M) HMT > LMT (resilience): relatively high – early fertility and mortality at pretransition as a perrmanent adaptive

state at carrying capacity. Changing during DT to low fertility. P expression with reduced M trade-off costs (already pre-empted/accounted for/subsumed in resilience capacity of of the inherent LHS setting, inherently low LE). Sustained Pm-type vitality (PM): reduced HMT-health trade-off ? for carrying capacity LHS-mode. Less decline thereof (as in Pm3: intensified M down costs: lower self-perceived health, Eikemo et al. 2008) with progression towards M > P and M4. And in new post DT, carrying capacity LHS mode.

E HMT specialists resilience high P early low M late high intrinsic mortality specialist type

NCS HMT-LMT generalists plasticity

From population equilibrium state PES to population increases, then homing in back to PES (P > M, M > P, M4, M(P↓↑)5). Increasing intolerance to foreigners W as towards M4 and MP5. E intrinsically.

EMPs

Table 2.2.2b. Two main physiological LHS-PM subtype settings are differentiated: LHS-**MP dispersal type** (*sensu* Geist 1978) setting with **generalist P-M plasticity** (pronounced P-fertility/M-longevity trade-off; e-r trade-off alleviated by cold-adaptation/low population density stress) and LHS-**P(M) maintenance type** (*sensu* Greist 1978) setting with **P-capacity specialist resilience** (predominance of the HMT-mode: Table 2.5.1.2e); restricted extrinsic early P-fertility-M longevity trade-off.

N M(P): LH Low fertility, low mortality (intrinsic high LE type) (late life performance, link to LE pattern)

C P-M: HL Moderate fertility, moderate mortality (intrinsic intermediate LE type 0) (late life performance, link to LE pattern)

S P-M: H↑L High fertility (early), high mortality (late) (intrinsic low LE -2)

E P(M): H High fertility (early), high mortality (later) (intrinsic low LE type -2/4)

Define PES for E, S, C, N.

Pre-transition PM LHS-modes: M(P), PM. P(M): generally extended life span performance (early to late).

N M(P): LH N-M(P) LMT > HMT (plasticity): priority of somatic investment (size, longevity, maintenance) and later life performance.
C P-M: HL C-PM: HMT ↔ LMT (plasticity): balanced/exchangeable somatic (size, longevity, maintenance) vs productive (reproduction/early to later life performance) investment. High P (competitive capacity related to population density stress: antiquity index), but not high early P fertility; traded off for increased M-longevity.
S P-M: H↑L S-PM HMT > LMT (plasticity): priority of investment into (early life) P performance traded off against later life M performance (size, longevity). High P(early life performance in the context of T-responsive functionality), but not high early P fertility; traded off for increased M-longevity.
E P(M): H E-P(M) HMT > LMT (resilience): fixed priority of investment into early life P performance at the cost of later life performance (increased mortality/reduced longevity/life expectancy). High resilience re f-LHS setting, inherently low LE

(Table 2.5.1.2e)

N LE up in both M and F, GAP down. M(P↓) SDT
E LE lower more so in M. GAP up. LHS-P(M) setting. HMT-mode predominance; reduced somatic investment/longevity. Male P predominance.

Plasticity (as genetically-based heritable characteristic: Pigliucci 2007) allows for high performance capacity realization; but the higher the plasticity scope, the lower is the capacity of resilience (involving protective factors/processes curtailing vulnerability to negative experiences under adversity: Pluess & Belsky 2013). A high plasticity scope underpins high performance breadth permitting both high P performance/fast LHS-mode and high M maintenance/slower LHS-mode expression. Resilience capacity, on the other hand, underpins invariant high P performance/fast LHS-mode realization in order to cope with and minimizing vulnerability to experienes of adversity. (Plasticity is here defined as flexibility in adaptability of an organism to environmental changes or challenges; whereas resilience relates to the capacity of endogenous protective factors and processes to prevent an individual from succumbing to or being harmed by some contextual adversity through the ability to restore or maintain any pre-perturbation functional state).

Health status affects the intensity of LHS trade-off constraints (Doblhammer & Oeppen 2003). Good health status apparently mediates a dampening of LHS trade-off relationships. For example, the fertility-longevity trade-off is absent in individuals of good health status (Doblhammer & Oeppen 2003); implying a weakening of trade-off relationships in respect of performance-maintenance/fast-slow LHS-mode expression.

Pluess & Belsky (2013): Here the concept of *vantage sensitivity* is advanced, reflecting variation in response to exclusively positive experiences as a function of individual endogenous characteristics (the emphasis is placed on the elucidation of *endogenous* factors associated with variability in response to *positive* influences).
Manuck and associates (Manuck 2011, op. cit. Pluess & Belsky 2013; Sweitzer et al. 2012, op. cit. Pluess & Belsky 2013) introduced the term vantage sensitivity. Vantage is short for advantage and implies benefit, gain or profit and is also defined as 'a position, condition, or opportunity that is likely to provide superiority or an advantage (Houghton Mifflin 2000, op. cit. Pluess & Belsky 2013). Vantage sensitivity relates to the notion that some individuals are more sensitive and positively responsive to environmental advantages to which they are exposed. The following concepts characterize variability in response to positive experiences: (a) *vantage sensitivity* reflects the general proclivity of an individual to benefit from positive and presumptively well-being- and competence-promoting features of the environment, just as *vulnerability* depicts the tendency to succumb to negative effects of adversity; (b) the degree of *vantage sensitivity* is a function of the presence of *vantage sensitivity factors* (i.e. promotive factors) just as *vulnerability/risk factors* increase vulnerability to negative effects of adversity in the diathesis-stress framework; (c) vantage resistance describes the failure to benefit from positive influences, just as *resilience* characterizes resistance to negative effects of adversity in the diathesis-stress framework; and (d) the degree of *vantage resistance* is a function of the presence of *vantage resistance factors* or absence of *vantage-sensitivity* ones, just as *protective factors* increase *resilience* to negative effects of adversity in the diathesis-stress framework.

According to the differential-susceptibility hypothesis, individuals generally vary in their developmental plasticity regardless of whether they are exposed to negative or positive influences. Both models accounting for environmental impacts, the differential susceptibility (Belsky & Pluess 2009) and the biological sensitivity to context (Boyce & Ellis 2005) models, share the notion that some individuals are disproportionately susceptible to both positive and negative developmental experiences and environmental exposures (Ellis et al. 2011a). The theoretical framework of *differential susceptibility* regards more susceptible individuals as not just especially vulnerable, but more generally developmentally plastic (Boyce & Ellis 2005; Ellis et al. 2011a). Accordingly, those disproportionately likely to be adversely affected by negative experiences and exposures are also likely to benefit more from supportive and enriching ones.

Vantage sensitivity should not be equated automatically with differential susceptibility. Whereas some individuals might be more sensitive to the benefits of a supportive or enriching environments as a function of vantage-sensitivity factors, the same individual attributes may not make them more susceptible to the negative effects of contextual adversity (thus not in line with differential susceptibility). A further distinction between the two concepts emerge when we consider that individuals may

be both highly responsive to environmental support (i.e. showing increased vantage sensitivity) and unresponsive to and protected from adversity (i.e. showing increased resilience), and this could be due to the very same endogenous characteristics. For example, children with high IQs tend to be more resilent in the face of adversity (e.g. Masten et al. 1999, op. cit. Pluess & Belsky 2013). Vantage sensitivity is exclusively about the positive benefit derived from an enriching or supportive experience, whether reflected in the reduction of problems or dysfunction (e.g. depression, antisocial behaviour) or the enhancement of competence/well-being (e.g. prosocial behaviour, academic achievement). Thus, whereas some individuals may be disproportionately likely to be affected positively and negatively by, respectively, positive and negative contextual conditions, others may only be susceptible to positive influences; thereby manifesting vantage sensitivity rather than differential susceptibility.

Resilience reflects the absence of problematic functioning despite exposure to contextual adversity. Whereas resilience is what protective factors and processes engender by preventing an individual from succumbing to or being harmed by some contextual adversity (Rutter 1987, op. cit. Pluess & Belsky 2013), vantage sensitivity refers to promotive influences (Sameroff 2000, op. cit. Pluess & Belsky 2013) and is about individual benefit, more than others, from a positive environmental experience or exposure. Vantage sensitivity is about variation in the promotion of well-being or competent functioning when exposed to an experience presumably having a beneficial effect, whereas protection (resilience) is about not having the well-being or competence undermined when subject to negative experiences. (**AS: Combination of vantage sensitivity, based on plasticity scope, and protective resilience; low plasticity-resilience trade-off constraints: low plasticity and low resilience costs. Underpinned by LHS PM realization: Table 2.2.2b**).
The concept of resilience reflects protective responses within a diathesis-stress framework and refers to individual differences in response to adversity.
The concept of vantage sensitivity pertains to individual differences in response to positive contextual conditions as a function of promotive factors. Differential susceptibility, on the other hand, is based on the view that the same factors that increase vulnerability to adversity will also increase vantage sensitivity in positive environments (**AS: high plasticity/low resilience; plasticity-resilience trade-off**) and that factors that make some resilient to adversity will also make them less responsive to positive experiences (**AS: high resilience/low plasticity**).

Heterozygosity. Boosting/amplifying P vs M LHS expression. Under high plasticity scope, P-M trade-off constraints come to bear: fP up sM down. fP down sM up. Increasing early life fertility vs longevity trade-off with shift from LHS-mode P > M to LHS-modes M > P/M4; particularly in S.

Homozygosity. Balanced P-M LHS PM longevity hotspots/Blue zone populations (endogamy). Low fertility-longevity and P-M trade-off consraints: early to late life performance/fertility-longevity combination. Diminished sexual dimorphism.

K-selection. Modes of dealing with life at carrying capacity.

W Dispersal-type mode. Sensitive to negative density-fertility feedback. Fluctuating phases between being at carrying capacity and population increase phases. Resource use and population density fluctuations. PM or MP: resource/space scarcity at carrying capacity/population equilibrium and P > M: surplus resource use response for population increases. Plasticity, high BMR for cold-adaptation more costly; thus higher M requirements and costs (plasticity scope is energetically costly; incurs high maintenance costs). Resource level sensitive i.t.o. food and space. Famine/starvation – feast abundance alternations (DR starvation). Capacity to utilize resource surpluses at cost of sensitivity to starvation. Per capita resource availability significant. M(P). Plasticity of HMT-LMT performance; sympathetic/parasympathetic. Early/later life. At minimum P-M costsunder PM but increased P-M costs under P > M, M >P, M4.

E Maintenance-type mode. Lower plasticity scope and thus less energy investment requirements for maintenance (including maintenance). In energy efficiency mode re DR (autophagy). Adler strategies. Resource level insensitive i.t.o food and space. Energy efficiency mode (DR autophagy). Resilience in the face of density effects. Constancy of carrying capacity. Constancy/perpetuation of high population densities under density-linked resource stress/scarcity. Per capita resource availability marginal under permanence at carrying capacity. P(M) HMT, sympathetic, youthful; ealy life performance capacity, resilience in the face of population density/anomy as experienced at persistent carrying capacity (per capita resource limitations, also ito space i.e. psychologically).

Life expectancy (LE):

N Base M(P). High LE sustained; lower P-M trade-off costs. From e-r. wide childbearing age span .TFRs up/stable.

C Plasticity. High LE base. High Pm expression re population density stressearlier on at cost of M relatively reduced LE up CHECK. P/M realization ratio up and TFRs down earlier on.

S Plasticity. fP up, LE down shifting to LE up under M4, especially sLHS M4. High P-M trade-off costs. LE up, TFR down. Inherently/historically LE down, but plasticity, LE increases (M4); shifting childbearing age span away from early fertility realization; TFRs down.

E Resilience. Low LE base. P(M) early life performance/resilience in face of population density stress (adaptation to persistence condions at carrying capacity: per capita resource and space limitations, and increased associated competitive

environment). P(M) to Pm3 delayed and incomplete shift to M4; low TFR and low LE sustained. P resilence sustained. Inherently/historically LE down, but not dramatically increasing, thus fixed to early fertility realization as shift to M4 (narrow childbearing age span) TFR down as P(M) to P > M to M4.

Plasticity scope vs resilience/specialization.

Adler p 405-408/450. W feast-famine phase dynamics (DR starvation) vs E ongoing famine dynamics (DR autophagy)

MP W PM E

Clarify modifying effects by homozygosity/heterozygosity and cold-adaptation

Wallace 2005 canalization/specialization to cope with population density stress at carrying capacity, i.e. population density effects.

Plasticity/stress tolerance/later life sustained performance vs resilience/stress resistance/early life peak performance. Longevity trade-off (unlike tropical stress resistance/low BMR Homozygosity link/endogamy (intolerance to foreighners). Less longevity costs when under PM.
Less population density stress sensitive than in plasticity dispersal types (geared for resource surplus use in new environments/population increases when not at carrying capacity)

E high BMR rate for resilience specialization/narrow metabolic amplitude specialization/neotonization. Specialized HMT – sLHS P(M) AU/W; pregnancy cueing P up; but with trade-off costs; early fertility (family important; per capita resource limitations: E-EMP), but constrained/narrow childbearing age span.
E In carrying capacity mode. 2006-2010. sLHS M4 to sLHS P(M). HMT sensitive pregnancy P cueing. Early to late fertility age span. TFRs up ? Evidence ?
Inherent basic LHS setting P(M) phenotypes; maintenance types-resilence-cold-adaptation-homozygosity. Early life performance. HMT-phenotype. Stress resistance capacity. Low plasticity scope of the HMT-phenotype. Inherent fertility-longevity trade-off.
W M(P). plasticity of HMT-LMT expression. Dispersal types, plasticity, tolerance capacity, cold-adaptation, homozygosity.
sLHS M(P↓) AU/W. PIE compromised persisting post SDT. Later fertility realization. Pregnancy P investment cueing; sLHS M(P↓) M investment supporting; more balanced P-M favourable for somatic investment; wider childbearing age span (e and r).

S P > M. Dispersal, heterozygosity, less cold-adaptation, rather temperature responsiveness adaptation. Strong P-M trade-off constaints; strong early fertility/longevity trade off. Pm-type expression and P/M ratio realization incur plasticity costs.

f-LHS M4 setting. Intensified P-M trade-off, as LE up (later life performance), fertility down. Trade-off intensity N lowest, C higher, S highest, E high. Relaxed for s-LHS M4 and more so for sLHS M(P) setting. The lower the P-M trade-off constraints, the wider the childbearing age span. And the lower the longevity-fertility trade-off, esp. for E.

Fast LHS settings in response to population density stress for P performance (competitive capacity; sympathetic ANS functionalty underpinning P-competitive capacity). High P-M trade-off constraints and PIE-related weakening of P-vitality; fre lowered energetic efficiency. Shift towards M > P to M4. Life expectancy up, mortality down, fertility down. PIE-linked CISD increases M investment requirements. Sympathetic ANS functionality at the cost of parasympathetic ANS functionality underpinning M processes. Population density stress resulting in sympathetic overdominance (P up) at cost of energy investment for parasympathetic ANS functionality (M: inter alia female reproductive success). P up, with M down trade-off costs. M demands increase with P up and PIE up at cost of P-vitality. PIE-based chronic disease load CISD compromizing P-vitality (thus at cost of male competetiveness and female fertility).

PM. Low PIE. P-M trade-off minimized based on efficiency of energy processing efficiency. M investment with minimum P costs and P investment with minimum M costs.

Bring in Chinese/mongoloids re Geist selected under conditions of continuous harshness

E Resilience combination of cold-adaptation/homozygosity and peak performance (specialization)

NW Plasticity cold-adaptation/homozygosity and plasticity scope of performance

S T-responsiveness for early life P > cold-adaptation; heterozygosity

7) European marriage patterns.

Hajnal (1982): The analyses pertain to populations of Europe in preindustrial times (seventeenth and eighteenth centuries). They were predominantly rural. All the populations treated in this paper had a 'young' age composition. They were all populations of high fertility compared with the levels found in Europe today. All of them had much higher mortality rates than those of modern Europe. (**AS: Historical predominance of high fertility-high mortality metabolic types, progressively changing to the predominance of lower fertility-lower mortality types over time**). The term Northwest Europe covers the Scandinavian countries, including Iceland, but excluding Finland, the British Isles, the Low Countries, the German-speaking area, and northern France. This area showed the European pattern of late marriage, back into the

seventeenth century. The data on household composition show a high proportion of "servants" and very small numbers of households comprising more than one married couple.
The servants recorded as household members, were not servants in he now customary meaning of the term. They participated in the productive tasks - mainly in farming or craft activities - of the households in which they lived. Servants lived as integrated members of the household; in particular thery often participated in meals. Servants were regarded as members of their master's household or family.
The characteristics of the institution of service in the rural populations of preindustrial Northwest Europe may be delineated as follows: (i) Servants were numerous, apparently constituting at least 6 percent, and usually over 10 percent of the total population. (ii) Almost all servants were unmarried and most of them were young (usually between 10 and 30 years of age). (iii) A substantial proportion of young people of both sexes were servants at some stage in their lives. (iv) Most servants were not primarily engaged in domestic tasks, but were part of the work force of their master's farm or craft enterprise. (v) Servants lived as members of their master's household. (vi) Most servants were members of their master's household by contract for a limited period. (vii) There was no assumption that a servant (usually the class of their parents), as a result of being in service, would necessarily be socially inferior to his or her master. The great majority of servants eventually married and ceased being servants.
Service was in general a stage for young people between leaving home and marriage, that is, a stage in the life cycle.

Two kinds of household formation system were compared:

1. Formation rules common to **Northwest European** simple household systems
a) Late marriage for both sexes (mean ages at first marriage over 26 for men and over 23 for women). About half of all women aged 15-50 years of age were married.
b) After marriage a couple are in charge of their household (the husband is head of household)
c) Before marriage young people often circulate between households as servants.

2. Formation rules common to joint household systems: **Eastern Europe**
a) Earlier marriage for men and rather early marriage for women (mean ages at first marriage are under about 26 for men and undedr 21 for women). Marriage was more universal (*ca* 70 % of women married).
b) A young married couple often start life together in a household of which an older couple is and remains in charge or in a household of which an unmarried older person (usually as a widower or widow) continues to be head. Usually the young wife joins her husband in the household of which he is a member.
c) Households with several married couples may split to form two or more households, each containing one or more couples.

Eastern Europe (Czap 1982, op. cit. Hajnal 1982):
Studied populations of Russian serfs in the first half of the 19th century. Households were large; the mean number of persons per household was over nine. They were fully integrated in spite of their size. Apart of heads and their wives and children, other relatives contributed to the large sizes of the joint households. In serf households there were very few, if any, persons unrelated to the head. The number of married men per

household was high (on average about two married men per household). The mean age at first marriage was under 20 years for both sexes.

Reher (1998): In Western Europe areas can be identified where families and family ties are relatively strong and others were they are relatively weak. Analyses were confined to areas west of John Hajnal's St. Petersburg – Triest line (setting apart Western and Eastern European family formation patterns: Hajnal 1982). The center and north of Europe (Scandinavia, the British Isles, the Low Countries, much of Germany and Austria; northern France) are characterized by relatively weak family links and the Mediterranean region (and southern France) by strong family ties.
In societies of Mediterranean Europe the departure of young people leaving the parental household coincide more or less closely with rheir marriage and finding a stable job. The years between adolescent maturity (ages 18-20 years) and marriage are spent largely within the parental household. In southern European countries, thus, a stable job, access to adequate housing, leaving the parental household, and marriage tend to be closely intertwined events. In contrast, from at least the latter part of the Middle Ages until the second half of the nineteenth century or the early years of this century, it was common in rural England for young adults to leave their parental households to work as agricultural servants in other households for prolonged periods. This was generally the case in respect of central and northern European populations. These data suggest that servants, despite local variations, were generally between two and four times more numerous in northern European societies than in Mediterranean regions. On the whole, probably between 50 and 80 percent of young people spent some of their young lives as servants before marriage in weak-family areas of Europe, as opposed to 15-30 percent in strong-family areas of the south. Service had important implications for nuptiality as it was, at least in part, the key to the fairly late marriage age characteristic of the European marriage patterns described by Hajnal (1965; Hajnal 1982). There is little evidence that these differences between regions of Europe have been reversed in recent years. In Spain, for example, the substantial increase since 1977 in age at which children leave their parental households has been strictly paralleled by the increase in age at marriage, with both indicators situated at extremely high levels. On the contrary, in England, Denmark, and the Netherlands, leaving home long before marriage has tended to be normative behaviour. Percent of men and women aged 25-29 still living with parents (1994. Fernández Cordón 1997, op. cit. Reher 1998): men (France, Germany, United Kingdom: 20.8-28.8) and (Greece, Italy, Spain: 62.6-66.0); for women (France, Germany, United Kingdom: 10.8-12.7) and (Greece, Italy, Spain: 32.1-47.6).
During the seventeenth and eighteenth centuries, life expectancy at birth in southern European countries was between 25 and 30 years, in contrast to northern European countries where it varied between about 33and 40 years.
The Industrial Revolution, based on an ethic in which the economic rationality and creativity of individuals was paramount, re-inforced an individual-orientated family system in the industrializing areas well before this same process began to take effect in most of southern Europe.

South-Western European marriage pattern.

Southern Europe: The distinguishing Northwest European features were not evidenced during the 17th and 18th centuries in parts of southern France and in Italy, where earlier ages of women at first marriage were experienced.

In the 15th century, a Tuscan women 21 years of age would be seen as past marriable age, the deadline for which was 19 years, and easily 97 percent of Florentine women were married by the age of 25 years while 21 years was the typical age of an English bride (De Moor & Van Zanden 2009). Early marriage for both sexes universal and high fertility was counteracted by high mortality (Kertzer & Barbagli 2001). High P-M trade-off (plasticity): high early life performance (lower life expectancy/ longevity) traded off against later life performance (high life expectancy/longevity); as LHS-mode shifts take effect from LHS-mode P>M to LHS-mode M↑:4 (early life fertility reduced/life expectancy increased: Table 2.3.3d).

North-Western European marriage pattern. Late and non-universal marriage restricted under conditions of resource limitations, i.e. in lower SES. The life phase of women from menarche (generally reached ate the age of 14 years or about 12 years in elite women: Hajnal 1965) to the birth of the first child was relatively long, averaging ten years (Seccombe 1992).Wealthier couples (*inter alia* noblewomen/gentlewomen) were likely to marry earlier. Moderate rates of fertility, mortality and marriage were tied to economic conditions. Under economically favourable conditions, early marriage and having more children were affordable, whereas under economically limiting conditions, delaying of marriage or non-marriage resulted in fewer children being born. Western European marriage pattern (EMP) was typically associated with conditions at carrying capacity (population stability) and underpinned by LHS PM setting, but conditions of resource surplus allowed for increasing population increase rates underpinned by LHS mode P > M (early age fertility realization; more prominent in higher SES, resulting in them realizing higher fertility rates than in lower SES befire c. 1900, but reversed thereafter: 2.2.2k). PM to slow M4 to M(P↓). Resource limitations at carrying capacity/population equilibrium associated with low fertility (late age of marriage/increased incidence of non-marriage) in low SES.

Eastern European marriage pattern. Early marriage for both sexes universal and high fertility was counteracted by high mortality (Kertzer & Barbagli 2001). High fertility even under resource shortages/competition for resources under sociospatial and economic density stress/anomy, but associated with higher mortality/reduced longevity/generally reduced LE (life expectancy). High inherent P-capacity LHS setting for resilience in terms of coping with sociospatial/population density

stress/socioeconomic stress/anomy (pre-adapted) under the LHS-mode P(M). Inherent resilience costs due to HMT (high metabolic turnover) setting associated with reduced life expectancy/increased mortality. High early fertility even under conditions of resource limitations at carrying capacity, but then associated with increased mortality rates.

c) Eastern-Northern/Western differentiated pathways towards the second demographic transition

Divergent fertility patterns during the FDT-SDT transition between Northern-Western and Eastern European country groupings were identified (Tables 2.3.3c, 2.3.3d, 2.3.3e and 2.3.3f).

Table 2.3.3f Correlation coefficients of fertility-linked factors within Northern-Western and Eastern European country groupings

Western-Northern Europe country group								
	TFR75	TFR02	FMR75	FMR02	DIV75	DIV02	EMB75	EMB02
TFR75		**0.69**					**0.64**	**0.73**
TFR02	**0.69**							**0.70**
FMR75					**-0.62**			
FMR02								
DIV75			**-0.62**				**0.74**	0.53
DIV02								
EMB75	**0.64**				**0.74**			**0.80**
EMB02	**0.73**	**0.70**			0.59		**0.76**	
POPD	-0.51	0.51					**-0.68**	**-0.72**
AgeM	0.50		-0.52		**0.76**		**0.88**	**0.84**
WellB								
URB								
Eastern European country group								
	TFR75	TFR02	FMR75	FMR02	DIV75	DIV02	EMB75	EMB02
TFR75					-0.61		**-0.83**	
TFR02								
FMR75								
FMR02							-0.58	**-0.69**
DIV75	-0.61							
DIV02								
EMB75	**-0.82**	0.53		-0.58	0.58			
EMB02				**-0.69**			**0.86**	
AgeM				**-0.73**		0.65		
WellB			**-0.79**					
URB					0.55	**0.73**	**-0.68**	

TFR75: Total fertility rate 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
TFR02: Total fertility rate 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
FMR75: Total first marriage ratio 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
FMR02: Total first marriage ratio 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)

DIV75: Total divorce ratio 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
DIV02: Total divorce ratio 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
EMB75: Proportion of extra-marital birth 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
EMB02: Proportion of extra-marital birth 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
URB: Urban population in percentage of total in 1960 (World Bank Data)
POPD: Population density per km^2 (Worldatlas)
PMOD: Percent post-modern (Van de Kaa 2001: World Values Surveys)
AgeM: Age at first marriage of women (Worldatlas)
WellB: Subjective well-being score (ex Inglehart 1997, op. cit. Van de Kaa 2001)

According to cross-country group analyses (Table 2.3.3f: within Western-Northern and Eastern European country groups and Table 2.3.3i: across these country groups), Western-Northern European countries in comparison with those of Eastern countries are characterised by relatively high TFRs 2002, Divorce 2002, urbanization, wellbeing scores, cancer incidence rates, childnessless, postmodernist scores, higher ages at first marriage (2014), lower percentages of births to women ≤ 20 years of age and lower priorities of having children in marriage (**features typically of the LHS-mode pM↑(4)** than in Eastern European group countries (Table 2.3.3i). Over countries ***within*** the Western-Northern group (1975/2002), fertility centered around high extramarital birth rates, being associated with countries of lower population densities and a reproductive mode characterised by late first marriage/late fertility realization (**LHS-modes pM > Pm → pM↑(4)**.

Eastern European countries had higher TFMR (higher total first marriage rates 1975), higher percentages of births of women with ages ≤ 20 years (2010) and perceptions that children are important in marriage (1990/2010); associated with lower levels of urbanization, lower Wellbeing scores, lower postmodernist scores, lower cancer incidence rates, lower ages at first marriage M (2014) and lower levels of childnessless (Table 2.3.3l).

Over countries ***within*** the Eastern country group **1975**:

Eastern countries with high TFR75, low DIV75 and low EMB75 (indicating family health/intactness); whereas those with high DIV75 and EMB75 rates are implicated to to exhibit low family health/intactness (Table 2.3.3f). TFRs are positively associated with family intactness.

Over countries ***within*** the Eastern country group **2002**:

Eastern countries with high TFR02 also already had relatively higher extramarital birth rates during 1975. Enhanced fertility thus was associated with high extramarital fertility, but low first marriage rates and later ages at first marriage (fertility

postponement), but lower levels of urbanization; resembling fertility patterns as in Western European countries. Eastern countries with relatively high rates of divorce (anomie effects) were associated with advanced ages of marriage and relatively high levels of urbanization (Table 2.3.3f). Fertility is no longer associated with family intactness, but with extramarital birth rates.

These data support the interpretation of a shift having taken place in LHS expression from LHS-mode mP↑(3) to LHS-mode pM↑(4) realization in eastern European countries.

Billingsley (2010): Two major theoretical perspectives dominate the discourse in fertility research of developed countries: those that emphasise ideational forces (SDT concept) and those that focus on economic forces. Under the SDT concept, Lesthaeghe and Surkyn 2004, op. cit. Billingsley 2010) contend that the desire for self-actualization was fueled by three revolutions: 1) a contraceptive revolution, permitting postponement of childbearing; 2) a sexual revolution, breaking the boundaries that kept sexual activity within marriage; and 3) a gender revolution, which allowed women independence from subservience to men and biology. Such ideational forces manifested in the expression of anti-authoritan sentiments, emphasis on higher order needs (self-actualization, individualistic and expressive orientations) and stronger postmaterialist political orientations (*vide* Inglehart 1990, op. cit. Billingsley 2010). The economic crisis concept involves, *inter alia*, a conflict between aspirations and resources, reducing the willingness for childbearing (Easterlin 1976, op. cit. Billingsley 2010); that is, childbearing is limited when current resource availability levels cannot sustain the aspirations of individuals which they had developed over time. Billingsley (2010) notes that the economic crisis concept may be particularly applicable to post-communist (Eastern European) countries. Causal mechanisms within the economic crisis concept relate *inter alia* to social capital and social anomie (Philipov et al. 2006). Fertility patterns under the SDT concept manifest in significant postponement of childbirth; unlike the economic crisis explanation where child stopping behaviour becomes prevalent when confronted with the challenge of securing material needs overrides family-size aspirations. The economic crisis is expected to explain the decline of fertility only until economic recovery sets in.

Fertility decline patterns were investigated for countries of the post-communist region from 1990-2003. In some countries a greater part of of the decline in fertility had occurred before postponement of childbearing had begun; implicating that stopping behaviour was involved in the fertility decline. Postponement of births contributed to fertility decline (*inter alia* via SDT processes) in a small number of countries. Two distinct processes were identified resulting in fertility declines: postponement of childbearing and economic crises effects. Furthermore, the likelihood of postponement of childbearing increased with improving economic conditions (1990 towards 2003). The average age at first marriage increased during the 1990s in all countries. Also an increase of births to non-married women was experienced.

The analyses revealed three Eastern European country-groups. Group 1: Czech Republic, Hungary, Poland, Slovakia and Slovenia; Group 2: Bulgaria, Estonia, Latvia, Lithuania and Romania; Group 3: Russia, Belarus, Moldova, Ukraine, Armenia, Georgia, and others.

Group 1: Czech Republic, Hungary, Poland, Slovakia and Slovenia
Improvement of economic conditions are linked to postponement of childbearing. Economic recovery and postponement of childbearing had begun by the mid-1990. TFR (1970/2000): Czech Republic 1.9/1.3; Hungary 2.0/1.3; Poland 2.2/1.3; Slovakia 2.4/1.3; Slovenia 2.1/1.3. (**AS: 1970: pre-FDT-SDT-transition phase**). Postponement of childbirth is implicated to be a prominent reason for period fertility decline towards 2000; whereas its effect appears rather more limited for group 2 and 3 countries. Mortality declining between 1989-2003. Postponement of childbearing, in the absence of sufficient recuperation, characterises most of the fertility decline. Countries exhibiting the most prominent increase in higher education enrolment rates (Group 1) were characterised by postponent rather than stopping behaviour. (**AS: Change over from LHS-mode mP↑:3 to pM↑:4 had taken place by 2000: 2.3.3c**). More stable economic development: postponement driving fertility decline.

Group 2: Bulgaria, Estonia, Latvia, Lithuania and Romania
TFR (1970/2000): Bulgaria 2.2/1.3; Estonia 2.2/1.4; Latvia 1.9/1.2; Lithuania 2.4/1.4; Romania 2.9/1.3. Mortality rising 1989-1994, then declining to 2003. Postponement increased to a lesser degree, after an initial decline. Postponement began around the end of the TFR decline (c. 1994). Postponement associated with fertility decline in the later half of the 1990s. Economic crisis effects during the early 1990s (**AS: anomie: LHS-mode mP↑(3): 2.3.3c**). Both postponement of childbearing and stopping behaviour (> postponement) appear to be involved regarding the fertility decline. (**AS: Change over from LHS-mode mP↑:3 to pM↑:4 had taken place during the later 1990s: post-ponement but inadequate fertility recuperation at later ages**).

Group 3: Russia, Belarus, Moldovia, Ukraine, Armenia, Georgia
Stopping behaviour (decline of higher order births) is linked to deteriorating economic conditions. TFR (1970/2000): Russia 2.0/1.2; Belarus 2.4/1.3; Moldovia 2.6/1.3; Ukraine 2.1/1.2; Armenia 3.2/1.1; Georgia 2.6/1.5. Mortality rising 1989-1994, then declining to 1998 and rising again to 2003. Postponement ratios decreased in the early 1990s, with a modest rise thereafter. Postponement began later in these countries than in Group 1 countries. Stopping behaviour characterises most of fertility decline. (**AS: Change over from LHS-mode mP↑:3 to pM↑:4 occurring even later than in Group 2 countries**).

A later onset of childbearing is known to decrease fertility quantum (Kohler et al. 2002; Billari & Kohler 2004). According to Philipov & Kohler (2001) fertility declines were due to tempo effects (progressively later ages at first births) in the Czech Republic, Hungary and Poland (Group 1); they were attributed to quantum effects (**AS: stopping behaviour: short reproductive age span associated with the LHS-mode mP↑:3**) in the early years of decline in Bulgaria and Russia (Groups 2 and 3). Between 1990 and 2003, postponement was linked to improvement in economic conditions, while worsening of economic conditions was related to stopping behaviour.

The results of Billingsley (2010) confirm research that had found a link between depressed economic conditions (**AS: as associated with anomie: 2.3.3c**) and declining fertility in countries where postponement of childbirth was not involved in the initial fertility decline; whereas under conditions of economic stability, postponement took effect.

Kalmijn (2007): Suicide and divorce rates (positively correlated) can be regarded as indicators of ***anomy*** (***a personal psychological state of isolation and anxiety under circumstances lacking social control and regulation; disorder, alienation, anarchy, low moral standards; reflecting a state of psychosocial stress***).
For the period 1990-2000, marriage rates, age at marriage and net divorce rates were recorded. Marriage rates: Western Europe (0.61), Northern Europe (0.55), South-eastern Europe, mainly Balkan countries (0.68) and Central-Eastern Europe (0.73).
Age at marriage: Western Europe (26.4), Northern Europe (27.9), South-eastern Europe, mainly Balkan countries (23.6) and Central-Eastern Europe (22.3).
Net divorce rates: Western Europe (9.5), Northern Europe (12.0), South-eastern Europe, mainly Balkan countries (3.8) and Central-Eastern Europe (12.8).
These cross-national analyses revealed that lower ages at first marriage (earlier in the East): and higher suicide rates of men were associated. Also, a strong positive association between suicide and divorce was established. Kalmijn (2007) interprets these patterns with reference to anomy (state of sociopsychological stress) which seemed to particularly prevail in eastern European countries. (**AS: The combination of early age at marriage and divorce in eastern European countries suggests the the prevalence of LHS-mode mP↑(3) as induced by anomie: 2.2.2e**).

Fialová & Kučera (1997): The demographic pattern in the Czech Republic from the 1950s to the end of the 1980s was characterized by a universally low age of marriage and a high proportion of men and women in marriage (prevailing two-child family model). Virtually all women married and they did so at relatively early ages (usually under the age of 23 years). Most women worked in order to sustain their standard of living, even when they were rearing small children at the same time. Within the context of increasing demands on the standard of living achievable, economists contend that marriage and the number of children in a family is often the result of a choice (partly subconscious) between possible gains and necessary costs (Becker 1981, op. cit. Fialová & Kučera 1997). Almost all women had children and the fertility rate was 1.96 children per woman throughout the 1980s. Relatively high rates of mortality prevailed. These characteristics of demographic behaviour were shared with other countries of Eastern Europe (Rychtaříková 1994, op. cit. Fialová & Kučera 1997). During the period from 1940 to 1990 childbearing was concentrated into a narrow age range, implying that mainly those aged 17-30 influenced the number of marriges and births. (**AS: LHS-mode Pm↑(3): 2.2.2e**).
Contrasting the above patterns, in Western European countries marriage rates had begun to fall and fewer people opted for matrimony. Children were generally raised within families with two parents; but extra-marital births increased and relation between partners, whether legal or informal, became less stable. Rates of divorce increased (Haskey 1993, op. cit. Fialová & Kučera 1997). After 1990 the demographic behaviour in the Czech Republic started to change towards resembling the patterns

prevalent in Western European countries. (**AS: transition from LHS-mode Pm↑(3) to LHS-mode p M↑(4)**. Divergence within population: some young people continued to enter into marriage at an early age, with half of the first children the product of pre-marital conceptions. The other, rapidly growing part of this generation has been postponing both marriage and childbearing. The marriage rate fell sharply. A large percentage of young people were postponing marriage and childbearing, resulting in a rise of the average age at marriage. A marked rise of children born outside of marriage was experienced during this period; and a higher proportion of people choosing to live together without marrying. Reduced mortality and birth rates was speeding up the ageing of the population. Marriage and family are no longer of foremost interest of young people.
Up to the beginning of the 1990s marriage was perceived to be a normal part of life and women considered a two-child family as desirable. Today reproductive patterns seem to be subject to conscious decisions. The new pattern of reproductive behaviour, as characterized by later marriage, postponing or rejecting marriage and the births of fewer children to older mothers, was being adopted by a growing number of the younger population; whereas some of their peers were still following the behavioural patterns of the preceding period characterized by early marriage, often due to pregnancy. (**AS: Underpinning LHS-mode shift – LHS-mode mP↑(3), 1940-1990 → LHS-mode pM↑(4), 1990 in Eastern European countries: the FDT-SDT transition period for eastern European countries**).

Philipov & Dorbritz (2003): The transition period (into the second demographic transformation) here discussed in respect of eastern European countries was divided into five phases: pre-transformation (coinciding with the final phase of the first demographic transition), collapse of the political system (market economy still dysfunctional; uncertainty in the future and impoverishment), structural caesura (demolishment of socialist economy), consolidation (stabilization of the political system, prevailing market economy through privatization, but rising unemployment and impoverishment) and sustained upswing (market economy prevails and becomes firmly established). Diverse countries passed through these five phases at a different pace: Economically more successful countries entered the transition at an earlier stage (Croatia, Czech Republic, Hungary, Poland, Slovak Republic, Slovenia, Estonia, Latvia, Lithuania), while those at a medium state of reform followed later along the transition (Albania, Armenia, Bulgaria, Georgia, Macedonia, Russia, Ukraine, Romania, Moldova). As the transition progressed, income increased to high levels in economically successful countries (however not reaching standards of Western European countries). In other countries, pre-transitional levels of real income were only reached towards the end of the 1990s. Even during the consolidation period middle class individuals (docters, teachers, scientists, specialist workers) experienced social decline and the economically lower classes were impoverished. Before the 1990s, total first marriage rates were high and the mean age at first marriage was very low in central-eastern and eastern European countries, especially in comparision with those experienced in western European countries. Total first marriage rates decreased and mean age at first marriage increased during the 1990s. During the 1990s cohabitation spread rapidly as a new behaviour. During the past two to three decades before the start of the transition the TFR was around replacement level in most of the central and eastern European countries (two child family model). The mean age at birth of the first child was low; typically lower than in western countries. ***Characteristic of childbearing in the East is a narrow age schedule as a result of both early start and***

early stopping of childbearing **(AS: as associated with the LHS-mode mP↑(3): 2.2.2e)**. The TFR declined to low levels and during the second half of the 1990s had dropped down to levels as low as 1.2 and was only rarely higher than 1.5. Before the onset of the transition, all populations in the region had a positive rate of population growth. Towards 2000 only 7 populations had sustained positive growth while 15 other populations experienced negative population growth. Behavioural modifications during the course of the transition typically included: 1) Remaining single and voluntary infertility becomes accepted by society, as observed in western European countries one to two decades earlier; 2) Entry into marriage and having a first child were postponed to later ages; 3) Extra-marital births increased, usually within a non-marital union.
The political and socioeconomic transformations which occurred during the transition brought much disorderliness associated with general uncertainty in the future, especially also in respect of economic uncertainty. A state of anomie was accordingly identified as overriding cause of demographic patterns during the transition.

LHS-mode mP↑ (3): Eastern European countries (2.2.2e). Response to exogenous stress/harshness (anomy) with fast life history strategy expression. Accentuation of fast-type > slow-type LHS expression trade-off due to some patho-information-engram load accumulation (less so than in the case of north-western European countries subject to the LHS-mode pM↑). Energy allocation demands for responding to exogenous impacts (anomie/harshness/unpredictability) in Eastern European countries underpins a high P/M realization ratio: stress resistance/tolerance coping mechanism (coping with stress and ***resilience to population density stress*** with high performance P-fast LHS expression). Early reproductive realization at the expense of later reproductive success (strong trade-off between current and future reproduction: 2.2.2c/d). Conditions of socioeconomic/psychological harshness cue for persistence and accentuation of the LHS-mode **LHS-mode mP↑ (3)** (fast-type LH strategy: early life performance and reproduction; manifesting in LHS-mode mP↑ expression). Inherent resilience in coping with anomie and ***population density stress effects*** in eastern European countries based on an inherent predisposition for fast-LHS mode realization (Table 2.3.3b). Inherent resilience capacity partially sustaining performance vitality notwithstanding the P vitality-reducing effects of procursive load accumulation (2.1.2) associated with and leading up to increasingly slow-type LHS-mode expression (LHS-mode pM↑:4). A delayed/incomplete shift from LHS-mode mP↑ (3) expression (sustained resilience) **to** LHS-mode pM↑:4 realization is likely to continue to constrain plastility scope realization underpinning wide childbearing age ranges for some time.

Eastern European populations have inherently higher resilience capacities (as associated with H-territory holding-maintenance phenotype predispositions: Table 2.3.3b); whereas western/northern European populations typically have greater plasticity scope underpinned by D-dispersal phenotype predispositions (Table 2.3.3b). High inherent plasticity scope and resilience capacity are combined under the LHS-mode PM (2.2.2e), but differential susceptibility applies as and when the efficiency of the endogenous energetic functionality declines due to patho-information-engram load accumulation (2.1.2). Then plasticity, when underpinning high P realization (relating to *inter alia* to competitive and reproductive performance) also involves higher vulnerability to negative experiences/adversity, manifesting in higher P *versus* health trade-off constraints (costs of plasticity). Thus, under conditions of increased fast-P *versus* slow-M trade-off constraints, differential susceptibility, as elucidated by Pluess & Belsky (2013), applies (2.2.1d). Furthermore, as higher plasticity costs are constrained through resilience, resilience costs are incurred, manifesting in, *inter alia*, an associated narrowed plasticity scope for fast versus slow LHS-mode expression (e.g. accentuated fast versus slow LHS-mode trade-off). This implies that the capacity for early fertility realization is at the expense of later life fertility realization (as associated with a narrowed scope for fast-slow LHS-mode expression: Table 2.3.3b). Resilience costs are then manifesting through *inter alia* a narrowed childbearing age range and associated lower fertility rates (2.3.3c).

Philipov (2003) considered explanatory approaches of demographic trends based on socioeconomic and ideational factors as insufficient for eastern European countries. Resulting from political and socioeconomic transformations, a state of disorderliness arose in society (corruption, rising crime levels, distrust towards governmental as well as newly privatised institutions, including banks; disruption of diverse social norms). Such a state of disorderliness and uncertainty in society is known as anomie (lack of rules and compromised possibilities of orientation); which Philipov (2003) and others considered of central importance in shaping fertility patterns during the FDT-SDT transition phase.

Inherent resilience capacity based on sensitivity to respond to psychosocial stress (Table 2.3.3b) with increased fast-LHS mode expression (LHS-mode mP↑:3), supporting P-vitality, but associated with lowered levels of subjective well-being.

Accentuated realization of this resilience capacity, when subject to conditions of increased P to M trade-off constraints, is progressively applicable during the FDT-SDT transition, but progressively counteracted by the prevalent fast to slow LHS-mode shift into the SDT (LHS-mode pM↑:4).

Eastern Europe: Low well-being scores/high anomie levels: combination of socioeconomic stress and high maternal stress. LHS-mode mP↑(3) in response to harshness /unpredictability (2.2.2c).

The FDT-SDT transition for eastern European countries: Late phase FDT → LHS-mode mP↑(3) in response to anomie → LHS-mode pM(4): delayed progression toward SDT fertility dispensation predominantly shaped by slow LHS-mode expression manifesting in LHS-mode pM(4) realization as in northern/western European countries. Inherent resilience capacity based on high P-fast-LHS expression (Table 2.3.3b) constrains later life fertility realization supported by slow-LHS-mode realization; thereby reducing the capacity for fertility recuperation, constricting childbearing age ranges and thus resulting in relatively depressed total fertility rates.

Relatively higher functional vitality of eastern European populations are taken to be the result of lower patho-information-engram loads (2.1.2 and 2.1.3). Inherent resilience capacity (2.3.3b), as based on high P-fast LHS expression, is furthermore anticipated to resist P-vitality depressing effects of patho-information-engram load accumulation. For Western/Northern European countries, Mennerich (1979) identified low functional vitality as reflected in, *inter alia*, in increased incidence rates of cancer. Germans (LHS-mode pM↑(4) seem to have only about two-thirds of the functional vitality than Russians, i.e. a third more time is required for treatment of Germans than Russians (particularly for Russians born before c. 1930; generally those with relatively lower accumulated patho-information engram loads).

Table 2.3.3g Mortality rates by main broad group of causes of death (European Region: 2006-2010): WHO-Europe (2012)						
	Age-standardized mortality rate per 100 000 thousand population, all ages					
	Neoplasms	Chronicity index [d]	Circulatory system	Digestive system [a]	External causes [b]	Infectious Parasitic [c]
North-West (Mortality ratings)[e]						

Iceland (1)	157.2	56.1	172.8	14.0	34.7	2.8
Norway (1)	159.8	17.4	151.8	16.1	39.1	9.2
Sweden (2)	145.4	18.4	182.2	16.7	35.4	7.9
Denmark (2)	212.6	22.1	193.5	38.5	39.0	9.6
UK (2)	175.9	25.1	169.2	31.7	27.5	7.0
Belgium (2)	175.0	13.2	182.7	27.6	49.0	13.3
Netherlands(2)	186.7	20.3	146.7	20.6	25.4	9.2
Average	173.2	20.6	171.3	23.6	35.7	8.4
Central (Mortality ratings)[e]						
Germany (3)	162.5	17.9	208.7	30.3	27.9	9.1
Switzerland(1)	149.1	27.1	161.4	20.5	37.7	5.5
Austria (3)	159.5	33.9	206.6	25.3	37.3	4.7
France (1)	174.5	17.6	126.1	24.7	44.4	9.9
Average	161.4	22.1	175.7	25.2	36.8	7.3
Southern (Mortality ratings)[e]						
Italy (2)	168.0	21.8	173.8	21.4	27.4	7.7
Spain (1)	157.7	16.1	143.1	26.6	24.4	9.8
Greece (3)	153.6	33.4	244.6	14.5	29.6	4.6
Portugal (2)	158.3	9.3	177.6	29.3	33.0	17.1
Average	159.4	16.3	184.8	22.9	28.6	9.8
Central-Northeast (Mortality ratings)[e]						
Poland (5)	207.6	38.4	356.3	37.0	57.6	5.4
Czechia (5)	198.2	58.3	344.1	34.2	48.1	3.4
Croatia (5)	210.8	39.8	370.8	39.7	52.7	5.3
Hungary (6)	246.4	74.7	421.2	65.6	59.0	3.3
Slovenia (3)	199.8	66.6	231.8	40.7	59.9	3.0
Slovakia (6)	198.9	40.6	446.6	49.8	51.0	4.9
Average	210.3	50.0	361.8	44.5	54.7	4.2
North-East (Mortality ratings)[e]						
Estonia (5)	187.9	24.9	408.3	35.6	76.3	7.6
Latvia (6)	194.8	16.9	479.5	37.4	86.7	11.5
Lithuania (7)	193.0	16.2	496.8	56.3	115.8	11.9
Average	191.9	18.6	461.5	43.1	92.9	10.3
Eastern (Mortality ratings)[e]						
Serbia (7)	205.9	51.5	506.6	32.4	42.8	4.0
Romania (6)	179.8	17.8	539.8	58.0	53.3	10.1
Bulgaria (6)	157.5	24.6	604.9	31.6	35.0	6.4
Average	181.1	26.6	550.4	40.7	43.7	6.8
Belarus (7)	162.9	14.5	587.2	43.1	133.6	11.2
Russia (7)	180.4	8.0	683.0	56.6	147.2	22.5
Ukraine (7)	158.2	5.2	732.7	51.4	88.4	30.4
Georgia (7)	92.2	17.4	476.0	21.8	27.3	5.3
Moldova (7)	164.1	8.7	715.2	118.5	97.3	18.8
Average	151.6	8.6	638.8	58.3	98.8	17.6

WHO-Europe 2012 (World Health Organization): [a] Chronic liver diseases/cirrhosis partly related to alcohol/processed food consumption, [b] Accidents, transport/traffic accidents, suicide/self-harm, assault/homicide [c] Including tuberculosis 40%. [d] Chronicity index = Neoplasms/Infectious. [e] GBD

(2019) Mortality ratings: Death per 100 000 population 1: <105, 2: 105 to <142, 3:142 to <189, 4: 189 to <249, 5: 249 to <313, 6: 313 to <397, 7: ≥397.

Supporting evidence that Northern and Western European countries have advanced further towards lower functional vitality (here taken to be the result of advanced patho-information-engram/procursive load accumulation) than Eastern European countries is presented below in the context of male reproductive health (Adami et al. 1994; Skakkebæk et al. 2001; Jørgensen et al. 2001; Jørgensen et al. 2002; Andersson et al. 2008).

Andersson et al. (2008): Adverse trends in male reproductive health have appeared over the past half a century. Particularly among Caucasians an increase in testicular germ cell cancer has been established. Several studies are suggesting that sperm concentrations below 40 mill/mL may be associated with longer time to pregnancy or even subfertility. Young men during the 1940s had sperm counts far above this value, with averages higher than 100 mill/mL. Recent studies of young men from general populations in Northern Europe show much poorer semen quality: in Denmark c. 40 % of men now have sperm counts below 40 mill/mL. Further decline of the implicated and associated poor male reproductive health is expected to result in even more infertile couples and lower fertility rates.

Adami et al. (1994): Age-standardized (World Standard Population) incidence rates of testicular cancer per 10^5 person-years of testicular cancer during 1980/1985-1989: Denmark (7.8/8.8); East Germany (5.9/7.6); Saarland, West Germany (4.8/6.0); Norway (5.4/7.0); Sweden (3.6/4.2); Finland (1.3/2.3); Estonia (1.9/1.5); Poland (1.7/2.2); Latvia (1.3/1.4); Lithuania (0.9/1.0). Age-standardized incidence doubles every 15-25 years and the incidence at age 25-29 every 12 to 20 years.

Skakkebæk et al. (2001): summarize existing evidence supporting a concept that poor semen quality, testis cancer, undescended testis and hypospadias are symptoms of an underlying entity, the testicular dysgenesis syndrome (TDS). The incidence of this syndrome has been rising during the last decades of the 20th century; being attributed to adverse environmental influences. Studies suggest that TDS is is a result of disruption of embryonial programming and gonadal development during fetal life. Growing evidence indicates a synchronized incidence of male reproductive problems (testicular cancer, genital abnormalities, reduced semen quality) and subfertility (Skakkebæk et al. 2006). Jørgensen et al. (2001) investigated reported trends of declining semen quality in some European countries. A study was carried out on the semen of fertile men from four European cities: Copenhagen (Denmark), Paris (France), Edinburgh (Scotland) and Turku (Finland). Lowest sperm concentrations and total counts were found for Danish men, followed by French and Scottish men, whilst Finnish men had the highest sperm counts. Men from Edinburgh had the highest proportion of motile spermatozoa, followed by men from Turku, Copenhagen and Paris. The analyses of Jørgensen et al. (2002) confirmed that young men from Denmark and Norway had a three-fold higher incidence of testicular cancer than those of Estonia and Finland. A largely congruent cross-country pattern was found for

median sperm concentration, total sperm counts and the frequency of normal sperm (Finland: 8.9 %; Estonia: 9.2; Norway: 6.9; Denmark: 6.4).

Develop PM to either $fP_R(M)$ E or $sM(P_P)$ W to fLHS P > M(1) ending up as sLHS $M(P_{R}\uparrow)$ E or sLHS $M(P_P\uparrow\downarrow)$ Hajnal 1982 Table 2.3.3b

d) Northern-Western-Southern-Eastern country groups: differentiated gradients in demographic responses

Table 2.3.3h Changing total fertility rates (TFR) in European countries (1975-2019)

	1975[a]	1997[b]	2000[c]	2004[c]	2008[a]	2011[c]	2019 [e]
Nordic Europe (Hg I1a)[d] and North-western Europe (Hg I1a)[d]							
Sweden	1.78	1.53	1.64	1.75	1.91	1.90	1.91
Norway	1.99	1.87	1.85	1.83	1.96	1.88	1.83
Iceland	2.61	2.04	2.08	2.04	2.14	2.02	1.92
Denmark	1.92	1.75	1.77	1.78	1.89	1.75	1.76
Netherlands	1.66	1.55	1.72	1.72	1.78	1.76	1.75
Belgium	1.74	1.59	1.67	1.72	1.82	1.81	1.80
UK	1.81	1.71	1.64	1.77	1.94	1.96	1.87
France	1.92	1.71	1.89	1.92	2.00	2.01	1.97
Average	1.93	1.72	1.78	1.82	1.93	1.89	1.85
Retainment of some fertility of maternal age classes 25-29 years (seemingly increasing after 1997-2011). R ≥ e combination (Table 2.3.3k). Scandinavian fertility levels are relatively high in the European context because relatively little loss at maternal ages 25-29 years and a strong recuperation effect at ages 30-39 years (Lesthaeghe & Moors 2000). From fast-LHS M-specialism: postponement (spring birth peak) to slow-LHS-M(P) mode generalism: (autumn birth peak). E and r realization. Increased TFRs from 2004 onwards indicate fertility reversal, both e and r involved.							
Central-Northern Europe (HgI1c)[d]							
Switzerland	1.60	1.48	1.50	1.42	1.48	1.52	1.55
Germany	1.45	1.39	1.38	1.36	1.38	1.36	1.47
Austria	1.82	1.36	1.36	1.42	1.41	1.42	1.51
Average	1.62	1.41	1.41	1.40	1.42	1.43	1.51
Postponement and some/little recuperation. From fast-LHS M-specialism: postponement (spring birth peak) to slow-LHS-mode M: some recuperation (autumn birth peak). TFRs remain low until 2011, showing some recuperation thereafter.							
Southwestern Europe (Hg Ib2)[d]							
Italy	2.21	1.22	1.26	1.33	1.34	1.40	1.49
Spain	2.79	1.15	1.23	1.32	1.46	1.36	1.39
Portugal	2.52	1.46	1.66	1.40	1.34	1.35	1.24
Average	2.51	1.28	1.38	1.35	1.38	1.37	1.37
Postponement and no recuperation. TFRs remain low between 1997-2019; having declined from 2.51 in 1975 (from e to persistent postponement).							

Eastern-Central Europe (Hg I 1b*)[d] /South-Eastern-Central Europe (Hg I 1b*)[d]							
Czech Rep	2.43	1.17	1.14	1.23	1.50	1.43	1.57
Slovakia	2.56	1.47	1.30	1.24	1.32	1.45	1.46
Slovenia	2.20	1.25	1.26	1.25	1.53	1.56	1.64
Hungary	2.35	1.38	1.32	1.28	1.35	1.23	1.40
Bulgaria	2.23	1.09	1.26	1.29	1.48	1.51	1.58
Romania	2.60	1.32	1.31	1.25	1.35	1.25	1.54
Average	2.39	1.28	1.26	1.26	1.42	1.40	1.53
Increasing postponement effects ≥ 1997; alleviated with some recuperation or earlier maternal age group fertility towards 2019. E-P(M): H; fast-LHS-mode Pm↑:3 TFRs remain low between 1997-2004; having declined from 2.39/2.14 in 1975 (from e to postponement). Then increasing from 2008-2019 (due to either e or r effects). Slow-LHS-mode M↑:4. TFRs remain low between 1997-2004; having declined from 2.39/2.14 (from e to postponement). Then increasing from 2008-2019 (due to either e or r effects; but not combined in the same mother).							
Baltic northern Europe and Eastern Europe (Hg I 1b*)[d]							
Latvia	1.96	1.11		1.24	1.45	1.36	1.57
Lithuania	2.19	1.39	1.39	1.26	1.47	1.76	1.66
Estonia	2.08	1.24	1.38	1.47	1.66	1.52	1.66
Russia	1.98	1.28			1.49		1.75
Poland	2.27	1.51	1.37	1.23	1.39	1.30	1.29
Belarus	2.17	1.39			1.42		1.71
Ukraine	2.02	1.40			1.39		1.56
Moldova	2.48	1.60			1.50		1.23
Average	2.14	1.36	1.38	1.30	1.47	1.48	1.55
Increasing postponement effects ≥ 1997; alleviated with some recuperation or sustained maternal earlier age group fertility. Extramarital births are positively associated with fertility of the age cohort 15-19 in Eastern European countries (relative to C and S: Table 2.3.3j); whereas nonmarital fertility is associated with reproduction at older ages occurring mainly in cohabiting couples in western and northern European countries (Lesthaeghe & Moors 2000). Pm3 to M4, E-P(M): H; fast-LHS-mode Pm↑:3. TFRs remain low between 1997-2004; having declined from 2.39/2.14 (from e to postponement). Then increasing from 2008-2019 (due to either e or r effects: Table 2.3.3k).							
TFR cross-country relationships: TFRs Year 1975 are negatively correlated with those of years 1997 (r = -0.48, P < 0.10), 2000 (r = -0.42, P = 0.15), 2004 (r = -0.55, P = 0.054), 2008 (r = -0.46, P 0.11) and 2011 (r = -0.55, P = 0.054).							
High TFR countries for the years 1997, 2000, 2004, 2008 and 2011, but not for the year 1975, exhibited higher rates of extramarital births as for 1997 (r = between 0.61 and 0.81, P generally < 0.05) and higher degrees of chosen childnessless (r = between 0.59 and 0.79, P generally < 0.05).							
[a] Myrskylä et al. (2011); [b] Lesthaeghe & Moors (2000); [c] EUROSTAT (2013); [d] Predominance of subhaplogroups (Rootsi et al. 2004) [e] World Population Review							

Subhaplogroup LHS settings	N M(P): LH	C PM: HL	S PM: H↑L	E P(M): H

E reduced P-health trade-off, resilience; some sustained vantage sensitivity? P up fertility trade-off with fertility, but not with health (resilience benefits) Sustained P-vitality (coping with psychosocial stress: resilience benefits), but restricted

childbearing age range: fertility down (resilience costs). Early fertility but at cost of later life fertility.

Resilience benefits (linked to reduced plasticity costs: less trade-off costs regarding health-early fertility; high early life fertility, but without fast-ageng effects such as in low SES and S populations) and costs (linked to reduced plasticity scope: narrow childbearing age span).

NCS Plasticity PIE up non-PM; differential susceptibility trsde-offs. Pm up accentuated P health/fertility trade-off; as P down and M up (LHS M > P; M4) accentuated plasticity costs for M up in the form of P down; but relaxation under LHS M(P)5

W (NCS) vs E Plasticity scope benefits and costs vs resilience benefits and costs

W (NCS) High P performance requirements at trade-off costs - differential susceptibility. High Pm-type performance realization/expression with plasticity costs re surplus resource use and competitive capacity in the context of high density population psychosocial environments. Pm-type plasticity costs (of vantage sensitivity): health/fertility down. Low SES: less plasticity scope re vantage sensitivity, but also less plasticity P-M trade-off costs. Thus less health/early fertility trade-off costs (less health down-fast ageing consequences). High SES: plasticity scope up, but less/reduced, allowing for both Pm and late life fertility combination; with plasticity costs (health-linked fertility down).

C Plasticity Intensified Pm up/health and fertility trade-off; but differential susceptibility, implying both vantage sensitivity and vulnerability to disease impacts.

N Plasticity. M-based fertility. Reduced trade-off constraints (cold adaptation/homozygosity). Reduced early vs later life fertility trade-off (plasticity scope benefits), but at the cost of P down (plasticity costs)

S Increased climate-linked (warm-cold gradient) proclivity to fast-LHS P-HMT mode realization (Table 2.3.3b). Benefits of high early life fertility and P capacity. Costs: increased early *versus* later life fertility trade-off constraints (fast ageing). With increasing postponement (M >P, M4) little plasticity scope for recuperation (narrow childbearing age span).

Table 2.3.3i Analyses of fertility and fertility-linked factors across Nordic/Northern-Western (N), Central-Northern (C), South-Western (S) and Eastern (E) European country groupings

Fertility-associated and differentiating factors	Nordic/ Northwest Europe: N	Central-Northern Europe: C	South-Western Europe: S	Eastern Europe: E
Notation of statistical significance. **76.7** ^{CNS} : the value 76.7 is higher than corresponding values of country groups C, N and S at P < 0.10, < 0-05 or lower; values in italics/bold are significantly lower				
TFR (total fertility rate) patterns over time (1975-2002)				
TFR 1975	2.06	***1.64***	**2.59** ^{C}	**2.21** ^{C}
TFR 2002	**1.76** ^{CSE}	1.37	1.33	1.25
TFRs: Employment (women)				
TFRs Employed	1.79 ^{C}	***1.14***	1.61 ^{C}	1.81 ^{C}
TFRs Non-employed	2.08 ^{SE}	2.00 ^{SE}	***1.13***	***1.15***
TFRs Education levels of women				
TFRs ISCED 0-2	1.67	1.59	1.54	1.98
TFRs ISCED 3-4	1.69	1.40	1.47	1.25
TFRs ISCED 5-6	2.05 ^{CSE}	***1.24***	***1.24***	1.56 ^{S}
Patterns of fertility (family and childbearing)				
TFMR 1975 (total first marriage rate)	***0.80***	***0.74***	**1.13** ^{NCE}	**0.99** ^{CN}
TFMR 2002 (total first marriage rate)	0.52	0.56	0.62	0.52
Divorce 1975	0.27 ^{S}	0.22 ^{S}	***0.03***	0.30 ^{S}
Divorce 2002	0.45 ^{S}	0.42 ^{S}	***0.22***	0.35 ^{S}
EMB 1975 (% extramarital births)	13.4	8.6	3.9	8.1
EMB-1997 (% extramarital births)	**35.7** ^{CSE}	10.0	13.7	23.8
EMB 2002 (% extramarital births)	**39.8** ^{S}	23.5	17.6	32.6
EMB 2009 (% extramarital births)	**47.8** ^{CS}	29.2	30.2	35.9
WomenchildPM: women need child	29.0	21.7	41.7	**82.6** ^{NCS}
Age at marriage (2014)	31.6 ^{E}	30.4 ^{E}	31.5 ^{E}	***27.6***
AFCH-97 (Maternal age at first child)	27.3 ^{E}	27.8 ^{E}	27.2 ^{E}	***23.5***
CHL60 Cohort childnessless-females	17.9	16.9	12.9	9.6
AvCLESS (Average childnessless)	**3.8** ^{E}	3.2	3.2	2.2
C-NB-M90 (Children important)	57.3	54.9	66.8	**76.7** ^{CNS}
C-NB-M2010 (Children important)	48.8	50.7	57.1	**67.3** ^{CNS}
PCoAge 26 (% fertility < 26 years)	41.3	43.3	49.1	**73.5** ^{CNS}
Pbirth20-1990: women ≤ 20 y	3.5	3.5	5.5	**12.8** ^{CNS}
Pbirth20-2010: women ≤ 20 y	2.4	2.0	2.6	**5.6** ^{CNS}
Psychosocial context (well-being-anomy; postmodern/liberalistic-conservative)				
WellB (Subjective well-being)	**80.1** ^{ES}	71.7 ^{E}	60.7 ^{E}	***19.1***
PMOD Postmodernism	26.7 ^{ES}	31.4 ^{ES}	***14.3***	***10.2***

TFR75: Total fertility rate 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
TFR02: Total fertility rate 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
TFRs: Employment: EUROSTAT (2013)
TFRs Education levels of women: EUROSTAT (2013)
TFMR75: Total first marriage ratio 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
TFMR02: Total first marriage ratio 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
DIV75: Total divorce ratio 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)
DIV02: Total divorce ratio 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
EMB75: Proportion of extra-marital birth 1975 (Council of Europe 2003, op. cit. Kohler et al. 2006)

EMB-97: Proportion of extra-marital birth (Lesthaeghe & Moors 2000)
EMB02: Proportion of extra-marital birth 2002 (Council of Europe 2003, op. cit. Kohler et al. 2006)
EMB 2009: Proportion of extra-marital birth 2009 (EUROSTAT 2009)
WomenchildPM: Agree that women need a child, Postmodern (Van de Kaa 2001: World Values Surveys, 1990s)
AgeMar14: Age at first marriage of women 2014 (Worldatlas)
AFCH-97: Maternal age at first child (Lesthaeghe & Moors 2000)
CHL60: Cohort childnessless-females 1960-1969. Data source op. cit. Miettinen et al. (2014)
AvCLESS: Average childnessless-females of 1940-1944 and 1960-1969 cohorts. Data source op. cit. Miettinen et al. (2014)
C-NB-M90: Children important for marriage 1990 Data source op. cit. Miettinen et al. (2014)
C-NB-M10: Children important for marriage 2010 Data source op. cit. Miettinen et al. (2014)
PCoAge 26 Contribution of mothers (%) < 26 to completed fertility (ex Zakharov 2008)
Pbirth20-1990: Percentage of births to women aged ≤ 20 years (2010)
Pbirth20-2010: Percentage of births to women aged ≤ 20 years (2010)
WellB: Subjective well-being score (ex Inglehart 1997, op. cit. Van de Kaa 2001)
PMOD: Percent post-modern (Van de Kaa 2001: World Values Surveys)

	Nordic/ Northwest Europe	Central-Northern Europe	South-Western Europe	Eastern Europe
Countries	Norway Sweden Finland Iceland Denmark Netherlands Belgium UK Northeastern France	Germany Austria Switzerland	Italy Spain Portugal	Latvia Lithuania Belarus Czech Republic Slovakia Slovenia Hungary Bulgaria Romania Russia Poland Ukraine
Subhaplogroups I	Hg I1a	Hg I1c (Hg I1a)	Hg I1b2	Hg I1b*

Subhaplogroups I: Rootsi et al. (2004): Table 2.3.3b

Ex Table 2.3.3i:

N TFR 1975-2002 down; TFR 2002, although higher than CSE, lower than in 1975 (postponement). Relatively low TFMR, declining to 2002. Divorce increasing to 2002/higher than C; EMB high and higher than in CSE notably increase and increasing 1997-2009.Age at marriage > E. Age at marriage and mean age at first child (as also CS) higher than E. Low Pbirth < 20y, declining 1990-2010 (postponement). Relatively high well-being score and postmodernism (as C).

C Low 975 TFR, but declining to 2002. Low TFMR in 1975, but declining to 2002. Divorce increasing towards 2002. Declining intactness of family and associated fertility. Relatively low, but increasing EMB towards 2009. Low rating women need child. Proportion of children below 20y low and declining1990-2010 (postponement as N and S).

S TFR 1975 and TFMR 1975 relatively high, but sharply declining towards 2002. Divorce vrery low in 1975, somewhat incressing to 2002 but still rel. low. EMB1975 very low but somewhat increasing to 2009. Women need child higher than N and C.

Age at marriage and mean age at first child relativly high; as N and C (postponement); but low levels of childlessness. Low and declining Pbirth below 20y (postponement). Low postmodernism score.

Ex Table 2.3.3i

E vs NCS (mainly NC: Western Eutrope)

Relatively high TFR 1975, decining to 1.25 in 2002

Relatively high TFMR 1975 0.99 ^{NC} to 0.52 in 2002; women need child high re NCS; Children NB in marriage high re NCS. Low age at marriage/maternal age at first child re NCS. High early fertility realization, below 20/26 y re NCS

EMB 1975 low, increasing towards 1997-2009. Low postmodernism scores re NC (WE). Low subjective well-being re NCS.

Employment

Education

These data suggest that in Western-Northern European countries a shift in underpinning LHS-modes between 1975 from LHS-mode pM > Pm(2) to LHS-mode pM↑:4 in 2002 had occurred; with a corresponding shift from LHS-mode Pm↑:3 in 1975 to LHS-mode pM↑:4 in 2002 in Eastern European countries.

Between 1975 and 2002, TFRs had declined only moderately in WN countries, whereas as those in E countries, having been somewhat higher than in WN countries in 1975, had declined substantially. In 1975, E countries had higher total first marriage rates than WN countries; but these had declined to somewhat lower levels than for WN countries by 2002 (Table 2.3.3i). Both divorce and extramarital birth rates had increased substantially between 1975 and 2002 in WN countries (psychosocial incoherence), while extramarital birth rates had also increased substantially in E countries during this period (Table 2.3.3i).

Two divergent pathways of the FDT-SDT transition towards low fertility are evident; then convergence towards the late phase of the SDT (LHS-mode pM↑(4).

Western-Northern European countries: Lower TFRs than of Eastern European countries during the end phase of the FDT (LHS-mode pM > Pm(2), fertility postponement, but then partially recovering due to fertility recuperation at ages > 30 years, but still basically remaining below self-replacement levels (LHS-mode pM↑(4);

advanced outcome of transgenerational procursive impacts associated with uninterrupted resource abundance and population density stress having resulted in substantial patho-information-engram loads (2.1.2).

Eastern European countries: Somewhat higher TFRs than of Western-Northern European countries during the end phase of the FDT towards the SDT. FDT-SDT transition: anomy-induced LHS-mode Pm↑(3); stress response adaptation mode; associated with a short reproductive age span and TFRs declining to below those of Western-Northern European countries. Incomplete transition towards fertility postponement (LHS-mode pM↑(4: Table 2.3.3i), with insufficient fertility recuperation at ages > 30 years (2.3.3e).

Lesthaeghe & Moors (2000): Current period total fertility rates are diverging due to differential recuperation in various western European countries. To bring back PTFRs to replacement levels would require substantially larger increases in in fertility past age 30 (recuperation) in the majority of countries; than is being witnessed to date. The FDT was characterized by increased fertility control manifesting in reductions of fertility mainly at higher ages, leading to declines in the mean age at childbearing, and being associated with declining ages at first marriage. The SDT is characterized by overall postponement of parenthood (fertility declines below age 30) and the adoption of new living arrangements. Of the 12 Eastern European countries, nine have early reproduction patterns with a mean age of first child below 24; all 12 have mean ages at first childbearing lower than 26 years. Nevertheless, this early start of reproduction has not prevented steep declines in PTFRs during the 1990s. (**AS: Trade-off between tempo and quantum effect: 2.2.2d**). Many Eastern European countries experienced declines in periodic TFRs after 1980 (1980-1997/1997), but with little increases in mean age of childbearing. Reduced quantum effects thus accounted for the overall decline in these populations (reduced higher birth order fertility). Younger cohorts in many Eastern European countries have started to shift towards postponement, characteristic of the SDT, but have not reached the stage with recuperation at older ages. For Southern European countries, PTFR declines were attributable to both tempo (fertility postponement) and quantum effects (low levels of childbearing at ages > 30 years). For most Western European countries PTFR declines since 1980 are accountable to tempo shifts (postponement). Despite increases in age at first birth, net rises in PTFRs are due to substantial increases in fertility after age 30 years (recuperation). The PTFR fell below 1.5 in West Germany (mid-1970s), Italy (1985) and Spain (1988), continuing to decline to even lower levels until the mid-1990s. In both Spain and Italy, an uninterrupted decline of fertility at ages 20-24 and 25-29 was exhibited by all cohorts since the one having reached adulthood in 1975; but no substantial recuperation after age 30 was experienced. Regarding Western Germany the PTFR of 1.28 in 1985 rose to 1.4 due to some recuperation; but substantially more recuperation would be required to maintain a PTFR that is still below 1.5. In the Netherlands substantial recuperation of fertility between the ages 30-40 years neutralized the postponement effect. The PTFR (1970) had changed from 2.47 in France and 2.45 in the United Kingdom to 1.71 in both countries by 1997.

Uninterrupted postponement starting with the cohorts reaching adulthood in the mid-1960s and an increasing recuperation effect after age 30 by the same and later cohorts is considered to be responsible for the relatively high PTFRs of these countries in the EU. Increases in PTFRs in Sweden to 2.14 in 1990 and to 1.81 in 1995 in Denmark lost momentum thereafter. These increases were attributable to substantial recuperation. The same applied to Finland and Norway (in these three countries fertility rates at ages 30-39 had nearly doubled by 1997). ***Scandinavian fertility levels are relatively high in the European context because relatively little loss at 25-29 ages and a strong recuperation effect at ages 30-39 years***. The western European countries have progressed much further than Eastern European countries, but regarding the former, two distinct groups in respect of recuperation are evident: those with strong recuperation, the Sandinavian countries, the United Kingdom and France; and those with insufficient recuperation: Mediterranian countries (such as Italy and Spain) and notably Germany and Switzerland. Extramarital births are positively associated with fertility of the age cohort 15-19 in Eastern European countries; whereas nonmarrital fertility is associated with reproduction at older ages occurring mainly in cohabiting couples in western and northern European countries. Extramarital births as a percentage of all births were exceeding 35 % in countries such as Iceland, Sweden, Estonia, Norway, Denmark, Finland, France and United Kingdom.

Factors systematically associated with independent living and cohabitation *versus* marriage: 1) Expansion of the welfare state (earlier independence and premarital cohabitation are effectively state subsidized); 2) Prolonged education and better access to advanced education (*inter alia* leading to greater economic autonomy for women and thus less reliance on marriage and opting for cohabitation/non-marital households is predicted on the basis of values concerning egalitarian gender roles); 3) Emergence of a more libertarian culture with tolerance for alternative lifestyles (followed by an overall weakening of authority and progression to post-materialist value orientations); 4) Intergenerational transition of family instability (associated with single living, cohabitation, single motherhood and divorce).

Determinants of postponements. 1) Advanced education (postponement of household formation); 2) Growing labour market flexibility (weakening of the economic basis of marriage); 3) Cycles characterized by weakened economic opportunities for new cohorts (increased youth unemployment leading to prolonged economic dependence on the parental household); 4) Unfavourable housing condition (relating to structural shortages, higher rents or purchase prices); 5) Rising consumerism (higher material/comfort aspirations to be met before establishing a new household); 6) Greater distrust in the institution of marriage (partially fostered by ideational change); 7) Social diffusion of alternative living arrangements (to all population strata). These factors are expected to produce powerful combination effects.

Countries with women cohabiting at ages 20-24, proportions above 25 %: Denmark, Sweden, Norway, Finland, Estonia. Together with Iceland, these countries also exhibit high prevalence of cohabitation combined with parenthood. Most nonmarital fertility takes place in cohabiting couples and these tend to be either more stable or are succeeded by partner changes and transitions to a next consensual union. Distribution of women aged 20-24 (1990s: Northern Europe, Western Europe, Southern Europe, Eastern Europe): cohabiting without children N 27/W 17/S 3/E 4; cohabiting with children N 12/W 3/S 0/E 4; married without children N 7/W 10/S 6/E 9; and married with children (regional means): N 12/W 9/S 13/E 32.

In populations of the Northern European countries procreation has been detached from the precondition of marriage and the effect of fertility postponement was therefore less

marked than in many Western European countries. **Scandinavian fertility levels are relatively high in the European context because relatively little loss at 25-29 ages and a strong recuperation effect at ages 30-39 years.**

Nordic, Northwestern, Central-Northern and Southwestern European countries had relatively high mean ages at first child, contrasting the situation in Northeastern-Central/Eastern Europe with characteristically lower values (Table 2.3.3j).

Table 2.3.3j Periodic total fertility, mean age at first child and percentages extramarital births for European countries 1995-1997 (Data ex Lesthaeghe & Moors 2000)

	Periodic total fertility rates	Mean age at first child	Percentage Extramarital births
Nordic Europe (Hg I1a)[a]			
Sweden (1.53/27.4/54) Norway (1.87/27.0/49) Finland (1.74/27.7/37) Iceland (2.04/25.0/49) Denmark (1.75/27.7/46)	1.79	27.0	47.0
Northwestern Europe (Hg I1a)[a]			
Netherlands (1.55/29.0/19) Belgium (1.59/27.5/18) UK (1.71/26.7/37) Ireland (1.92/27.0/27) France (1.71/28.3/39)	1.70	27.7	28.0
Central-Northern Europe (Hg I1c)[a]			
Switzerland (1.48/28.3/8) Germany (1.39/28.4/14) Austria (1.36/26.7/8)	1.41	27.8	10.0
Southwestern Europe (Hg I1b2)[a]			
Italy (1.22/27.9/8) Spain (1.15/27.8/13) Portugal (1.46/25.8/20)	1.28	27.2	13.7
Eastern-Central Europe (Hg I1b*)[a]			
Czech Republic (1.17/24.1/18), Hungary (1.38/23.4/25), Slovakia (1.47//14), Slovenia (1.25/25.6/32)	1.32	24.4	22.2
Eastern Europe (Hg I1b*)[a]			
Bulgaria (1.09/22.6/30) Latvia (1.11/23.5/35), Lithuania (1.39/23.1/17), Romania (1.32/23.1/22), Poland (1.51/23.1/11) Russia (1.28/22.8/25), Belarus (1.39//15) Ukraine (1.40//14) Moldova (1.60/22.4/17)	1.34	22.9	20.7
Estonia (1.24/23.4/52) represents an outlier to the above pattern as it combines low mean age at first child (eastern characteristic) with high percentage of extramarital births (Nordic characteristic)			

For the period 1995-1997, across all countries, Periodic Total Fertility Rates were positively correlated with percentage extramarital births (r = 0.52, P = 0.005). Within northern, western and southern European countries this correlation was positive (r = 0.74, P = 0.001), but negative within the north-eastern central/eastern European country grouping (r = -0.75, P = 0.003).
[a] Predominance of subhaplogroups (Rootsi et al. 2004)

Three country groupings can be distinguished as manifesting during the SDT (Table 2.3.3j):

1) Nordic and northwestern European countries (Northern Europe): relatively high fertility (1995-1997), associated with relatively high percentages of extramarital births; high mean ages at first birth (postponement); i.e. in alignment with LHS-mode pM↑(4) realization: slow LHS expression; pM-type predominance). However, Scandinavian fertility levels were relatively high in the European context because relatively little loss at 25-29 ages and a strong recuperation effect at ages 30-39 years (Lesthaeghe & Moors 2000), i.e. due to a relatively wider childbearing age range (re Table 2.3.3j; Table 2.3.3b).

2) Central-northern and southwestern European countries (Western Europe): relatively lower fertility rates (1995-1997), low incidence of extramarital births; high mean ages at first birth (postponement). Fertility determined by family-based childbearing associated with postponement, but little recuperation of births at later ages (Table 2.3.3b).

3) North-eastern central and eastern European countries (Eastern Europe): relatively low fertility rates (1995-1997), intermediate incidence of extramarital births; lower mean ages at first child. Early fertility realization was positively linked to family-based childbearing (then still remnant effects of LHS-mode mP↑:3; fast LHS expression; combined with relatively higher functional vitality: 2.3.3c; and associated high performance mode expression).

For the period 1995-1997, periodic total fertility rates (PTFR) and percentage extramarital births were positively correlated within the northern, western and southern European country group (r = 0.74, P = 0.001), but negatively within the north-eastern central/eastern European country grouping (r = -0.75, P = 0.003). In respect of the Nordic/northwestern/central-northern and southwestern country assemblage, countries with higher PTFRs and percentage extramarital births are also those exhibiting wider childbearing age ranges (as discussed with reference to Table 2.3.3j). Attenuation of the fast-slow LHS trade-off in populations subject to inherently higher degrees of cold-

adaptation, i.e. in more northern European countries, supports a wider childbearing age span and thereby relatively higher fertility (Table 2.3.3b).

1-2) Nordic Europe (Hg I1a)/Northwestern Europe (Hg I1a: inherently D-phenotypes: Table 2.3.3b). Advanced LHS-mode pM↑(4): slow LHS-mode expression; low P-vitality: psychosocial incoherence; increased rates of exramarital births. Accentuated P to M trade-off constraints resulting in extremized P-type and M-type expression (2.2.2e). Extremized P-types are in high performance LHS-mode (high metabolic turnover) at the expense of health (2.2.1a/d; 2.2.2j). Extremized M-types exhibit low P-vitality and slow-LHS-mode realization (late fertility realization). However, attenuation of the fast-slow LHS trade-off in populations subject to inherently higher degrees of cold-adaptation, i.e. in more northern European countries, supports a relatively wider childbearing age span and thereby relatively higher fertility (Table 2.3.3b).
2) Central-Northern Europe (Hg I1a/Hg I1c: inherently D-phenotypes: Table 2.3.3b) and Southwestern Europe (Hg I1b2: inherently D-phenotypes)
Fertility postponement, but relatively low levels of extramarital births. Relatively sustained fast-P-LHS-mode expression/vitality than in more northern European countries (as anticipated according to north-south gradients of inherent LHS-mode predispositions: Table 2.3.3b). With increasing P to M LHS-mode trade-off constraints and shift towards slower LHS mode expression under the LHS-mode pM↑(4), fertility postponement is supported, but inherent predisposition towards faster LHS expression constricts childbearing age ranges; more so towards more southern European countries (Table 2.3.3b).

Dispersal phenotypes (D-phenotypes) are characterised by generalist plasticity, whereas maintenance/holding phenotypes (H-phenotypes) are typified by specialization and resilience (Table 2.3.3b). This underlies divergent life history strategy and associated demographic responses in respect of western/northern/southern in comparison with eastern Eastern European countries (Table 2.3.3b). Plasticity of P ↔ M LHS-mode expression of inherent D-phenotypes and inherent resilience capacity in inherent H-phenoptypes (restricted plasticity: prevalence of a fast LHS-mode realization when subject to increased P to M trade-off constaints: 2.2.1d).

3) North-eastern central and eastern European countries (Eastern Europe: Hg I1b*: inherently H-phenotypes: Table 2.3.3b). The H-phenotypes have inherently higher resilience capacity, and when subject to high P to M LHS trade-off constraints, as during the FDT-SDT transition phase, this translates into constricted childbearing age ranges associated with the LHS-mode mP↑(3). Subject to this LHS-mode (anomy-induced LHS-mode mP↑(3); stress response adaptation mode), resilience costs are incurred, manifesting in, *inter alia*, an associated narrowed plasticity scope for fast versus slow LHS-mode expression (e.g. accentuated fast versus slow LHS-mode trade-off). This implies that the capacity for early fertility realization is at the expense of later life fertility realization (as associated with a narrowed scope for fast-slow LHS-mode expression: Table 2.3.3b). Resilience costs (reduced plasticity) are then manifesting through *inter alia* a narrowed childbearing age range (2.3.3c).

The evolution of fertility trends in industrialized countries during the SDT is basically related to fertility postponement. However, fertility levels varied greatly with some countries keeping PTFRs (periodic total fertility rates) above 1.70 or close to replacement level, while others maintained values below 1.50. The main cause explaining these differentiated fertility patterns is the degree of fertility recuperation at older ages (above age 30 years) among cohorts which had initiated or continued the tempo drift, i.e. shift towards postponement (Table 2.3.3k).

Table 2.3.3k Fertility (TFR), age of women at first birth (fertility postponement) and proportion of fertility attributable to second and higher order births (index of fertility recuperation) (EUROSTAT 2013/2015)

	Total fertility rate (live births per woman)	Mean age of women at birth of first child (a)	Proportion of fertility TFR2+	Proportion of fertility TFR3+ (b)	Maternal childbearing age span index (MCASI) [30 - (a-b)]
Cold temperate climate zone (N)	Wide MCAS based on r ≥ e combination in congruence with the inherent LHS-setting N-M(P): LH (cold-adaptation) supporting plasticity, but subject to reduced P-M trade-off constraints.				
Sweden	1.85	29.2 H	56.1	20.0 H	20.8 W(r)
Norway	1.72	28.9 I	57.0	19.5 H	20.6 W(r)
Finland	1.65	28.8 I	59.1	24.3 H	25.5 W(r)
Iceland	1.80	27.5 L	62.5	25.1 H	27.6 W(e-r)

Cool temperate climate zone (N)	As above, wide MCAS based on r ≥ e combination, underpinned by inherent LHS setting N-M(P): LH (cold adaptation): e/P-r/M trade-off alleviated.				
Denmark	1.71	29.2 H		16.7 I	17.5 I(p)
Netherlands	1.66	29.7 H	53.5	17.7 H	18.0 I(p)
Belgium	1.70	28.7 I		21.8 H	23.1 W(r)
United Kingdom	1.80	28.7 I	58.2	24.4 H	25.7 W(r)
Cool temperate climate zone (C)	Postponement, little r. Subject to the constraints of the inherent LHS-setting C-PM: HL (relative prevalence of HMT-P functionality: increased P-M trade-off constraints). When subject to RUR metabolic energy use mode functionality and mounting population density stress effects, LHS shifts occur from fast-LHS-P>M specialism to fast-LHS M>P specialism to slow-LHS M generalism supporting some r (2013/2015).				
Switzerland	1.54	30.6 H	50.3	14.7 L	14.1 N(p)
Germany	1.50	29.5 H	50.0	16.6 I	17.1 I(p)
Austria	1.49	29.2 H		16.4 I	17.2 I(p)
Warm temperate climate zone (S)	The applicable inherent LHS setting S-PM: H↑L underpins a prevalence for temperature responsive HMT specialized functionality associated with pronounced trade-off constraints in respect of HMT-P and LMT-M specialist functionality. Shifts of LHS settings from fast-LHS-P > M specialism (e capacity) to fast-LHS M specialism (postponement/longevity) during the SDT. Initially (specialized e capacity realization) left no scope for later life fertility realization (i.e. for r) and subdsequent specialized later life M metabolic performance realization left no scope for e nor r. Extremized postponement left no scope for r, but favoured longevity. Increased fast-LHS-mode P>M/fast-LHS-mode M specialism trade-off (fertility/longevity trade-off: high life expectancy at birth 2006-2010 at the expense of earlier life fertility: Table 2.3.3d)				
Italy	1.35	30.8 H		14.9 L	14.1 N(p)
Spain	1.33	30.7 H	45.3	10.9 L	10.2 N(p)
Greece	1.33	30.2 H	48.2	12.2 L	12.0 N(p)
Portugal	1.31	29.5 H	44.7	11.3 L	11.8 N(p)
Central-northeastern Europe (E: CN Baltic)	Wide MCAS based on e and r. Combined influences E-P(M): H/N-M(P): LH. Somewhat more e effects underpinned by inherent LHS setting E-P(M): H) than some r effects underpinned by LHS setting N-M(P): LH also involved.				
Estonia	1.58	27.2 L		20.6 H	23.4 W(e-r)
Latvia	1.70	26.5 L		19.9 H	23.4 W(e-r)
Lithuania	1.70	27.1 L		14.9 L	17.8 I(e)
Central-eastern Europe (E: CE)	TFRs not linked to e effects nor to r effects (TFR3+). Mothers starting early experience lower later life fertility. Within-individual trade-offs between early and late fertility (resilience, but low plasticity). Inherent LHS setting E-P(M): H (resilience of HMT-P specialized functionality). When subject to RUR metabolic energy use mode functionality, LHS-mode specialization does no provide for a combined e and r realization within the same individual (contrasting the situation experienced				

	in northern countries with inherent LHS settings N-M(P): LH where e/P-r/M trade-off constraints are alleviated).				
Czech Republic	1.57	28.2 I	51.0	14.7 L	16.8 N(p)
Hungary	1.45	27.9 L	52.1	21.3 H	23.4 W(e-r)
Slovakia	1.40	27.1 L	49.4	17.3 H	20.2 W(e-r)
Slovenia	1.57	28.7 I	50.3	14.1 L	15.4 N(p)
Poland	1.32	27.0 L		14.8 L	17.8 I(e)
Southeastern Europe (E: SE)	TFRs based on e effects (no r); as anticipated under enhanced specialized HMT-P functionality supported by the inherent LHS setting E-P(M): H (early life performance).				
Romania	1.58	26.3 L		16.3 I	20.0 I(e)
Bulgaria	1.56	26.0 L		12.3 L	16.3 N(e)
Serbia	1.46	27.7 L		14.9 L	17.2 I(e)
Subhaplogroup LHS settings N-M(P): LH, C PM: HL, S-PM: H↑L, E P(M): H for Northern, Central, Southern and Eastern Europe respectively (2.3.3b:6; Table 2.3.3b; Table 2.3.3e).					
Correlation between country-specific TFRs and TFR2+: r = 0.92, P = 0.000; TFR and TFR3: r = 0.69, P = 0.000; TFR and MCASI: r = 0.68, P = 0.000; MCASI and TFR3+: r = 0.95, P = 0.000; MCASI and mean age at birth: r = -0.49, P = 0.012.					
Data ex Eurostat (2013) and Eurostat (2015)					

In Table 2.3.3k, a strongly significant positive correlation between realized fertility (2013) and fertility recuperation at later ages (indexed by the proportion of two and more children off all children born: TFR2+) is identified. This association follows a latitudinal gradient, with northern countries in the coldest, strongly seasonal climate zone exhibiting greater realization of fertility recuperation at later ages (slower LHS expression: later life performance; in alignment with inherent LHS predispositions: Table 2.3.3b) than southern countries under warm temperate zone conditions (faster LHS expression: early life performance). A less constricted childbearing age span (earlier mean age of women at first birth and higher recuperation capacity) typically applies to cold temperate climate zone countries (Nordic countries), followed by northernmost cool temperate zone countries and with the childbearing age span becoming progressively more constricted towards warm temperate southern European countries (Table 2.3.3k).

Table 2.3.3k

N e-r in same individual plasticity reduced P-M trade-off constraints eP-Mr combination. E high mean MCBAS, but e and r not in same individual e-resilience.

C S no e no r but postponement (average). But r or e individuals may be present.

Page 253 Myrskyla et al. 2011, op. cit. Myrskyla et al. 2013

Myrskylä et al. (2011): A change in the fertility-development relationship has occurred in highly developed countries (1975-2008), suggesting an association between further socioeconomic development and a reversal of the fertility declining trend. The underlying mechanism of this fertility reversal was investigated by analyzing the links between development and age of cohort fertility patterns, as well as the role of gender equality. The results indicate that the reversal exists in respect of both period and cohort fertility and is largely driven by ***increasing older reproductive age fertility***. Fertility above age 30 is key to the reversal of the development fertility relationship (from negative to positive). Regarding fertility below age 30, cross-sectional and longitudinal analyses showed a continuous fertility decline (continued negative fertility-development association). ***Recuperation of fertility at higher ages is apparently essential for reaching increased levels of fertility in advanced societies***.

Lesthaeghe & Moors (2000): ***Scandinavian fertility levels are relatively high in the European context because relatively little loss at 25-29 ages and a strong recuperation effect at ages 30-39 years***. The western European countries have progressed much further than Eastern European countries, but regarding the former, two distinct groups in respect of recuperation are evident: those with strong recuperation, the Sandinavian countries, the United Kingdom and France; and those with insufficient recuperation: Mediterranian countries (such as Italy and Spain) and notably Germany and Switzerland. **Extramarital births are positively associated with fertility of the age cohort 15-19 in Eastern European countries; whereas nonmarital fertility is associated with reproduction at older ages occurring mainly in cohabiting couples in western and northern European countries. Extramarital births as a percentage of all births were exceeding 35 % in countries such as Iceland, Sweden, Estonia, Norway, Denmark, Finland, France and United Kingdom.**

AS 2007-2011: SES reversal in nordic countries. Wide childbearing age span: attenuated fast-slow trade-off or already in LHS-mode pM5.

E high mean MCBAS, but e and r not in same individual e-resilience.

Integrate: SE fast LHS up; with less plasticity costs (less fast LHS-health trade-off), but resilience costs: narrow fertility age range. North plasticity gains and costs.
Fertility based on P-fast expression (heterozygosity). When PIE up, increased fast-P vs M-slow LHS trade-off constraints: P down, slow M, i.e. early fertility capacity down, in the face of low capacity for later life fertility (TFR down).

Pronounced cold adaptation and childbearing age span

Wallace (2005): Adaptive mutations are clinically relevant as became apparent from studies which correlated mtDNA (mitochondrial DNA) haplogroups with longevity and degenerative diseases. All age-related degenerative diseases (including cancer predisposition), as well as ageing itself, seem to be directy related to mitochondrial production of ROS and the resulting accumulation of mtDNA mutations.
Specific mtDNA lineages were found to promote longevity (De Benedictis et al.1999; Rose et al. 2001; Niemi et al. 2003). However, some of the same variants associated with increased lifespan and protection against certain diseases, increased the predilection of developing other degenerative diseases. Cold-adapted mtDNA uncoupling mutations would generate less ATP per calorie consumed and would thus be more prone to clinical problems due to energy insufficiency. However, certain individuals with uncoupled mitochondria (**AS: healthy individuals with minimized/ low PIE loadings and thus minimized P-M trade-off constraints**) would burn calories more rapidly to generate both the required ATP plus increased heat; resulting in ETCs (mitochondrial electron transport chains) of uncoupled individuals to be more oxidized, thereby minimizing the production of mitochondrial ROS (favouring health and healthy ageing in such individuals). (**AS: under conditions supporting the LHS-mode PM**). mtDNA haplogroups harbouring adaptive mtDNA uncoupling adaptations can thus have a reduced rate of ageing and neurodegenerative diseases. Those harbouring mtDNAs with uncoupling polymorphisms would have reduced mitochondrial ROS (reactive oxygen species) and be less prone to somatic mtDNA mutations (reduced mitochondrial ROS associated with low levels of oxidative stress).

In cold-adaptive mtDNA variants harbouring uncoupling adaptations, plasticity benefits are realized to a greater extent, involving a wider range of Pm versus Mp realization due to attenuated fast-slow LHS trade-off constraints. Wider adaptability amplitudes associated with reduced/attenuated LHS trade-off constraints (attenuated fast-slow LHS trade-off) have plasticity costs as and when these trade-off constraints are intensified as a result of lowered vitality of functional energetic efficiency (due to PIE accumulation associated with uninterrupted food abundance and population density stress). Attenuation of the fast-slow LHS trade-off supports a wider childbearing age span; more so for more populatioms subject to higher degrees of cold-adaptation (Nordic/northern European countries: Table 2.3.3b). However, plasticity costs (vulnerability to procursive impacts: 2.1.2a) arise as fast-slow LHS trade-off constraints are increased under conditions of cumulative PIE accumulation, manifesting in the associated increased prevalence of chronic illness (degenerative diseases).

From data presented in Table 2.3.3l, a correlation between country-specific incidence of cancer and the chosen childnessless index (Aassve et al. 2013) was identified. This is consistent with cancer as index of low vitality due to progressive patho-information-

engram accumulation (2.3.3c). Relevant information gleaned from Bach (2002) indicate that incidence rates of multiple sclerosis and type I diabetes in children (ex Kurtzke 2000, op. cit. Bach 2002; Green & Patterson 2001, op. cit. Bach 2002) follow similar patterns as cancer incidence rates across country groupings.

Table 2.3.3l Cancer incidence rates, chosen childnessless indices and percentages extramarital births according to geographic groupings of European countries

	Cancer [a] (MS)[b] (Diabetes)[c] (Mortality)[g]	GDP [d] per capita: 2018 (Nominal)	Chosen childnessless index [e]	Extramarital births [f] (as % of total live births)
Nordic Europe				
Sweden (270/53/3.59/54.6)2[g] Norway (318/74/4.05/55.0)1[g] Finland (259/46/3.73/40.7)3[g] Iceland (284/55//64.1)1[g]	283 (90) (28) (1.7)	57 (65)	3.79	53.6
Northern Europe				
Denmark (338/52/4.48/46.3)2 Netherlds (305/57/3.92/41.2)2 Belgium (321/48/3.61/42.0)2 UK (273/46/3.25/45.4)2	309 (85) (17) (2)	51 (51)	3.81	43.7
North-Central Europe				
Switzerland (287/65/653.24/17.0)1 Germany (284/53/2.94/31.8)3 Austria (254/52/3.52/38.8)3	275 (c. 90) (13) (2.3)	57 (61)	3.21	29.2
Southwestern Europe				
Italy (279/39//22.2)2 Spain (249/40/3.29/32.1)1 Portugal (246/32/3.19/36.2)2	258 (c. 45) (13) (1.7)	37 (29)	3.24	30.2
South-eastern Europe				
Romania (224/26/2.24/27.4)6 Hungary (285/32/2.46/39.5)6	254 (35) (10) (6)	29 (14)	2.35	33.5
North-eastern Europe				
Estonia (243/33/2.15/59.1)5 Latvia (/29/2.33/43.5)6 Lithuania (252/35//28.5)7	247 (45) (8) (6)	32 (20)	2.24	43.7
Central southeastern Europe (Slavs)				

Czech Republic (294/37//36.3)5 Slovakia (/35/2.46/30.1)6 Slovenia (296/37/2.99/54.7)3 Bulgaria (235/23/1.63/51.2)7	275 (c. 38) (13) (5.2)	33 (26)	2.51	43.1
Eastern Europe (Slavs)				
Russia (/29/1.90/26.9)7 Poland (230/32/2.67/19.9)5 Belarus (219/20//20.1)7 Ukraine (/9/1.64/20.9)7	234 (c. 31) (c. 6) (7)	22 (9)	1.41	21.9
Correlation between country-specific incidence of cancer and chosen childnessless index: r = 0.71, P = 0.001; cancer and mortality ratings: r = -0.59, P = 0.005.				
[a] Cancer incidence: Age-standardised rates of all cancers per 100000 diagnosed in 2012 (World Cancer Research Funds); Estimated mean incidence of multiple sclerosis [b] and type 1 diabetes in children [c] (cases /100 000) for country groups as derived from Kurtzke 2000 (op. cit. Bach 2002) and Green & Patterson 2001(op. cit. Bach 2002). [d] International Monetary Fund World Economic Outlook (2018): GDP per capita $ PPP and GDP per capita $ (Nominal) country group means [e] Chosen childnessless index value (Aassve et al. 2013) [f] EUROSTAT (2009) [g] GBD (2019) Death per 100 000 population: Mortality ratings 1: <105, 2: 105 to <142, 3:142 to <189, 4: 189 to <249, 5: 249 to <313, 6: 313 to <397, 7: ≥397.				

Comparison of country groupings allow further unpacking of results presented in Table 2.3.3l. Nordic and Northern European countries exhibit high incidence of cancer rates, high values of the 'chosen childnessless index' and high rates of extramarital births; whereas intermediate values apply to North-Central and Southwestern Europe. In the eastern European country group, relatively high/intermediate cancer incidence rates are recorded for Central South-eastern Europe (Czech Republic, Slovakia, Slovenia and Bulgaria), also somewhat elevated rates of chosen childnessless and proportion of extramarital births within the eastern European group. Relatively lower levels of cancer incidence and low values of the chosen childnessness are characteristic of south-eastern, northeastern and eastern European countries (Table 2.3.3l).

Subject to LHS-mode PM, functional vitality is sustained due to the absence of significant performance-maintenance trade-off constraints (minimal patho-information-engram loads: low PIE loads: 2.2.2e). As PIE loads accumulate transgenerationally, performance-maintenance trade-off constraints intensify, ultimately leading to either extremized **Pm-type** expression (extremized LHS-mode **mP↑(3)** expression: sustained performance capacities at the cost of compromised maintenance capacities) or extremized **Mp-type** realization (extremized LHS-mode **pM↑(4)** expression: sustained maintenance capacities of later life performance at the

cost of performance vitality; i. e. reduced competitive and reproductive vitality). Extremized **Pm-type** expression implies fast LHS realization with early life performance at the cost of later life performance (high early reproduction at the expense of reproduction at later ages). Conversely, extremized **Mp-type** expression implies slow LHS realization with later life performance at the expense of high/early reproductive output, i.e. life time reproductive success. In both cases the reproductive/childbearing age span is constricted (extremised Pm: low capacity for fertility recuperation at later ages or extremised Mp: postponement capacity at the expense of early reproduction, respectively). Decreased **Mp-type/Pm-type** trade-off expression accordingly supports increased childbearing age spans.

Caucasian metabolic functionality is subject to the peri-arctic metabolic performance mode which involves resource use efficiency through broad metabolic amplitudinal adaptability (2.5.1.1a; Table 2.5.1.1a). The peri-arctic metabolic performance mode is characterized by the combination of sustained metabolic performance settings (resource-level buffered) and stress tolerance (sustained metabolic performance over time facing resource level and temperature fluctuations). The associated stress tolerance mode is relatively resource-costly (relatively high BMRs) and reproduction only possible above a relatively high level of resource availability (relatively high reproduction-resource level threshold). Accordingly, reproduction is resource level sensitive (2.5.1.1b: relatively high nutritional and space requirements for successful reproduction: sensitivity to resource deficits and high population densities). Relatively high BMRs enable sustained performance in the face of fluctuating resource conditions. The more pronounced the low-temperature seasonality (higher latitudes, higher altitudes), the greater the fitness advantages of full expression of the peri-arctic metabolic performance mode based on resource use efficiency through broad metabolic amplitudinal adaptability (plasticity), supported by relatively high BMRs; manifesting in genetic/epigenetic types with relatively enhanced childbearing age spans (buffered/attenuated fast/slow LHS trade-off constraints: decreased early *versus* later life reproduction trade-off: decreased **Pm-type/Mp-type** trade-off expression); ***but with increased vulnerability/sensitivity to population density stress*** (2.5.1.1b) and to procursive impacts generally (***elevated plasticity costs***). This is in agreement with Lutz & Qiang (2002) who note that, with respect to contempory European fertility levels, the low density regions of northern Scandinavia (e.g. also northern *versus* southern

Sweden:) have significantly higher fertility than the high density areas of central and southern Europe.

Variation in human (mammalian) life history strategies can be described to occur on a slow to fast continuum (Promislow & Harvey 1990, op. cit. Brumbach et al. (2009). At any given point of this continuum, life history traits cluster to form coherent, integrated sets. At the faster end of this continuum we have early reproduction, relatively smaller body size, high mortality rates and reduced longevity. Life history traits at the slower end of this continuum are associated with slower rates of reproduction and population turnover: fewer children, greater energy investment per child (offspring quality) and longer life spans (Section **2.2.2d**). Fast life history strategy: based on capacity for high process rates (high metabolic turnover functionality: early and fast rates of reproduction (***early life performance but faster ageing***). Slow life history strategy (***later life performance***): offspring quality > quantity; based on efficient maintenance to secure fitness benefits over time, i.e. into the future (health, extended growth-size/storage, longevity).

Body size favours fasting endurance (through energy storage) under conditions of seasonality (Lindstedt and Boyce 1985); supporting energy storage important for metabolic competence in periarctic populations (Table 2.5.1.1a). As adaptation to severe cold stress, northern populations have elevated basal metabolic rates. BMRs independent of body size are elevated in northern groups (Leonard et al. 2002); consistent with a strong negative association between BMR and mean annual temperature (Leonard et al. 2005, op. cit. Snodgrass & Leonard 2009).

The Nordic populations subject to pronounced cold climate seasonality would inherently (genetically) tend to slower life history (Table 2.3.3b) modes supporting large body size/energy storage and later life metabolic performance (capacity for reproduction retained at more advanced ages; longevity). This would also apply in progressively decreasing extent for cool temperate zone populations southwards. As mean annual temperatures rise and cool temperature seasonality declines (increasing incidence of warm summers), as towards south-western Europe (Southern European populations), faster life history modes are applicable (smaller body size, early life reproductive performance, faster ageing). This is consistent with lower fertility recuperation capacities at later ages for Southern European populations, as reflected in Table 2.3.3k (lowest mean group TFR2+; lowest mean group TFR in 2013).

Subject to the influence of transgenerationally procursive impacts and associated diminishing functional vitality (largely uninterrupted food abundance and mounting population density stress effects: patho-information-engram load buid-up), there is a shift from faster-type to slow-type LHS-modes (Section 2.2.2e): LHS-mode Pm > pM(1) (early life performance) to LHS-mode pM > Pm(2) and LHS-mode pM↑(4): later life performance, during the second demographic transition. These slower life history modes underpin reproductive postponement (high mean ages of women at first births: Table 2.3.3j). Slower life history modes are more in alignment with inherent life history strategies of cold/cool temperate zone populations (Table 2.3.3b), supporting later life performance and hence fertility recuperation at later ages. The declining recuperation potential and realisation from north to south is reflected by the proportions of TFRs realised in birth orders 2 plus (TFR 2+) in Table 2.3.3j and can be taken to causally explain the progressively lower TFRs over this gradient. The fertility of Southern European countries (inherently tending to faster life history strategies: early life performance: Table 2.3.3b) is more compromised by fertility postponement and low recuperation potential (reduced childbearing lifespan) than the fertility of more northern countries (inherently tending to slower life history strategies: performance extended into later life). Taking Italy to represent Southern European countries (De Rose et al. 2008), mean ages at first births by birth cohorts were considerably lower prior to 1960 (1933-1947-1960: c. 25.9, 24.8, 25.5) than 30.0 years in 2013 (Table 2.3.3j). The percentages of children born of birth order 2 and more per cohorts in Italy progressively declined from c. 70 % in 1935 to c. 55 % in 1960; indicating fewer higher order children being born as the extent of postponement increased (Percentages of children born 3 or more per cohorts in Italy were above 30 % during 1930 and 1940; c. 18 % in 1960).

Castro Martin (1992): During the last decade younger cohorts in Spain have been increasingly postponing marriage and delaying childbearing after entering marriage. The traditional pattern of low fertility in Northern Europe and high fertility in Southern Europe has become inverted: in 1989 Sweden with a TFR of 2.02, Norway (1.84), the United Kingdom (1.85) had higher fertility than Portugal (1.53), Greece (1.50), Spain (1.30) and Italy (1.29). The low fertility rates in Scandinavian countries during the 1970s were partly due to delayed childbearing; whereas during the 1980s fertility rates had increased again as postponed births were made up at older ages (fertility recuperation). The particularly low fertility levels recorded for Spain were partly attributed to changing family formation patterns in younger generations involving postponement of marriage and deferment of first births. Whereas most women of the

late 1960s and early 1970s cohorts had their first child right after marriage (linkage between marriage and motherhood role), a pattern of delayed childbearing emerged in the mid-1970s and 1980s when most of the women in the last marriage cohort (who were not pegnant at marriage) postponed their their first birth beyond the second year of marriage. Late age at marriage, high education, low religiosity, small family size, urban residence and work experience before marriage all led to the postponement of first births. 80 % of women with no education had their first birth within two years of marriage, whereas only 57 % of women with a college degree had become mothers in the same time span. Also, women out of the labour force are more likely to become premaritally pregnant. Most societal trends led to an increasing dissociation of marriage and motherhood in Spain. With reference to fertility postponement, Castro Martin (1992) contends that the timing of reproductive events of women is likely aimed at optimally synchronizing non-family and family roles.

According to the life history strategy (LHS) explanatory framework (2.3.3e), increased postponement is consistent with a shift from fast-LHS P > M to LHS-mode M > P realization. An associated increased trade-off between P-fast-LHS (inherent), supporting early-life fertility realization, and M-slow-LHS fertility realization resulted in a narrowing of the childbearing age range; thereby depressing fertility.

The traditional pattern of high fertility in Southern Europe and low fertility in Northern Europe has become inverted by in 1989 (Castro Martin 1992). The low fertility rates in Scandinavian countries during the 1970s were partly due to delayed childbearing; whereas during the 1980s fertility rates had increased again as postponed births were made up at older ages (fertility recuperation). This is consistent with the interpretation that pre-SDT fertility in southern Europe was underpinned by a relatively faster-type LHS-mode predominance: early and relatively high fertility; as would be expected on the basis of an inherited fast-LHS-mode predisposition (Table 2.3.3b). With increasing fast-slow LHS trade-off constraints coming to affect during the SDT, increasingly slow-LHS expression supported fertility postponement, but recuperation of births at later ages was/is constrained due to the inherent predisposition for fast-LHS realization (early fertility realization) applicable to southern European populations now experiencing lower fertility rates than northern European populations subject to inherent predispositions to slower LHS realization (Table 2.3.3b), allowing for fertility recuperation and supporting a wider childbearing age range.

Southern regions of Spain exhibited the fastest transition to first births, while northern and eastern regions displayed slower rates of transition (Castro Martin 1992). This is

in agreement with faster LHS expression as expected for southern regions and slower LHS expression in more northern regions (Table 2.3.3b).
(AS: It is of interest to note here that the implicated underpinning gradient of fast-type to slower-type life history strategies from sowth-western to north-eastern regions within Spain is congruent with that over south-western to north-eastern Western European countries: Section 2.3.3).

e) Demographic transitions: a life history strategy (LHS) explanatory framework

Fitness maximization, especially according to the K-reproduction strategy (peri-arctic mode), notably requires LHS optimization of offspring number x quality, requiring investment allocation to cater for both production and maintenance (LHS-modes PM, P-M/M-P). Such LHS modes were maintained during conditions of variably alternating resource conditions during pretransitional resource availability conditions (feast/famine). During the initial stage of the demographic transition fertility was relatively high, then declining (progressive LHS-mode Pm > pM (fertility high/mortality high) to LHS-mode pM > Pm shift (fertility declining/mortality declinig). In order to allow for maximum utilization of affluence/wealth (industrialization) the LHS-mode Pm > pM (relatively fast LHS) took effect. Under the sustained impact of procursive impacts associated with chronic affluence and population density effects progressively higher patho-information-engram (PIE) loads became lodged within biocybernetic regulation systems (transgenerationally accumulated and transmitted to succeeding generations through epigenetic mechanisms: **2.1.2**; **2.1.3.1**).

First demographic transition (FDT): Increasing trade-off accentuation and associated shift to a slower LHS: less fertility/greater maintenance demand.
Second demographic transition (SDT): sustained affluence and increasing transgenerational exposure to population density stress. Further accentuation of trade-off due to further accumulation of PIE loading: metabolic functional efficiency progressively more compromised (chronic immune system dysregulation syndrome: **2.2.2i**) and low instinct vitality (**2.3.1**; **2.3.2**). LHS shifting even more to the slow extreme, leaving little energy for high turnover performance (reproduction and male competitive performance). Quantity-quality trade off under population density stress:

As population density (conspecific competition) increases the importance of competiveness among offspring increases and a shift from the production of large numbers of offspring towards inceased investment in fewer, highly competitive offspring is favoured by selection (MacArthur & Wilson 1967, op. cit. Low 1994).

Table 2.3.3m Main demographic eras: pre-industrialization, first demographic transition (FDT) and second demographic transition (SDT): Northern-Western-Southern Europe

Pre-industrial	First demographic transition (FDT): early phase	Second demographic transition (SDT)
c. < 1750	**1870-1930** (1931-1960)	**1975-2000+**
LHS-mode PM	**LHS-mode Pm > pM (1)**	**LHS-mode pM↑ (4)**
Low levels of PIE loadings; implying relatively weak performance/maintenance trade-off constraints (2.2.2e)	Increasingly higher PIE loadings (strong P > M trade-off constraints) (2.2.2e)	High PIE loadings (strong M > P trade-off constraints) (2.2.2e)
As initiated during the Industrial Revolution (1760-1840), LHS mode shifts ensued from PM to P > M to Pm > pM (1): early phase of FDT; progressing to pM > Pm (2): late phase of FDT (1931-1960) and finally to pM↑ (4): representing the Second Demographic Transition (1975-2000+) (2.3.3e)		
Balanced P/M realization ratio (2.2.2e)	High P/M realization ratio by Pm-types (2.2.2e)	Low P/M realization ratio by Mp-types (2.2.2e)
	Competitive mode changing from win-win to win-lose	**Predominance of low vitality win-lose competitive mode**
Both early and later life metabolic performance	Fast-type LHS (early life performance)	Slow-type LHS (later life performance)
Maximising fitness (2.2.2d: Korpelainen 2003) requires the combination of early reproduction (tempo effect) and high life time reproductive success (quantum effect). This combination is facilitated when the investment trade-off between fast and slow life history traits is minimal, as in the case of the LHS-mode P-M.	High early life reproductive performance: tempo effect realization at the expense of life time reproductive success (quantum effect): maximum fitness not achieved Korpelainen (2003). (2.2.2d; 2.2.2e)	Later life reproductive performance: quantum realization (postponement) at the expense of early reproduction: maximum fitness not achieved (Korpelainen 2003). (2.2.2d; 2.2.2e)
Curbed population growth through late ages at marriage and many in lower socioeconomic classes never marrying; external mortality	**Marriage**[a]: rise in proportions marrying, declining age at first marriage (low or reduced cohabitation, low divorce rates)	**Marriage**[a]: fall in proportions married, rise in age at first marriage; rise in cohabitation and divorce rates
Total fertility moderately high (ranging between 4 and 6 children per women on average)	**Fertility**[a]: decline in marital fertility at older ages, lowering of mean ages at at first parenthood; low levels of childnessless among married couples	**Fertility**[a]: further decline in fertility via postponement, increasing mean age age at first parenthood. Rising extra-marital fertility, but also of childnessless
Central role of family as unit of successful childrearing	**Societal background**[a]: preoccupation with material needs, community oriented networks. Solidarity prime value. Strengthening of social cohesion. Segregated gender roles, familistic policies.	**Societal background**[a]: individual autonomy, self-actualization. Tolerance prime value. Weakening of social cohesion. Retreat of the State. Secularisation and refusal of authority. Rising symmetry in

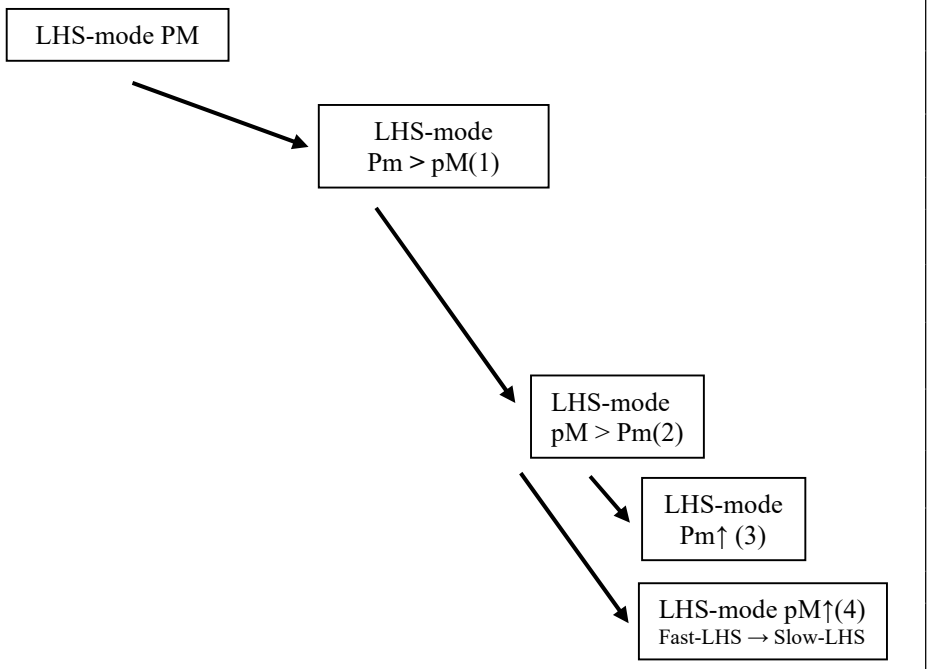
	Dominance of one single family model	gender roles and female economic autonomy
Psychosocial resilience; variable according to external circumstances	Psychosocial tensions	Psychosocial incoherence (2.2.2e) Increased prevalence of scramble competition by both males and females for power, partners and economic resources (2.2.2e)
Patriarchy intact (differentiation of gender roles; equal status of men and women within a role-differentiated context). (2.2.2e) Gender role complementarity	Patriarchal predominance (Family structure maintained) Interference competition: patriarchal family territoriality (2.2.2e) Gender role complementarity	Patriarchal family structure as central unit of childrearing weakening/in dissolution (2.3.3e). Gender role competiveness
Strong female households embedded within a generally patriarchal dispensation	Strong patriarchal dispensation providing protection and provisioning to the female childrearing unit	Patrirchal family unit in disintegration. Advantages of the family unit for childrearing lost ()
Prevalence of infectious diseases. [b] Atherosclerosis, cardiovascular diseases	Prevalence of tuberculosis (high metabolic turnover disease states)	Prevalence of chronic immune system dysregulation (CISD) syndrome (cancer, autoimminity: degenerative diseases): 2.2.2i
Balanced and relatively high male-female reproductive vitality. Both male and female fitness maximization optimally pursued within the defended monogamous family unit (2.2.2e)	Relative accentuated male performance vitality; pursuing to sustain the traditional patriarchal family unit as entity of procreation (through interference competition). Low levels of extra-marital childbearing. (2.2.2e)	Male performance vitality and associated male role capacity compromised. Tendency to pursue reproductive fitness through scramble competition by both males and females. Rising extra-marital proportion of childbearing. (2.2.2e)
Slower-type LHS: especially in high latidude-altitude regions: birth peaks in autumn/winter (2.2.2g)	Fast-type LHS: birth peaks in spring/summer: high P/M realization ratio types (2.2.2g)	From fast to slow-type LHS: Fast: birth peaks in spring; Slow: birth peaks in autumn (2.2.2g)
[a] Lesthaeghe & Neels (2002); [b] Fogel (2004)		

Refer to Demographic transitions for Europe, interpreted in the context of life history strategies below (Table 2.3.3n).

(Re Table 2.3.3n: TFR = total fertility rate = number of births in a given year by the average number of women of reproductive age. Marital fertility Ig = fertility relative to an observed maximum, that of a twentieth century religious group, the Hutterites, who married early and prohibited contraception).

Table 2.3.3n Life history strategies and demographic transitions (Europe)	
TFR (Ig Marital fertility)	
	⇦ LHS-mode PM
(0.7-0.8)	

1700-1800	
4-5 (0.7-0.8) 1800-1890	
3-4 (0.5-0.7) 1890-1910	
2-3 (0.2-0.4) 1920-1940	
1.7-2.1 (1955)	
1.2-1.9 (1980+)	



	Pre-Industrial		Industrial Revolution 1760-1840	Demographic Transition		Second Demographic Transition
	1650-1700	1690-1800	1740-1890	1870-1930	1931-1960	1975-2000+
Resource availability status	Temporally dynamic (feast-famine)	Low Variable	Variable Improving to high	Relatively good and basically uninterrupted	High (Chronic feast)	High (Chronic feast)
Daily caloric supply [a]	2095 (1700)	2237 (1800)		2857 (1910)	3231 (1954)	3304 (1965)
Height (cm) [b]	(c. 160.0)	c. 166.0	c. 167.8	(c. 168.9)	(c. 172.3)	c. 175.8 (-180)
BMI [c]		(c. 18) (1705)	c. 23.4 (1864)	c. 23.2 (1894)	c. 25.9 (1961)	c. 26.6 (1991)
Fertility/ high SES relationship [d]	Positive	Positive	Positive	Negative	Negative	Negative
Marital fertility	High	High	High	Declining	Low	Low
Mortality rates	High to moderate	High	High → Declining	Declining	Low	Low
Life expectancy at birth	Variable to high 30-40	c.40-60	c. 60-70		70+	c. 75-80
Fertility/longevity	Positive	Positive	Negative	Negative		Negative
Age at first marriage	Increasing	High	High Decreasing	Relatively low	Increasing	Delayed (postponement)
Never marrying (proportion)	Increasing	Relatively high	Relatively high	Decreasing 1810-1900	Low Increasing	Increased
Natural population increase rates [e]	Low Variable	Declining 1760-1800	Increasing 1800-1830	Stabilizing 1830-1910	Declining	Declining (fertility below replacement)

Fogel 2004: [a] Estimated calories per capita for Great Brittain; [b] Estimated average final heights; [c] Mean BMI at age 45; [d] Skirbekk (2008); [e] Botev (1990): Denmark, Norway, Sweden. (also Wrigley 1985a/b, Voland 1998, Knodel & Wilson 1981, Zakharov 2008, and others cited in text: 2.3.3a)

In response to prevailing/anticipated conditions/circumstances the body adopts particular LHS settings which support fitness maximization

Resource use efficiency (RUE) *versus* resource use reactive metabolic mode functionality (2.2.2f)

Under the assumption of a constant area beneath the performance curve, a **trade-off between maximal performance (performance specialism) and performance breadth** (performance generalism) is implicated (*vide* Gilchrist 1995).

Following Gilchrist (1995), natural selection favours increased efficiency during even limited times of optimal conditions (narrow performance breadths-specialism) rather than extending the range of conditions (wide performance breadths-generalism) that support fitness-enhancing activity. The same specialist phenotype, characterized by a narrow performance breadth, is favoured in both constant and in environments with substantial within- and among-generation variation. In a variable environment, specialization is made possible by the existence of some period of suitable conditions for metabolic investment in reproduction or some other fitness-related processes. Specialists are favoured if specialization on those conditions provides enough of an increase in efficiency during those times. Selection favours broad performance breadths (functional generalism) only in environments characterized by considerable among-generation but little within-generation variation (Gilchrist 1995).

It is contended that (2.2.2f), under the RUR metabolic energy use mode (pronounced P-M trade-off constraints), high peak performance specialism is favoured by natural selection. RUE metabolic energy use mode (reduced P-M trade-off constraints): Slow LHS-PM settings underpin broad performance breadths embracing both efficiency of P and M functionality (efficiency generalism)

P-M trade-off constraints. EUE *versus* EUR specialism. From P-HMT specialism under LHS-mode P>M:1 to LHS-mode M>P:2 to LHS-mode M↑:4 (M-LMT specialism).

From fast LHS P>M setting to fast LHS M>P setting (mortality down, life expectancy up, P vitality down as P-M trade off costs constraints increase) to fast LHS M↑:4 setting (strong P-M trade-off performance specialist LHS phenotypes) to slow M↑:4 /LHS M(P) settings (Table 2.3.3o). This LHS sequence is driven in response to increasing population density stress, as intensified by P-M trade-off constraints due to endogenous energetic insufficiency on the basis of PIE load accumulation (Tables 2.3.3n and 2.3.3o).

Life history strategy sequence (Table 2.3.3n/Table 2.3.3o) and season of birth (2.2.2g)

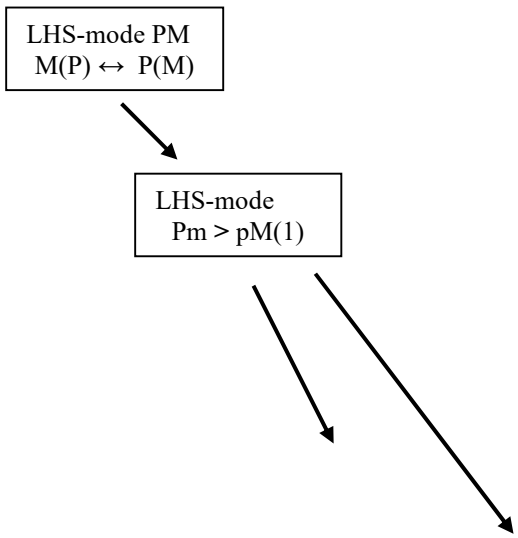
Life history strategy sequence (Table 2.3.3n) and season of birth (1750-1990+): LHS-mode PM: 1750-1825 (high P vitality: slow LHS: autumn/winter) → LHS-mode Pm > pM(1): 1870-1930 (fast LHS: spring) → LHS-mode pM > Pm(2): 1931-1960 (fast LHS towards slow by c. 1980) → fast-slow LHS-mode pM↑(4): ≥ 1950 (declining P vitality: as M-expression increases, underpinning: postponement/recuperation) → slow LHS pM↑(4): 1981 + (autumn/winter).

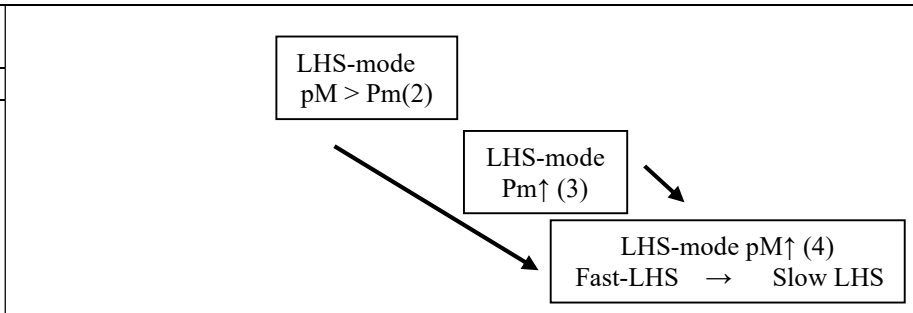
Life history strategy sequence: pre-transition, first demographic transition phase to second demographic transition phase.

From LHS-mode PM (resource use efficient metabolic energy use mode; autophagy: absence of patho-information-engram load accumulation) into the demographic transition from LHS-mode P>M (HMT early life performance) in response to resource overabundance (resource use reactive metabolic energy use mode; autophagy insufficient; patho-informatio-engram load accumulation resulting in lowered energetic functional capacity/vitality and associated increased P-M) trade-off constraints); shifting to LHS-mode M>P and LHS-mode M↑4 in the SDT-phase; responding to increasing population density stress (LMT later life performance realization). Unpacked Table 2.3.3o.

Table 2.3.3o Life history strategy sequences across demographic transitions (Europe)

TFR (Ig Marital fertility)	
(0.7-0.8) 1700-1800	
4-5 (0.7-0.8) 1800-1890	
3-4 (0.5-0.7) 1890-1910	
2-3 (0.2-0.4) 1920-1940	



1.7-2.1 (1955) **1.2-1.9** (1980+)						
	Preindustrial	First Demographic Transition		Second Demographic Transition		
	1750-1825	1870-1930	1931-1950	1940-1980	1950-1980	1980+
Resource status: Nutrition		Persistent abundance of (HMT) nutrition (High metabolic turnover nutrition: Table 2.5.1.2e)				
Resource status: Space (low stress environs)		Increasingly limited (Urbanization)		Chronically limited (fertility-limiting psychosocial population density stress)		
LHS-modes (Table 2.3.3e)	PM: M(P), PM, P(M)	Pm > pM(1)	pM > Pm(2)	Pm↑(3) E Europe	pM↑(4)	pM↑(4) M(P↓)
Natural population increase rates [a]	Variably stable to declining 1760-1800	Increasing 1800-1830 Stabilizing 1830-1910	Stabilizing	Stabilizing	Declining	Declining (Stabilizing)
Energy resource use strategies (2.2.2f)	Nutrient-recycling, efficient resource use strategy	Adaptive resource re-allocation resource use strategy (responsive to feast *versus* famine conditions; providing for population increase capacity during feast conditions at the cost of pronounced unbuffered population declines under 'space famine' conditions; i.e. persistent overpopulation and associated sociospatial density stress)				
Supporting energy use metabolic modes	Energy use efficient EUE-LHS-PM mode	Adaptive resource re-allocation resource use strategy Energy use reactive EUR-LHS-energy use metabolic modes: high-level use of nutritional resources				
Autophagy as healing process	Functional	Blocked	Blocked	Blocked	Blocked	Compro-mized
Accumulation of patho-information engram loads	Minimal or absent	Ongoing	Ongoing	Ongoing	Ongoing	
P-M trade-off constraints: P or M performance specialism *versus* PM tolerance generalism	Absent or relaxed	Increased (as associated with high plasticity scope) P_{max} /M performance specialism predominant (Limited PM tolerance generalism) (Gilchrist 1995)				Reduced
Functionality breadth	Wide	Narrow			Narrow	Broadened
P_{max} –capacity vs M-tolerance trade-off intensity	Absent or relaxed	High (plasticity costs)	High (plasticity costs)	Low (buffered)	High (plasticity costs)	Reduced
Performance specialism vs tolerance genralism	P-M tolerance generalism	High P-HMT perfor-mance specialism		Resilience: P_{max} per-formance specialism	High M-LMT perfor-mance specialism	Enhanced M LMT ≥ HMT generalism
Fast-slow LHS settings	Slow	Fast	Fast	Fast	Fast	Slow
LHS settings	PM slow	P > M fast		P > M fast	pM↑ fast	M(P↓) slow

Season of birth peaks [b]	Autumn/ winter	Spring	Spring	Spring	Spring-early summer	Autumn (late summer)
Mean maternal ages at first child				22-25: 1997 26-29: 2013	27-28: 1997: Table 2.3.3j	28-31: 2013: Table 2.3.3k
Early births (e) Recuperation (r): 2013 Table 2.3.3k						N: e-r C: some r S:no e nor r E: e or r
Inherent LHS settings: 2.3.3b:6.		Fertility patterns during the SDT as influenced by inherent LHS settings:				
Northern Europe N-M(P): LH		Increased TFRs from 2004 onwards indicate fertility reversal (1.93: 2008), both e and r involved				
Central Europe C-PM: HL		TFRs remain low until 2011 (1.43), showing some recuperation thereafter (1.51: 2019)				
Southern Europe S-PM: H↑L		TFRs remain low between 1997-2019; having declined from 2.51 in 1975 to c 1.37: 2000-2019 (from e to persistent postponement)				
Eastern Europe E-P(M): H		TFRs remain low between 1997-2004; having declined from 2.39/2.14 (from e to postponement). Then increasing from 2008-2019: 1.48-1.55 (due to either e or r effects).				
Critical fertility-promoting resources	Nutritional resources ≈ space as a resource	Nutritional resources > space as a resource		Nutritional resources and space important	Space as a resource of increasing importance	Space as a resource of increasing importance
Tolerance to foreigners	Endogamy	Variable	Increased	Progressively declining tolerance to foreigners as their proportion in the population increases and space is perceived as a limited/ing resource in the native population (consciously or subconsciously)		
Marital fertility	High	High	High	Declining	Low	Low
	1750-1825	1870-1930	1931-1950	1940-1980	1950-1980	1980+
Life expectancy at birth W [c] (Riley 2005) E	30-40	45-65 35-55	45-65 35-55	65-70 55-70	65-70 55-70	70-80+ 65-70+
[a] Botev (1990): Population density increase rates for Denmark, Norway, Sweden; [b] Lerchl et al. (1993) Knodel & Wilson 1981; [c] (Riley 2005): approximations						

Eastern *versus* Western Europe (Table 2.3.3o)

LHS-mode mP↑(3). Eastern European countries. **I**nherent LHS setting E-P(M): H (early life performance). Inherent resilience of the prevalence of P-HMT functional expression, supporting early fertility realization unconstrained under densely packed conditions (Eastern European marriage pattern: 2.3.3b:7). Resilience reflects the absence of problematic functioning despite exposure to contextual adversity; it is about not having a particular competence compromised when subject to perturbing influences.

With onset of the demographic transition, resource use reactive responses to relative resource abundance, the LHS-mode mP↑(3) represents LHS-mode P-HMT (high metabolic turnover) specialism (in support of peak performance). Resilience in sustaining P-HMT functionality is diminished and P-M trade-off constraints intensify. Vulnerability to exogenous stress/harshness (anomy) increases as LHS-mode settings shift to converge towards those of LHS-mode M↑:4. Accentuation of fast-type LHS-

mode P-HMT expression (2.2.2c/d) coping with anomy underpins low well-being scores (in contrast to north-western European countries subject to LHS-modes M>P and pM↑:4). For Eastern European countries: Inherently reduced P-M trade-offs due to representing an inherent genotypic P-HMT type involving reduced P-HMT(P-performance)-M-LMT (life expectancy/health) trade-off constraints; a resilience thus underpinning a reduced P-health trade-off (sustained P-vitality, but restricted childbearing age range during the SDT: fertility down; resilience costs).

Fertility transitions and seasonality of births (Table 2.3.3o)

As reported in 2.2.2g, the findings of Dahlberg & Andersson (2018) for Sweden reveal two basic patterns of birth seasonality over the study periods (1940-1959, 1960-1979, 1980-1999, 2000-2012). Pronounced spring peak and November-December trough, with the pattern relatively sustained over the study periods; II) Relatively weak spring peak, progressively flattening out towards a weak autumn peak during the period 2000-2012. Pattern I reflects that of the higher educated, of mothers of ages 25-29/30-34 years, of parity 2 offspring; and in respect of offspring with same partners compared to offspring with new partners (P-HMT early life performance Pm-type specialism). Pattern 2 reflects that of the lower educated, mothers of ages ≥ 35 years and for third and higher order births (M-LMT Mp-type specialism). For the population as a whole, seasonal birth variation is consistent with the predominance of pattern 1 for the periods 1960-1979/1980-1999 and concurrent prevalence of patterns 1 and 2 during 2000-2012.

Pattern 1 relatively sustained over study periods, including period 1980-1999 (for western-central European countries where the change over to autumn birth peaks had already occurred from 1980 onwards). Provide link to N country inherent LHS features. Pattern 1 is typically in alignment with P performance requirements (HMT-P early life performance) as underpinned by a fast-LHS-mode-P>M; whereas pattern 2 is typically in alignment with M performance requirements (LMT-M later life performance), as underpinned by LHS-modes slow-LHS-M↑:4 or slow LHS-M(P). Over time, increasing M performance requirements are reflected in shifts towards LHS M>P specialist realization (later life M performance) at the cost of P performance LHS P>M specialist realization (early life P performance); reflecting pronounced P-M trade-off constraints. Fast-LHS specialist realization of either P or M (LHS-mode P>M and

LHS-mode M>P or LHS M↑:4) during FDT and early SDT (in alignment with predominantly spring births of offspring: 2.2.2g; Table 2.3.3o).

Fertility trends during the SDT (Table 2.3.3o)

For variable periods into the SDT, TFRs declined further due to postponement effects (p); recovered due to variable degrees of recuperation of births at maternal ages beyond 30 years (r) or through sustained early age births (e) or combined early age births and recuperation (e-r). TFRs during the SDT were determined by the combined effects of p, r and e as these factor effects shaped the maternal childbearing age span (Table 2.3.3k). Changing fertility patterns differed between northern, central, southern and eastern European countries in alignment with underlying subhaplogroup-based LHS-PM settings (Table 2.3.3b and Table 2.3.3e).

For variable periods into the SDT, TFRs declined further due to postponement effects (Tables 2.3.3h/k).

Northern European countries (Table 2.3.3b and Table 2.3.3e): From fast-LHS M-specialism: postponement (spring birth peak) to slow LHS-M↑:4/slow-LHS-M(P) mode generalism: (autumn birth peak). Increased TFRs from 2004 onwards indicate fertility reversal, based on both e and r being involved. Slow LHS-M↑:4/slow-LHS-M(P) generalist realization (autumn birth peaks) implies patterns 1 (early life P performance) and 2 (later life M performance) realization in the same individual.

(On the basis of relaxed P-M trade-off constraints inherent to N-M(P): LH generalism. Increased TFRs from 2004 onwards indicate fertility reversal with both e and r involved (Table 2.3.3k).). Wide maternal childbearing age spans ($r \geq e$ combination) are underpinned by inherent LHS setting N-M(P): LH (cold adaptation/ slow metabolic turnover environments): e/P-r/M trade-off alleviated. Scandinavian fertility levels are relatively high in the European context because relatively little loss at 25-29 ages and a strong recuperation effect at ages 30-39 years (Lesthaeghe & Moors 2000).

Retainment of some fertility of maternal age classes 25-29 years (seemingly increasing after 1997-2011: Table 2.3.3h). e and r combination (Table 2.3.3k). From fast-LHS M-specialism: postponement (spring birth peaks) to slow-LHS M↑:4/slow-LHS-M(P) mode generalism: (autumn birth peaks). Pattern 1 of birth seasonality (Sweden: spring peak: 2.2.2g) is relatively sustained over the study period, including period 1980-1999

(reflecting e and r combination in northern countries); whereas for western-central European countries the change over to autumn birth peaks had already occurred from 1980 onwards; but the underpinning slow LHS modes did not involve substantial e and r combination (see below).

Central European countries (Table 2.3.3b and Table 2.3.3e). From fast-LHS M-specialism: postponement (spring birth peak) to slow-LHS-mode M↑:4: some recuperation (autumn birth peak). C-PM: H ≥ L (Plasticity of combined P-HMT and M-LMT functional capacity, with some prevalence of P-HMT functionality) allowing for some recuperation. TFRs remain low until 2011, showing some recuperation thereafter (Table 2.3.3k: postponement, little r). Subject to the constraints of the inherent LHS-setting C-PM: HL (relative prevalence of HMT-P functionality: increased P-M trade-off constraints), TFRs remain relatively low hen subject to RUR metabolic energy use mode functionality and mounting population density stress effects. Under such conditions, LHS shifts occur from fast-LHS-P>M specialism to fast-LHS M>P specialism to slow-LHS M generalism, supporting some r (2013/2015). Insufficient recuperation experienced notably in Germany and Switzerland (Lesthaeghe & Moors 2000). Postponement and some/little recuperation. From fast-LHS M-specialism: postponement (spring birth peak) to slow-LHS-mode M: some recuperation (autumn birth peak). TFRs remain low until 2011, showing some recuperation thereafter (Table 2.3.3h).

Southern European countries (Table 2.3.3b and Table 2.3.3e). S-PM: H↑>L: implying inherent predominance P-HMT functionalty underpinning early fertility. TFRs remain low between 1997-2019; having declined from 2.51 in 1975 (from e to persistent postponement: Table 2.3.3k). Insufficient recuperation encountered in Mediterranian countries such as Italy and Spain (Lesthaeghe & Moors 2000). The applicable inherent LHS setting S-PM: H↑L underpins a prevalence for temperature responsive HMT specialized functionality associated with pronounced trade-off constraints in respect of HMT-P and LMT-M specialist functionality. Shifts of LHS settings from fast-LHS-P>M specialism (e capacity) to fast-LHS M specialism (postponement/longevity) during the SDT. Initially (specialized e capacity realization) left no scope for later life fertility realization (i.e. for r) and subdsequent specialized later life M metabolic performance realization left no scope for e nor r. Extremized postponement left no scope for r, but favoured longevity. Increased fast-LHS-mode

P>M/fast-LHS-mode M specialism trade-off (fertility/longevity trade-off: high life expectancy at birth 2006-2010 at the expense of earlier life fertility: Table 2.3.3d).

Eastern European countries (Table 2.3.3b and Table 2.3.3e). The inherent E-P(M): H setting is characterized by resilience in sustaining the prevalence of P-HMT functionality under LHS-PM promoting conditions (RUE/EUE metabolic energy use functionality). Under RUR metabolic energy use functionality, as applicable during demographic transitions, individuals become vulnerable to anomy (low well-being scores) as an LHS shift occurs to LHS-M↑:4. As M-LMT functionality increases (postponement), P-HMT functionality (e: early fertility) is severely compromised. Thus, mothers starting early experience low later life fertility.

TFRs remained low between 1997-2004; having declined from 2.39/2.14 (from e to postponement). Then increasing from 2008-2019 (due to either e or r effects). Slow-LHS-mode M↑:4. Separate e vs r performers (Table 2.3.3k: E: CE). TFRs not correlated with e effects or to r effects (TFR3+). Within-individual trade-offs between early and late fertility (resilience, but low plasticity). Inherent LHS setting E-P(M): H (resilience of HMT-P specialized functionality). When subject to RUR metabolic energy use mode functionality, LHS-mode specialization does no provide for a combined e and r realization within the same individual (contrasting the situation experienced in northern countries with inherent LHS settings N-M(P): LH where e/P-r/M, trade-off constraints are alleviated).

(E: South-East: 2.3.3k). TFRs (1.46-1.58) based on e effects (no r); as anticipated under enhanced specialized HMT-P functionality supported by the inherent LHS setting E-P(M): H (early life performance).

E-Baltic (Table 2.3.3k): Wide maternal childbearing age spans are based on the combination of e and r in the same mothers; supporting country-specificTFRs of between 1.58-1.70. Combined influences E-P(M): H/N-M(P): LH. Somewhat more e effects underpinned by inherent LHS setting E-P(M): H) than some r effects underpinned by LHS setting N-M(P): LH also involved.

In general, countrygroup-specific current mean TFRs are inversely related to the extent they exceed population densites at population equilibrium carrying capacities (PECC: maximum sustainable population densities where populations neither increase nor decline; as they are in equilibrium with material and sociospatial resource availabilities). Overarching influences on fertility levels

appear to be involved as well, such as population density effects (refer to section 2.3.3:5 outlinig the pronounced significance of population density in shaping fertility levels) and factors reflected in the *State Antiquity Index* (Aassve et al. 2013; 2.3.3b:3). Present-day countries which were sited on preceeding nation-states, kingdoms or empires over longer time spans of history were found to be associated with features linked to lower present-day fertility; supporting the contention that differences in current attitudes to demographic behaviour stem from differences in characteristics of economic and institutional development exhibited before modern times (Aassve et al. 2013). State antiquity correlates positively with economic development and associated modernist attitudes in respect of fertility behaviour (high rates of cohabitation, high extramarital childbearing, high divorce rates, high levels of female empowerment and emancipation). Children lost their centrality, being no longer perceived as essential for parental achievement of personal satisfaction and realization (Aassve et al. 2013).

Five demographic phases have been identified (Table 2.3.3n) and their characteristic features are outlined below.

Pre-Industrial phase (Pre-transition era): < 1750

Resource availability levels were temporally dynamic (variable, but relatively low; alternating feast- and famine conditions). Such circumstances support an equilibrium between procursive impacts and recursive elimination thereof (minimal/zero accumulation of patho-information-engrams: sustained health and vitality). Predominant **LHS-mode PM**: minimal trade-off constraints between performance expression and maintenance processes (2.2.2e; Le Bourg et al. 1993: absence of early fertility-longevity trade-off). Furthermore, two subtypes of the LHS-mode PM can be differentiated: P-M and M-P. P-M-types: realization of somewhat enhanced performance capacity under conditions requiring/favouring faster-type LHS expression (surplus resource/nutrient use) and supporting interference competition in both males and females (territoriality: breeding and resource territoriality). M-P-types: some predominance of maintenance realization under conditions requiring/favouring slower-type LHS expression; when coping with pronounced periarctic conditions such as in areas subject to cold seasonality and in arid, nutrient-poor areas: traditional healthy

living populations: 2.5.1.2). Competitive interactions: male family territoriality and inter-female competition through matriarchal household territoriality (Section 2.2.2e).

Ferility levels during this era varied between 4 and 8 births per woman (Hirschman 2001). Population growth variable to low or declining; delayed marriage and proportions of the population never marrying relatively high (Table 2.3.3n). Fertility and longevity were positively associated (when subject to LHS-mode PM); as was fertility and wealth (Table 2.3.3n). Relatively low body heights and body mass indices; with estimated daily caloric intakes of between 2100 and 2300 for Britain (Fogel 2004; Table 2.3.3n). Alternating feast-famine conditions minimized the accumulation of patho-information-engrams in the biocybernetic regulation system of the body (2.1.2, 2.1.3, 2.5.1.4a). Omran (2005) identified successive stages of epidemiologic transition. This era was termed the age of pestilence and famine (incidence rates of infectious disease mortality is high and fluctuating, curbing sustained population growth; life expectancy low and variable: 20-40 years). During 17th century London c. 55 % of deaths were related to infectious diseases and diarrhea. ***Subject to LHS-modes PM and Pm > pM, high performance vitality (low patho-information-engram loadings) was conducive to acute interactions with disease (fever, infections, inflammation) which prevented or reduced procursive impacts to result in patho-information-engram accumulations (chronic disease factors can only be eliminated through acute healing processes: Section 2.1.2).***

Industrialization phase (c. 1750-1870)

This phase is characterized by increasing resource availability levels and food security for increasing proportions of populations (Table 2.3.3n). Under such circumstances the life history strategy mode for optimal resource utilization is the **LHS-mode Pm > pM**: Maximized use of uninterrupted resource affluence (feast), progressively at the expense of M capacity via LHS-mode Pm>pM(1) specialism and at the expense for autophagous self-healing patho-information-engram-clearing processes, which require transient conditions of resource deficits, i.e. transient famine. Associated trade-off constraints imply high birth and death rates (Table 2.3.3n).

At the beginning of this era, the European marriage system had already ensured that the average family size involved only about 4 to 5 births per couple, even without within-marriage control of fertility (Hirschman 2001). Ages at first marriage were

initially high, then decreasing and proportions never marrying remained relatively high (Table 2.3.3n). Persisting resource level gradients underpinned sustained positive fertility-wealth relationships. Populations increasing (1800-1830; Table 2.3.3n). **Omran (2005)**: Age of receding pandemics (mortality declined progressively as epidemic peaks were less severe or disappeared; average life expectancy at birth increases from c. 30-50 years; sustained and increasing population growth). Following the stage of pestilence and famine, wich had prevailed during the pre-modern and early modern periods, mortality started to decline gradually.

Demographic transition (1870-1930)

LHS-mode Pm > pM (1):

Life history trait combination congruent with energy investment optimization in response to prevailing circumstances. Performance (P) expression maximizing surplus resource use and competitive prowess under conditions of high interference competition requirements (high population density stress), but costly in terms of health and fertility (accentuated P-M trade-off: plasticity scope costs). Fast LHS Pm > pM setting supporting Pm-type expression and early life fertility as underpinned by high metabolic turnover functionality; requiring a fast-LHS setting promoted and actuated by spring births (2.2.2g). Intensified P > M trade-off constraints: growth > maintenance, fertility at the cost of longevity (relatively high mortality; reduced life expectancy; current reproduction at the cost of survival/future reproduction). Fast ageing: increasingly costly in respect of health and health-based fertility.

Use of uninterrupted resource affluence (feast) via LHS-mode Pm > pM at the expense of pM capacity (autophagus self-healing patho-information-engram-clearing processes: activated under conditions of resource deficits, i.e. transient famine). First stage of procursive load accumulation; but which had started already earlier in time in high SES individuals (2.2.2j). Central to the elimination and prevention of the accumulation of patho-information-engrams are autophagous maintenance processes (catabolic) which cannot occur under conditions of chronic overfeeding (feast > famine conditions) and procursive stress impacts (2.1.2). Circumstances of uninterrupted food availability and increased population density stress generally co-occur, resulting in ***procursive overload*** (progressively reduced metabolic functional efficiency). As a

result, the performance-maintenance trade-off increases in intensity, which is associated with an elevated P/M realization ratio: stress proneness, sympathetic ANS overarousal (yang, male functionality) at the expense of parasympathetic functional efficiency (yin, female functionality: 2.3.2a; Table 2.3.2a).
High male competitive performance expression (interference competition): both male and female fitness maximization within the defended monogamous family unit (perceived as a childbearing territory). Prevalence of high performance realization (Pm-types: interference competition manifesting in patriarchal family territoriality).

Maximised utilization of uninterrupted resource affluence (feast) *via* LHS-mode Pm > pM at the expense of pM capacity (at the expense of effective maintenance processing: autophagus self-healing patho-information-engram-clearing processes which reqire activation under conditions of resource deficits, i.e. transient famine). Central to the elimination and prevention of the accumulation of patho-information-engrams are autophagous maintenance processes (catabolic) which cannot occur under conditions of chronic overfeeding (feast > famine conditions) and stress impacts (2.1.2). Circumstances of uninterrupted food availability and increased population density stress prevailed, resulting in ***procursive overload*** (reduced metabolic functional efficiency: 2.2.2e). Progressively increasing fertility-longevity trade-off constraints (2.2.2e; Doblhammer & Oeppen 2003), implying that relatively high fertility is associated with increased mortality/reduced longevity.
Classical models of the demographic transition involve socioeconomic development and modernization as causal drivers (Hirschman 2001); as initiated during the industrialization phase, and a causal link to declining mortality is generally implicated (2.3.3a). During this phase both death and fertility rates are starting to decline (Table 2.3.3n), but birth rates remain relatively high (decreasing age at first marriage; increasing marriage rates consistent with LHS-mode Pm > pM expression as fast-type life history strategy: early life metabolic performance, early reproduction). This is in alignment with expected trade-off constraints of the applicable LHS-mode with Pm > pM vitality (2.2.2e). Fertility-wealth relationship becoming negative during this phase (Table 2.3.3n); attributed to a relaxed effective socioeconomic wealth gradient and the reproductive vitality of the wealthy having been disproportionately compromised by an earlier transgenerational onset of patho-information-engram accumulation

(procursive impacts: Section **2.2.2j**); as induced by relatively higher levels of resource availabilities and population density stress impacting more on the wealthy.

Susceptibility to degenerative diseases increases concurrently with rising living standards/levels of affluence (Frame et al. 1998). Omran (2005): Era of degenerative and man-made diseases starting to emerge (life expectancy rising, gradually exceeding 50 years). Mortality starting to decline gradually; decline progressively more pronounced towards the turn of the 20th century, by which time fertility had started to decline. The author notes that socioeconomic factors were the primary derterminants of this transition; augmented by the sanitary revolution in the late 19th century and medical and public health progress in the 20th century. Degenerative and man-made diseases replaced infections as leading causes of mortality and morbidity in the second and third decades of the 20th century. A gradual shift in disease patterns involved the steady decline of infectious diseases (including tuberculosis and diarrhea) and the moderate increase in cancer and cardiovascular disease (as exemplified in England and Wales up to 1920).

Demographic transition (1931-1960)

LHS-mode pM > Pm (2)

With increasing patho-information-engram load accumulation and associated decline in metabolic functonal efficiency (endogenous energy deficits) and associated increased performance-maintenance trade-off constraints, performance capacity is increasingly compromised and a greater demand for maintenance processes arises (*inter alia* self-healing processes in order to cope with chronic disease loads). In response to these changing energy investment demands the appropriate LHS-mode pM > Pm is associated with declining Pm-type expression and increased investment in maintenance (later life performance/extended life span, fertility postponement, longevity).

Representing a LHS optimization shift to LHS M > P in order to reduce high P-HMT plasticity scope costs: high costs associated with high metabolic turnover functionality. Shift to later age fertility realization (postponement); less health-compromizing lower metabolic turnover functionality; supporting quality rather than quantity of offspring. Continuation of fast LHS setting supporting sustained P capacity realization.

With increasing patho-information-engram load accumulation and associated decline in metabolic functional efficiency (endogenous energy deficits), performance capacity is compromised (accentuated performance-maintenance trade-off, progressively at the expense of performance capacity: 2.2.2e) and a greater demand for maintenance processes arises (*inter alia* self-healing processes in order to cope with chronic disease loads); progressively manifesting in compromised LHS Pm-type expression (reduced P-vitality). In response to these changing energy investment demands the appropriate LHS-mode pM > Pm caters for increased investment in maintenance through a slower-type life history strategy (later life performance/extended life span, fertility postponement, longevity). (2.2.2e).

Conditions of uninterrupted and relatively secured food resource availability (daily supply 3231 calories per capita estimated for England (as an indication for European countries) and associated increased mean body heights and and BMIs of 172.3 cm and 25.9 respectively (Fogel 2004; Table 2.3.3n). Uninterrupted high dietary caloric consumption is an important risk factor for a spectrum of human degenerative diseases and studies have established that increased body weight or body mass index (BMI) is positively correlated with a number of morbidity indices and the incidence of disease manifestations (Frame et al. (1998; 2.5.1.4). As the era of degenerative and man-made diseases unfolds, the decline in infectious and rise in degenerative diseases becomes more distinct after 1930; with 10 % of deaths being attributable to infectious diseases and c. 50 % to heart diseases and cancer by 1960 (Omran (2005).

(**AS: Continued lowering of performance vitality in association with low P/M realization ratios in favour of maintenance processes; subject to accentuation of the P-M trade-off relationship). Low performance vitality for acute disease interactions result further increases of the chronic degenerative disease load (on the basis of accumulating patho-information-engram loadings**).

Mortality continues to decline, eventually approaching stability at low levels, life expectancy rises gradually exceeding 60 years and TFRs decline towards c. 1.7-2.1 (Table 2.3.3n). The fertility wealth relationship remains negative as food security applies to all socioeconomic classes (securing resources for reproductive success for all) and high performance types (generally wealthier) being disproportionately more negatively affected due to higher transgenerationally accumulated and epigenetically

inherited PIE load accumulation (2.2.2j). As individuals are progressively more exposed to population density stress, they tend to suffer from irritability, undue aggressiveness, sense of chronic fear or states of nervous exhaustion and generally increased aggression levels within society (Knaul 1985). Associated with and in response to procursive sequence effects there is a progressive shift towards the LHS-mode pM↑ (4) in the next phase (Second Demographic Transition).

FDT-SDT transition

Two divergent pathways of the FDT-SDT transition towards low fertility are evident; then convergence towards the late phase of the SDT (LHS-mode pM↑(4).

Western-Northern European countries: Lower TFRs than of Eastern European countries during the end phase of the FDT (LHS-mode pM > Pm(2), progressively shifting towards fertility postponement and later involving partial recovery due to fertility recuperation at ages > 30 years, but with fertility still basically remaining below self-replacement levels (LHS-mode pM↑(4): advanced outcome of transgenerational procursive impacts associated with uninterrupted resource abundance and population density stress having resulted in substantial patho-information-engram loads (2.2.2e).

Eastern European countries: Somewhat higher TFRs than of Western-Northern European countries during the end phase of the FDT (LHS-mode pM > Pm(2). FDT-SDT transition: anomy-induced LHS-mode mP↑(3) as stress response adaptation mode. Associated with a short reproductive age span and TFRs declining below those of Western-Northern European countries. Transition towards fertility postponement (LHS-mode pM↑(4), but with insufficient fertility recuperation at ages > 30 years (2.3.3e; Table 2.3.3k). Slower/delayed progression along the FDT trajectory in Eastern European countries due to relatively lower levels of patho-information-engram load accumulation (2.3.3c); reflected in *inter alia* somewhat higher fertility levels towards the end phase of the first demographic transition (2.3.3c).

Predominance of **LHS-mode mP↑(3)** in Eastern European countries; representing a response to exogenous stress/harshness (psych-social/socioeconomic stress: anomy) with fast life history strategy expression. Accentuation of fast-type > slow-type LHS expression trade-off due to some patho-information-engram load accumulation (fast-type LHS: enhanced early life performance, early fertility realization). Energy allocation demands for responding to exogenous impacts of harshness/unpredictability

in Eastern European countries traded off against and thus at the expense of slow LHS features (later life fertility); resulting in a reduced reproductive age span and low TFRs (2.3.3c).

Second Demographic transition (1975-2000+)

LHS-mode pM↑ (4). Due to advanced patho-information-engram load accumulation (procursive overload), resulting in low functional vitality (endogenous energetic constraints) a high demand for maintenance processes continues to prevail; inducing even greater accentuation of maintence processes (M): allocation of energy to survival at the expense of current/early reproduction (trade-off between current and future reproduction: 2.2.2d); but supporting survival (longevity) and later life reproduction (postponement and recuperation of fertility through births at maternal ages above 30 years). Diminished Pm-type expression (reduced male P-vitality); but some sustained P expression capacity through continued fast LHS setting required for coping with prevailing population density stress.

Due to advanced patho-information-engram loads (procursive overload) resulting in low functional vitality (endogenous resource constraints) there is a high demand for maintenance processes. Poor health vitality status is associated with intensified trade-off constraints between LHS traits subject to this LHS-mode (Section 2.2.2e; Doblhammer & Oeppen 2003); implying low performance capacities, especially in males. The associated slow LHS expression (allocation of energy to survival) is at the expense of current/early reproduction; but favourable for survival (longevity) and later reproduction (accentuated fertility-longevity trade-off: low birth rates and low mortality rates apply). Slow-type LHS-mode expression supporting later in life performance (fertility postponement). Accentuated energy allocation demands for responding to endogenous maintenance requirements. Higher and accentuated maintenance investment traded off against performance capacity under the LHS-mode pM↑(4), as induced by associated high PIE loads, imply reduced functional energetic potency/ efficiency/vitality; resulting in *inter alia* impaired brain functional integration, low levels of instinct vitality (2.3.1), low fight-flight reaction thresholds, vulnerability to chronic stress impacts and low levels of male role performance (2.3.2e). Overall, reduced performance vitality (low fight-flight threshold) is evident in response to

coping with stress. Low-vitality stress protective response manifesting in an over-aggressive reaction to minor challenges (fight mode) or flight in reaction to major and persisting (stress resistance through stress escapism).

Widespread manifestation of the chronic immune system dysregulation (CISD) syndrome (2.2.2i). The dysregulated immune system is characterised by functional weakness with low reaction fight-flight thresholds, that is, over-reactive fight responses to weak challenges (allergenic) and flight/escapist responses to strong challenges (non-resolution of acute/subacute disease insults resulting in further accumulated chronicity). The CISD syndrome includes pathological manifestations of what Ruiz-Núñez et al. (2013) termed '***chronic systemic low-grade inflammation induced energy reallocation syndrome***' (reduced insulin sensitivity, increased sympathetic nervous system activity, increased activity of the HPA-axis (hypothalamus-pituary-adrenal) gland stress axis (cortisol resistance in the immune system), decreased activity of the HPG-axis (hypothalamus-pituary-gonadal gland axis), IGF-1 resistance (insulin-like growth factor-1) and the occurrence of sickness behaviour; 2.2.2i).

Continued chronic resource overabundance and population density impacts, further rise in life expectancy, a persisting negative fertility/wealth association, negligible population growth, country-specific TFRs ranging between 1.2-1.9 after c. 1980 (Table 2.3.3n) and declining native European population sizes (2.3.3f). Contrasting fertility-related features, as exhibited during the early phase of the FDT, those of the SDT are characterized by lowered fertility due to postponement of childbearing, fall in the proportions married, increased cohabitation and divorce rates, rising proportion of extramarital childbearing; but also increased rates of childnessless. Furthermore an increasing symmetry in gender roles and female economic autonomy is being experienced (Table 2.3.3m). Fitness measure λ (Korpelainen 2003) involves both fertility timing (tempo) and life time reproductive success (quantum: LRS-life time reproductive success). Late fertility realization compromizes individual fitness in terms of the tempo component, thereby limiting life time reproductive output. Late fertility realization (postponement) and recuperation in the more northern European countries is facilitated by a genetic adaptational predisposition to slow life history modes selected for under cold/cool seasonal climatic conditions; explaining the comparatively higher TFRs of northern relative to southern European countries during this phase of the second demographic transition (2.3.3d).

Consequences of advanced procursive load accumulation, with specific reference also relating to population density stress effects (Knaul 1985; Table 1.2a: Section 1.2), manifesting and mediated by the LHS-mode pM↑(4): Procursive impacts result in transgenerational accumulations of patho-information-engrams, pre-programmed already in parents and grandparents when subject to uninterrupted feast/density stress impacts (2.1.2; 2.1.3; also Knaul 1985). Weakened social hierarchical order and social cohesion (psychosocial incoherence: 2.2.2e). Prevalence of an anti-elitist/anti-authoritan mentality: individuals with special competencies, skills or moral standing no longer receive due respect. Gender differences in roles and behaviour are reduced. Reduced gender differentiation in respect of sexual behaviour and phenotype. Family aspirations and the rearing of children are no longer of high priority (reduced fertility and increasing childnessless). Reduction of sexual vitality (impotence; infertility). Declining reproductive success more pronounced in higher social classes. Diseases of civilization particularly prevalent in urban environments, as expected from intensified population density effects (as paralleled in animal studies under conditions of food overabundance and space deficit; Knaul 1985; Section 1.2: Table 1.2a).

Sympathetic overdominance (Table 2.3.2a) in males, as associated with allostatic load (Table 2.1.2b) results in loss of male performance vitality and in females underpins competitive assertiveness and compromised reproduction associated with decreased/impeded parasympathetic functionality (negative energy balance). Gender role complementarity, as manifesting in a win-win patriarchal value system underpinning male protection and provisioning roles (Table 2.3.2b: Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution), has changed towards an increasing preponderance of gender role competitiveness (for power) in parts of the population. Erosion of patriarchal value system in low vitality males leading to male win-lose competitive behaviour. Generally, manifestations of declining gender role differentiation are evidenced (*vide* Knaul 1985). Female sympathetic overdominance (energy-expensive), manifests at the expense of suppressed parasympathetic functionality (compromised energy balance/body condition for female reproductive vitality; stress proneness: low response reaction thresholds).

Modernist-postmodernist/liberalistic attitudes and associated fertility behaviour (2.3.3a) are proximately underpinning TFRs fluctuating between below replacement

levels and replacement levels (c. 1.5-2.1 and country-specific TFRs after 1980 of between 1.2-1.9); but ultimate causality is attributed to the applicable LHS-mode pM↑(4), influencing both fertility attitudes and low fertility rates partly independently (2.2.2e).
Pronounced population density stress effects (*vide* Knaul 1985: Table 1.2) manifest, *inter alia* relating to aggresive behaviour in sympatheic overdrive (Table 2.3.2a), diminishing gender role differentiation (2.3.2c) and breakdown of social hierarchy and family intactness; generally leading to and representing a state of psychosocial incoherence (Table 2.3.3m).

The second demographic transition, subject to the LHS-mode pM↑(4), is manifesting in the predominance of slow-LHS expression, shaped by accentuated fast-slow LHS-mode trade-off constraints (2.2.2e), and associated with psycho-social incoherence and chronic immune system dysregulation (2.2.2i).

As a result of substantial accumulated patho-information-engram (PIE) loads intensified P-M/fast-slow LHS trade-off constraints prevail during the SDT, as subsumed in the LHS-mode pM↑4. Basic P-vitality compromised; high P-M trade-off constraints associated with high P realization (accentuated trade-off costs).
In response to such trade-off constraints various LHS phenotypes can be differentiated.

High Inherent Performance-Plasticity (HIPP) and Low Inherent Performance-Resilience (LIPR) types.
Plasticity as here defined implicates flexibility in adaptability of an organism to environmental changes or challenges; whereas resilience relates to the capacity of endogenous protective factors and processes to prevent an individual from succumbing to or being harmed by some contextual adversity through the ability to restore or maintain any pre-perturbation functional state (2.2.1d). Plasticity (as genetically-based heritable characteristic: Pigliucci 2007) allows for high performance capacity realization; but the higher the plasticity scope, the lower is the capacity of resilience (involving protective factors/processes curtailing vulnerability to negative experiences under adversity: Pluess & Belsky 2013). Thus, a high plasticity scope underpins high performance breadth permitting both high P performance/fast LHS-mode and high M maintenance/slower LHS-mode expression. Resilience capacity, on the other hand,

underpins invariant high P performance/fast LHS-mode realization in order to cope with and minimizing vulnerability to experienes of adversity (2.2.1d). Furthermore, the results of a study by Inouye et al. (1984) on the heritability of plasma uric acid levels indicate a genetic basis of blood uric acid level, which may have resulted from polymorphisms in purine metabolism pathway, the end product of which is uric acid (2.2.1c). The significant correlation between plasma uric acid level and IQ indicates a contribution of partly common gene loci to the two quantitative traits. Uric acid as an endogenous cortical stimulant (metabolic performance catalyst: 2.2.1c), accordingly promoted the full expression of IQ rather than causing it per se.

The combined genetically inherent capacities for high performance and plasticity scope form what are here defined as High Inherent Performance-Plasticity types (HIPP-types); usually associated with individuals of higher socioeconomic status (higher SES). LIPR-types (Lower Iinherent Performance-Resilience types) represent the combination of lower peak performance, but higher resilience capacities; a combination often associated with individuals of lower socioeconomic status (lower SES).

Summary: **LHS-mode pM↑**(4)

I) LHS optimization shift from predominantly fast to slow-LHS settings

High PIE loading: low P vitality; strong fast-slow LHS-mode trade-off constraints. High SES: Responding to high maintenance demands resulting in further intensified LHS P-M trade-off constraints, supporting slow LHS-mode traits: long-term view; offspring quality > quantity and enhanced later life performance: longevity, fertility postponement and fertility recuperation at maternal ages > 30 years. Plasticity gains of persistent fast-M LHS setting: sustained relatively high performance capacity realization (plasticity scope allowing for combined Pm-type and pM-type expression). Plasticity costs: reduced capacity of resilience under adversity; such as *inter alia* population density stress affecting fertility negatively). Low SES: Responding to *inter alia* high population density stress in predomintantly fast LHS-resilience mode (Fast LHS-mode: early life performance vitality supporting early life fertility realization. Resilience gains: enhanced coping capacity in the face of economic or social adversity; minimized vulnerability to experienes of adversity; relatively higher reproduction rates

subject to conditions of population density stress than in high SES individuals. Resilience costs associated with accentuated fast LHS expression: poorer health status and associated higher mortality rates; restricted later life performance: reduced childbearing age span).

Subject to divergent demands for LHS-mode optimization, differentiation into **LHS-mode phenotypes** became manifest.

HIPP-Pm-type performance realization. Higher SES: higher inherent P capacity and higher inherent plasticity scope (2.2.1c; 2.2.2d). Sympathetic ANS performance (Table 2.3.2a); realization of achievement-orientated behaviour (2.2.1c: competitiveness, social dominance, endurance, cognitive competence, assertiveness); representing plasticity benefits, but associated with plasticity costs. Plasticity benefit-costs trade-off constraints: compromised parasympasthetic ANS functionality (low energy efficiency for the maintenance of normoadaptive body condition: Table 2.5.1.5c and reduced reproductive success, especially in females: Table 2.3.2b). High P/low health-low fertility trade-off combination.
HIPP-Mp-type realization: Somewhat reduced high P/low health-low fertility trade-off constraints in comparison with Pm-type expression (reduced plasticity P benefits and reduced M costs in respect of health and fertility). Mp-type realization (realization of enhanced maintenance investment at the cost of compromised performance capacity: 2.2.2e); but some later life fertility sustained.

LIPR-Pm-type realization. Lower SES: lower inherent P capacity and lower plasticity scope, but inherently greater resilience; 2.2.1c; 2.2.2d). Relatively lower P capacity realization, but resilience in the face of harshness and unpredictability: 2.2.2c; based on fast-LHS realization: 2.2.2d; but less fertility-compromized. Accentuated fast LHS realization: low health status (fast ageing: 2.2.2k) and early life fertility realization sustained due to resilience in the face of poor health status.
LIPR-Mp-type realization. Low SES: resilience capacity in the face of harshness underpinned by fast-LHS expression restricts later life fertility realization; thus resulting in low life time fertility realization. This fast LHS-based low health status trade-off somewhat ameliorated by more investment in maintenance; potentially reducing any P versus health-fertility trade-off constraints.

II) Accentuated P-fast/M-slow LHS-mode trade-off constraints

Accentuated P-M trade-off constraints result in extremized Pm-type and Mp-type expression (2.2.2e). Extremized P-types are in high performance LHS-mode (high metabolic turnover) at the expense of health (2.2.1a/c; 2.2.2j). Extremized M-types exhibit low P-vitality and slow-LHS-mode realization (late fertility realization). Increasing proportions of males and females manifesting as low P-vitality males and assertive/low fertility females, respectively; *inter alia* reflecting diminishing gender role differentiation. A progressive separation into four LHS-mode types is observed: male high performance types with compromised health and low fertility (accentuated fast LHS-mode expression), female high performance types with compromised health and low fertility (accentuated fast LHS-mode expression); and, male and female low performance-vitality types with moderately compromised health and depressed fertility (increased slow LHS-mode expression).

III) Chronic immune system dysregulation

On the basis of low endogenous energetic efficiency due to advanced patho-information-engram accumulation, immune system functionality has become dysregulated; manifesting in the ***chronic immune system dysregulation*** (**CISD**) syndrome (2.2.2i). This manifests as chronic systemic low-grade inflammation *vide* Ruiz-Núñez et al. (2013); and sympathetic ANS (autonomous nervous system) over-dominance (**2.2.1a;** Table **2.3.2a**). The dysregulated immune system is characterised by functional weakness with low reaction fight-flight thresholds, that is, over-reactive fight responses to weak challenges (allergenic) and flight/escapist responses to strong challenges (non-resolution of acute/subacute disease insults resulting in accumulated chronicity). The associated levels of aggression and escapism furthermore underpin psycho-social incoherence.

IV) Psycho-social incoherence: Increasing prevalence of a state of psychosocial incoherence in populations (2.2.2e). Disintegration of traditional social institutions (family/church), dominance hierarchies (largely based on socioeconomic position) and value systems (based on duty rather than rights). Also linked to the build-up of transgenerational population density stress effects (Knaul 1985).

Weakening/dissolution of patriarchy and its fitness maximizing role (Table 2.3.2b: Gender role specialization and complementarity: Energetics, reproductive ecology and

human evolution). Gender role complementarity, as manifesting in a win-win patriarchal value system underpinning male protection and provisioning roles has changed towards an increasing preponderance of gender role competitiveness (for power) in parts of the population. Erosion of patriarchal value system in low vitality males leading to male win-lose competitive behaviour. Generally, manifestations of declining gender role differentiation are evidenced (*vide* Knaul 1985). Assertive competitiveness in female with sympathetic overdominance (energy-expensive), manifests at the expense of suppressed parasympathetic functionality (compromised energy balance/body condition for female reproductive vitality; stress proneness: low response reaction thresholds).

2.3.4 Demographic status assessments

a) Persistence of low fertility

(Table 2.3.2b: Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution)

Doblhammer & Oeppen (2003): After statistical correction for the effects of differences in health and mortality selection before the age of 50, a strong and significant positive correlation was found between parity and late-life mortality for British peerage women. This is consistent with other studies where the generally observed positive relationship between fertility and late-life mortality (fertility-longevity trade-off) was similarly detected; in historical (Korpelainen 2000; Lycett et al. 2000) as well as contempory populations (Doblhammer 2000). In natural fertility populations the fertility *versus* late-life mortality trade-off (negative relationship between fertility and longevity) is mediated by health status. Good health status positively affects both fertility and survival (life span) and can thus result in a dampening or elimination of this trade-off; permitting the concurrence of relatively high fertility and longevity (as applicable to traditionally healthy populations: Section 2.5.1.2). Müller et al. (2002), for historical French-Canadian cohorts (1600-1800s), found that increased fertility was linked to increased post-reproductive survival and that the extended postreproductive life expectancy was tied to late births.
According to the Darwinian theory of evolution all organisms, including humans, are expected to maximize their fitness within relevant socioecological constraints (Voland 2000). Children produced at an early age contribute more to fitness of the female parents than children produced later in life (Stearns 1992, op. cit. Korpelainen 2003). An indicator of fitness, life time reproductive success (LRS) does not take variation in generation length into account. The indicator of fitness λ includes rate measures sensitive to both reproductive quantity (LRS) and timing (parental age of reproductive

events): McGraw & Caswell 1996 (op. cit. Korpelainen 2003). Thus the combination of early reproduction and high LRS implies high fitness (λ). (**AS: This is achieved under the LHS-PM setting: 2.2.2e:2**).

Mueller (2001): Seemingly, given the relatively favourable conditions in industrialised societies, parents could easily have additional children to the few they have, often hardly above replacement level, but they chose not to. Various sociological explanations are implicated: *inter alia* increasing economic costs of rearing children, changing value orientations, alternate sources of satisfaction, long years spent in the educational system and special burdens of working mothers. From an evolutionary perspective however such explanations can only be considered proximate factors. Although prevailing economic and technological conditions may be associated with low mean fertility levels, Mueller (2001) contends that there would still be room for an individual competition for maximum fertility. The author investigates stabilizing selection as an approach to explain the demographic transition in the context of natural selection; an approach not requiring additional assumptions regarding human reproductive decisionmaking. Stabilizing selection implies that some intermediate value of a trait (such as number of children) is optimal in respect of long-term reproductive success. Of the members of the European royality (born between1790-1939) surviving to age 50, 29 % remained childless and the average number of children born had been 2.87. Earlier cohorts had more children. The demographic transition of this population took effect c. 1789-1799 (French revolution).
Results derived from five populations analysed: a monotonic positive association between long-term fitness as reflected by total offspring fertility and lineage survival: the more children, the more grandchildren, the more great-grand children and great-great-grand children. The more children, the greater the number of expected generations to lineage extinction. Thus, the more children the higher the lineage survival probability. No decrease of marginal fitness gain by number of children was detected. These results provide no support for stabilizing selection, i. e. any intermediate optimum of fertility for reproductive fitness. Based on these findings, Mueller (2001) concludes that the maximum number of children is the optimum number of children for reproductive fitness. This is consistent with Kaplan et al. (1995) who showed that men with the most children had the highest number of third generation descendants, in contrast with the observed modal fertility of two children in the population as such. Thus, additional children mean additional fitness gains at a nondecreasing marginal rate. This implies that descendants of families with average fertility can be displaced by the descendants of small numbers of large families.
The majority of individuals of the high-status populations investigated, who could have had a higher number of offspring, refrained from having such. According to the findings of Mueller (2001) descendants of individuals with such average fertility are expected to be displaced by descendants from a small numbers of large families. Accordingly it can be concluded that large families play a disproportionately crucial role in the demographic dynamics of societies.

b) Populatiom replacement

Low and below-replacement fertility make European native populations vulnerable to (genetic) replacement through the influx of non-European migrants (Section 3.1.3: Demographic colonization of Europe).

Immigration into Europe from countries outside of Europe with vigorous population increase rates, still only partly through their fertility transition and with youthful age strcuctures, proceeds at a rapid pace (Coleman 2009). European Union-15 received over one million immigrants per year; with numbers grenerally trending upwards. The gross inflow into EU-27 countries amounted to 3 million during 2006, 60 % of which originating was from non-EU countries (Coleman 2009). Net international migration exceeds natural increase in most European countries (the latter includes births to existing immigrants). One in four or more births in the United Kingdom, France, Germany and other countries are born to immigrant mothers (Coleman 2009). Net immigration has prevented or slowed down population decline where natural increase has ceased (e.g. Germany, Greece, Italy, Russian Federation). According to 2008-EUROSTAT (op.cit. Coleman 2009) projections of population increases for some European countries were between 15 % and 26 % by mid-century, primarily or entirely supported by international migration (Ireland, Norway, UK, Sweden, France and Spain). Of the more prosperous central European countries, such as the Czech Republic and Slovenia, have attracted immigration at levels moderating what would otherwise have represented a large projected population decline (Coleman 2009). It follows from basic rules of demography that populations with sub-replacement fertility and subject to a regular net inflow from foreign populations, will diminish as a proportion of the total population, and be eventually replaced by immigrant-origin populations. Western countries, as subject to sub-replacement fertility and positive immigration, face that outcome unless birth or migration rates change (Coleman 2009).

In summary, the confluence of the second demographic transition in Europe and relative high fertility rates in first world, often wealth-incompetent countries, with their associated poverty and competitive conflicts/crime from which an increasing number of people want to escape (3.1.1), sets the context for genosuicide made possible by an evolution-incompetent leadership failing to maintain the territorial integrity of European countries (3.1.3: Demographic colonization of Europe).

c) Dysgenic reproduction

During the current/advanced stage of the SDT with country-specific TFRs generally below replacement level, the negative relationship between fertility and higher SES is seemingly reversed in Nordic countries when taking education level as proxy for SES. For the years 2007-2011(Eurostat 2013), TFRs (annual averages) of women with low education (ISCED 0-2) ranged between 1.82-1.86, intermediate education levels (ISCED 3-4) between 1.35-1.47 and for those with high educational levels (ISCED 5-6) between 1.53-1.58. Generally, the fertility of women with medium education (ISCED 3-4) had decreased more so than of women with low and high education (Eurostat 2013). In contrast to countries such as Austria, Spain and of eastern Europe (Czech Republic, Slovakia, Slovenia, Estonia, Romania), in Nordic countries of Denmark, Finland and Norway women with the highest education had the highest fertility. This deviation from the general trend of an inverse association of fertility and high SES performance expression during the SDT can be explained by an attenuation of fast P/slow M-LHS-mode trade-off constraints prevalent in more northern European countries on the basis of inherent LHS predispositions shaped by cold-adaptation and low levels of heterozygosity (Table 2.3.3b), supporting relatively increased childbearing age spans in Nordic countries (2.3.3d).

Table 2.3.4a Total fertility rates of European women (TFR: 2007-2011) for categories of employment status and levels of education

	Employment status [a]			Education [a]		
	Employed	Non-Employed		ISCED 0-2	ISCED 3-4	ISCED 5-6
Nordic Europe (Hg I1a)[b] and North-western Europe (Hg I1a)[b]						
Sweden				2.07	1.70	2.05
Norway	1.82	2.42		1,73	1.67	2.07
Finland	1.68	2.25		1.81	1.80	2.01
Denmark	1.87	1.60		1.48	1.60	2.06
Belgium	1.79	2.06				
Central-Northern Europe (HgI1c)[b]						
Germany	0.92	2.43				
Austria	1.36	1.58		1.59	1.40	1.24
Southwestern Europe (Hg Ib2)[b]						
Spain	1.76	1.02		1.77	1.54	0.99
Portugal	1.47	1.25		1.31	1.41	1.49
Eastern-Central Europe (Hg I 1b*)[b] /South-Eastern-Central Europe (Hg I 1b*)[b]						
Czech Rep				2.03	1.45	1.47

Slovakia				3.05	1.17	1.50
Slovenia	1.56	1.32		1.85	1.33	1.80
Hungary	2.01	0.83		1.51	1.08	1.47
Romania	1.31	1.48		1.97	0.89	1.73
Baltic northern Europe						
Estonia	2.10	1.09		2.04	1.55	1.48
Eastern Europe (Hg I 1b*)[b]						
Poland	2.08	1.02		1.45	1.32	1.45
Countries with relatively high TFRs during 1975 (Southern and Eastern Europe) exhibited low TFRs in non-employed women (r = -0.75, P = 0.003); whereas in countries with relatively high TFRs during the years 1997-2011 (Northern Europe), non-employed women had higher TFRs than employed women (r = 0.60- 0.65, P < 0.05). In coutries where TFRs of non-employed women are relatively high (Northen Europe), generally high TFRs positively associated with increased educational level (ISCED 0-2: r = 0.18, P = 0.60; ISCED 3-4: r = 0.55, P= 0.08; ISCED 5-6: r = -0.71, P < 0.02).						
EUROSTAT (2013); [b] Predominance of subhaplogroups (Rootsi et al. 2004)						

Attenuated fast-P versus slow-M LHS realization when subject to pronounced cold-adaptation, particularly prevalent at higher latitudes (2.3.3b:5: Population density stress).

Facilitating wider fertility age spans; also for P-types (of higher socio-economic status) and notably reduced plasticity costs under conditions of lower population density stress.

When subject to relatively lower population densities, disproportionate relative fertility advantages can result (2.3.3b:5; e.g. in low density refugia of higher status individuals).

For the years 2007-2011, in Belgium, Germany, Austria, Romania, Finland and Norway, non-employed women (unemployed and inactive women) had higher fertility than those employed (Eurostat 2013). Germany is a particularly extreme example (Eurostat 2013). The TFR for Germany is around 1.37, that of employed women c. 0.92 (about two-thirds of women of childbearing age) and for non-employed women c. 2.43 (about one-third of women of childbearing age). Income per capita is a strong indicator of level and quality of educational attainment (Aassve et al. 2013).

Pronounced dysgenic fertility patterns: Arden, R., Luciano, M., Deary, I. J., Reynolds, C. A., Pedersen, N. L., Plassman, B. L. McGue, M. Christensen, K. & Visscher, P. M. (2016). The association between intelligence and lifespan is mostly genetic. *International Journal of Epidemiology* 45 (1): 178-185.

INTELLIGENCE-EDUCATION-FERTILITY
FERTILITY-EDUCATION-heiland
FERTILITY-kohler-Education
FERTILITY-GENETICS-rodgers
INTELLIGENCE-nisbett

Earlier onset of procursive impacts in lineages with higher performance capacities drive down fertility. Performance expression is associated with greater vulnerability to procursive load accumulations (2.2.2j). Nobel prize winner Bertrand Russell had already taken note (1957) of the progressive extinction of the best lineages in Western civilization (in people of the Occident).

Mueller (2001): Seemingly, given the relatively favourable conditions in industrialised societies, parents could easily have additional children to the few they have, often hardly above replacement level, but they chose not to. Various sociological explanations are implicated: *inter alia* increasing economic costs of rearing children, changing value orientations, alternate sources of satisfaction, long years spent in the educational system and special burdens of working mothers. From an evolutionary perspective however such explanations can only be considered proximate factors. Although prevailing economic and technological conditions may be associated with low mean fertility levels, Mueller (2001) contends that there would still be room for an individual competition for maximum fertility. The author investigates stabilizing selection as an approach to explain the demographic transition in the context of natural selection; an approach not requiring additional assumptions regarding human reproductive decisionmaking. Stabilizing selection implies that some intermediate value of a trait (such as number of children) is optimal in respect of long-term reproductive success.
Results derived from five populations analysed: a monotonic positive association between long-term fitness as reflected by total offspring fertility and lineage survival: the more children, the more grandchildren, the more great-grand children and great-great-grand children. The more children, the greater the number of expected generations to lineage extinction. This implies that descendants of families with average fertility can be displaced by the descendants of small numbers of large families. The majority of individuals of the high-status populations investigated, who could have had a higher number of offspring, refrained from having such. According to the findings of Mueller (2001) descendants of individuals with such average fertility are expected to be displaced by descendants from a small numbers of large families. Accordingly it can be concluded that large families play a disproportionately crucial role in the demographic dynamics of societies.

d) Parental age effects

Following Kohler et al. (2006), in advanced low fertility countries few women will have children prior to age c. 28-29 years and childbearing at parity one and two will be concentrated in women in their thirties; with very few higher parity births, particularly

regarding in women with a late onset of childbearing. This outlines a situation with very few births after the thirties, but also with few births during the twenties. Increased negative parental age effects are however already experienced for births of mothers between 30-40 years of age relative to those aged 20-30 years.

Young maternal age was most important as predictor of exceptional survival (Gavrilov & Gavrilova 2013). Some empirical evidence indicates that the quality of female eggs in humans sharply declines with age (Comings & MacMurray 2006). Another hypothesis is based on the telomere theory of female reproductive senescence according to which eggs ovulating in older females have shorter telomeres due to a later exit from the oogonial production line, with incomplete restoration by telomerase (Keefe et al. 2005). Also, Gloria-Bottini et al. (2005) reported on negative mother-foetus relationships (negative effects on foetal developments and predisposition to diseases) related to maternal age.

The findings of Dockerty et al. (2001) indicate a higher incidence of childhood cancers born to older mothers and fathers. The risk of childhood lymphoblastic leukaemia was significantly higher among children of older mothers and fathers and significant trends with increasing maternal and paternal ages were found (Dockerty et al. 2001). Individulals born to older parents have increased chances to suffer from deleterious mutations (Tarín et al. 1998); furthermore maternal ageing is associated with higher odds of conceiving a trisomic child or individuals suffering from mitochoncrial DNA disorders (Tarín et al. 1998). According to Bingley et al. (2000), high maternal age increases the risk of type 1 diabetes and this risk of childhood diabetes has increased substantially during the 1980s and 1990s relative to the 1950s/1970s; in parallel with rising ages at first births typical for developed countries.

Gloria-Bottini et al. (2005): The fertility transition in Western countries, as associated with ***delayed childbearing, has detrimental effects on intra-uterine development and increased susceptibility to disease and could bring about change in the genetic composition of the population***. For example, a strong association was found between increasing maternal age at delivery and diabetes in the child. Paternal age was also associated with an increase in risk, but to a somewhat lesser extent (Bingley et al. 2000).
Furthermore, the socioeconomic pressures that have determined in Western countries the drastic reduction in number of children in the family and the childbearing displacement toward an older maternal age could exert a negative pressure on the more

fertile genotypes (which tend to produce early), resulting in similar long-term effects on gene frequencies at the population level (MacMurray et al., op.cit. Gloria-Bottini et al. 2005). It is likely ***that changes in the maternal environment at a stage of life characterized by differentiation and developmental problems and during which intense selection forces are aleady operating will induce adaptive modification of gene frequencies***. Under natural primitive conditions the zygote was best adapted to a maternal environment corresponding to an age closer to 20 years than to 30 years; a displacement of the maternal age to 30 years and beyond could represent a significant change that may induce a negative effect on the survival and development of zygotes, favouring genotypes more resistant to these changes. Over the course of generations this would bring about changes in gene frequencies at the population level. Our preliminary observations suggest that for some genetic systems such changes are indeed taking place.

e) Population ageing

Population ageing involves the narrowing of the population pyramid at the bottom (due to low fertility) and widening at the top (due to extended longevity). Such a demographic situation, as is increasingly experienced in European countries in the context of demographic transitions, results in serious socio-economic problems, especially in relation to the financing of pensions and health care systems (Lutz & Qiang 2002). Diminished relative proportions of the labour force in younger age classes results in perspectives that the problem could be counteracted through facilitating immigration from non-European countries. In the report by the United Nations on replacement migration (United Nations 2000; determined for 2000-2050) it was concluded that the potential of immigration to substitute domestic births was limited (Kohler et al. 2006). Refer also to Alonso (2009) and Grant et al. (2006). In any event any such replacement immigration would accelerate the demographic colonization of Europe (Section **3.1.3**).

f) Population declines of Europe 2000-2100

Lutz & Qiang (2002): For the period 1995-2000, total fertility rates and population growth rate percentages were: World 2.8/1.35, North America 2.0/1.04, Europe 1.4/-0.04, Asia 2.7/1.41, Latin America and Carribean 2.7/1.57, Oceania 2.4/1.37 and Africa 5.3/2.41 (ex United Nations 2001, op. cit. Lutz & Qiang 2002). Currently thus, Europe represents the only continent with below-replacement fertility rates and shrinking populations (see below: Population sizes and percentage changes relative to those in 2000 (ex data Lutz & Qiang 2002).

For the period 1995-2000, total fertility rates and population growth rate percentages (United Nations 2001, op. cit. Lutz & Qiang 2002) of less developed countries (LDC: 3.1/1.62) were considerably higher than those of more developed countries (MDC: 1.6/0.30). In the year 2000, the population size ratio of LDC (4865 millions) to MDC (1191 millions) was 4.1 (United Nations 2001, op. cit. Lutz & Qiang 2002). Towards the year 2075, predicted population size ratios of countries from which migrations targeting Europe are already ongoing/to be anticipated (North Africa, Sub-Saharan Africa, Middle East: 2271 millions) in relation to Western Europe (433 millions) are 5.2 and in relation to all European countries (western and eastern Europe: 679 millions) 3.3 respectively. In 2000, Europe represented 13.4 % of the world's population; predicted for 2100 only 7.2 %. Europe is on the road to demographic eclipse in relation to the rest of the world, as its population proportion will fall from 22 % in 1950 to 7 % of the global population by 2050 (Coleman 2009). The European political, economic and military dominance, which had lasted from the 18th to the 20th century has come to an end, and its old identity is threatened (Coleman 2009).

Table 2.3.4b Worldwide demographic patterns and the latitudinal poverty gradient

	Poverty levels[a]	**Population sizes (in millions) and percentage changes relative to those in 2000 (adapted ex data Lutz & Qiang 2002)**				
World regions*		**2000**	**2025**	**2050**	**2075**	**2100**
World		6055	7827	8797	8951	8414
			29.3	**45.3**	**47.8**	**39.0**
North Africa	22.5	173	257	311	336	333
			48.6	**79.8**	**94.2**	**92.5**
Sub-Saharan Africa	46.0	611	976	1319	1522	1400
			59.7	**115.9**	**149.1**	**145.5**
North America	12.2	314	379	422	441	454
			20.7	**34.4**	**40.4**	**44.6**
Latin America	26.9	515	709	840	904	934
			37.7	**63.1**	**75.5**	**81.4**
Central Asia	14.4	56	81	100	107	106
			44.6	**78.6**	**91.1**	**89.3**
Middle East	22.9	172	285	368	413	413
			65.7	**114.0**	**140.1**	**140.1**
South Asia	17.2	1367	1940	2249	2242	1958
			41.9	**64.5**	**64.0**	**43.2**
	14.6	1408	1608	1580	1422	1250

China region [b]			**14.2**	**12.2**	**1.0**	**-11.2**
Pacific Asia	25.0	476	625	702	702	654
			31.3	**47.5**	**47.5**	**37.4**
Western	15.9	456	478	470	433	392
Europe			**4.8**	**3.1**	**-5.1**	**-14.0**
Eastern	15.8	357	335	290	246	215
Europe			**-6.1**	**-18.6**	**-31.0**	**-39.8**
Poverty levels[a] : Population below poverty line (%): The World Fact Book (CIA)						
	*World regions as defined in Lutz (1996): pages 437-440. [b] China region: China, Cambodia, Mongolia, Hong Kong, Taiwan, Laos, Vietnam.					

Coleman & Rowthorn (2011): The last generations to completely replace themselves in Western Europe were those born in the 1950s (Sobotka 2008). Subreplacement fertility results in populations becoming older for about two generations, after which a new structure is established at an older, but stable age-distribution; ***with population sizes tending towards extinction over time***. Small reductions in fertility have an increasingly large effect on population size. Perceived negative consequences of lowered population sizes of countries: population ageing, negative effects in respect of economic growth/prosperity, relatively lowered military security, decreasing strategic impact of smaller populations on the international level.

Given these demographic circumstances applicable to Europe (Table 2.3.4b), any migration influx has existential consequences. Based on proportions of populations below the poverty line and projected population sizes (2025), 976 million people in Sub-Saharan Africa suffer poverty, 191 million in Latin America, 157 million in Pacific Asia, 62 million in the Middle East and 58 million in North Africa. For these world regions with poverty levels above 20 % (Table 2.3.4b), nearly a billion people (916 millon) are expected to have strong motivation to seek a better life through migration towards the primarily targeted regions of North America, Western and Eastern Europe (which themselves have estimated 2025 population sizes of 379, 478, and 335 million respectively). These estimates must be considerd minimum eastimates of potential migrants since in these regions sizable proportions of the populations even above the poverty line also suffer from relative poverty and crime. The estimated number of potential economic migrants from Sub-Saharan Africa, the Middle East and North Africa (569 million) targeting Europe exceed the population numbers of Western Europe (478 million). Given these statistics, the threat to Europe is enormous (3.1.3: Demographic colonization of Europe) and the overall potential to releave poverty through allowing refugee immigration is minimal. Poverty alleviation can only be

effectively addressed in the poor countries themselves, based on an understanding of poverty dynamics applicable to the relevant countries (2.3.4g).

g) Latitudinal poverty gradient in the context of life history strategy trade-off constraints

Differentiated life history strategies are characterized by evolutionary superiority under the conditions of their selection. Any differences in value systems associated with particular strategies are to be respected. Attaching value judgements would be unprofessional and highly inappropriate.

As will be shown, poverty is primarily a function of the relationship between population size and economic capacity. In terms of fitness maximization, three basic reproduction strategies are involved (Table 2.5.1.1a): the r-Selection reproduction strategy, the K- Selection reproduction strategy and T-responsive reproduction strategies (high T response: fast LHS expression; low T response: slower LHS expression; Table 2.3.4c).

Table 2.3.4c Poverty, reproduction strategies and economic capacity

Latitudinal deviation from the equator: N/S	World regions	Poverty [a]	[b] Population growth (annual %): 1960/2017		Climate	Ancestral selection domains and Life history-reproduction strategies (LHS)
Tropical Zone: Aseasonal or weakly seasonal (Tropical, high temperatures)						
0-10°	**Sub Saharan Africa**	44.9	2.19	2.70	Tropical	SSA: r-Selection reproduction strategy (fast-LHS)
	Pacific Asia	31.7	2.02	1.44	Tropical	PA: Pacific Asia T-R-high: fast LHS
	Latin America	23.2	3.16	1.16	Tropical	LA: T-responsive T-R-high: fast LHS
	South Asia	15.6	2.48	1.55	Tropical	NEC Asia: K-selection: slow LHS[c]
10.1-20°	**Sub Saharan Africa**	50.0	2.15	2.82	Tropical	SSA: r-Selection reproduction strategy (fast-LHS)
	Latin America	33.4	2.81	1.32	Tropical	LA: T-responsive T-R-high: fast LHS
	Pacific Asia	24.1	3.21	1.09	Tropical	PA: T-responsive T-R-high: fast LHS
	China Region	15.5	2.62	1.43	Tropical	NEC Asia: K-selection: slow LHS[c]
Subtropical Zone: Seasonal (spatial differentiations: spatial differentiations: w-ST: warm subtropical; Wt-ST: warm temperate subtropical)						

20.1-30°	**Sub Saharan Africa**	36.9	2.23	1.64	w-ST	SSA: r-Selection reproduction strategy (fast-LHS)
	Latin America	27.6	2.66	1.11	w-ST	LA: T-responsive T-R-high: fast LHS
	North Africa	25.4	2.64	1.84	w-ST	MED: T-responsive T-R-high: fast LHS
	Middle East	24.5	2.29	1.68	w-ST	MED: T-responsive T-R-high: fast LHS
	South Asia	23.9	2.32	1.05	w-ST	T-R-high: fast LHS
	China Region	10.7	1.36	0.2	w-ST	NEC Asia: K-selection: slow LHS
	Pacific Asia	20.0	3.38	1.12	w-ST	PA: T-responsive T-R-high: fast LHS
30.1-40°	**Middle East**	25.1	3.05	1.96	Wt-ST	MED: T-responsive T-R-high: fast LHS
	Southern Europe	23.1	1.48	0.48	Wt-ST	MED: T-responsive T-R-high: fast LHS
	Latin America	17.7	1.48	0.67	Wt-ST	LA: T-responsive T-R-low: slow LHS
	Central Asia	15.9	3.30	1.89	Wt-ST	NEC Asia: K-selection: slow LHS
	North Africa	15.3	2.19	1.21	Wt-ST	Ancestral K-selection: slow LHS[d]
	China Region	9.7	1.36	0.20	Wt-ST	NEC Asia K-selection slow: LHS
Temperate Zone: Cold winter seasonality (c-W)						
40.1-50°	**Central Asia**	16.2	3.59	1.68	c-W	K-Selection reproduction strategy Propensity towards slow LHS realization
	Western Europe	15.0	1.43	0.46	c-W	
	Eastern Europe	13.1	1.44	-0.09	c-W	
50.1-72°	**Western Europe**	13.2	1.13	0.64	c-W	
	Eastern Europe	17.6	1.45	-0.37	c-W	

[a] Percentage of population in poverty/below poverty line (The World Fact Book, CIA)
[b] Population growth. Annual percentage: 1960/2017 (The World Bank Data)
[c] Ancestral Northeast Asian genetic origin (Kim et al. 2000; Bellwood 2018; Matsumura & Hudson 2005): Malaysia, Indonesia, Vietnam, Cambodia.
[d] Franco-Cantabrian genetic origin (SW Europe) of Berbers (Achilli et al. 2005): Morocco/Tunisia.

All world regional populations, excepting some of Sub-Saharan Africa, exhibit declining rates of population growth between 1960 and 2017 (Table 2.3.4c). This is attributed to world-wide demographic transition effects driven by increasing population densities. Demographic transition effects are resisted/counteracted/slowed in populations subject to r-Selection reproduction strategies (robust fast-LHS realization), since reproduction under this strategy is insensitive to negative feedback of population density stress (2.5.1.1b). At the other extreme we have European populations for which the K-Selection reproduction strategy applies as a result of

having been subject to K-selection under conditions of pronounced cold winter seasonality (2.5.1.1; Table 2.5.1.1a; Table 3.1.2a). The K-Selection reproduction strategy is sensitive to population density effects (2.5.1.1b); which have manifested in pronounced declines of population increase rates subject to demographic transition effects between 1960 and 2017 (Table 2.3.4c). In terms of fitness maximization, the r-Selection reproduction strategy seems superior to the K-Selection reproduction strategy in a globalizing world with ever increasing population densities (Table 2.3.4b). The downside to the former is, however, higher poverty levels experienced by the populations involved; notably at advanced stages along the boom-bust trajectory, as the discrepancy between increased population numbers and the economic capacities to support these, increases. A pervasive pattern was revealed of mean poverty levels (Table 2.3.4c) over world subregions grouped according to climatic zones and associated with fast-LHS (tropical zone: 34.5; warm-subtropical zone: 27.7; warm temperate zone: 22.7) or slow-LHS expression (temperate zone with cold winter seasonality: 14.4). Poverty level ranges for Tropical latitudes (0-20°): 50.0-15.5; Subtropical latitudes (20.1-40°): 36.9-9.7; Temperate zone latitudes (40.0-72°): 17.6-13.1. However, poverty level variation was more closely linked to ancestral selection domains which determined whether fast- or slow-LHS realization predominated than latitudinal position of residence *per se*. Poverty level means and ranges (low to high latitude gradient) for ancestral selection domains (from highest to lowest mean poverty levels): Sub-Saharan Africa 43.9 (50.0-36.9); Latin America 25.5 (33.4-17.7); Pacific Asia 25.3 (31.7-20.0); Mediterranean (Middle East/Southern Europe/North Africa) 24.5 (25.4-23.1); Northeast-central Asia 13.9 (15.9-9.7) and North-eastern Europe 14.7 (17.6-13.1). When subject to to ancestral r-selection, fast LHS epression prevails and poverty levels are relatively high (mainly tropical zone). Intermediate levels of poverty are exhibited (around 25) in populations inhabiting tropical/subtropical zones (Pacific Asia, Mediterranean domains) subject to the T-responsive reproduction strategy (Table 2.5.1.1a; Flexible utilization of temperature as resource: high temperature use through fast-LHS expression: early and high reproduction rates. Under lower temperature conditions: shift towards slower LHS expression: later and lower reproductive rates). Populations of ancestral K-selection domains (Northeast-central Asia, North-eastern Europe), with a predisposition to slow-LHS expression, exhibit the lowest poverty levels.

Sinding (2009): A broad consensus has developed over time that as income rises, fertility tends to fall; but tere is little debate about the causal relationship between rising prosperity and declining fertility. That there is a causal relationship running from improved living standards to lower fertility is no longer in much dispute according to the National Research Council (op. cit Sinding 2009). According to Malthus high rates of population growth (fertility) result in societies remaining in permanent states of underdevelopment (poverty; high fertility leading to poverty); whereas Marx argued that high fertility was a symptom, not a cause, of poverty; and that only by bringing about a radical transformation in the underlying causes of poverty would living standards rise and birth rates begin to fall (poverty leading to high fertility). In the absence of longitudinal household information, it is nearly impossible to address the issue of what economists call the 'endogeneity of fertility problem' and thus the direction of causality: does poverty reinforce high fertility or does high fertility lead to poverty? Sinding 2009 conclude that the burden of evidence from micro-analysis is that fertility reinforces poverty and makes an escape from poverty more difficult.

Poverty is a matter of low *per capita* wealth levels which arise as emphasis is placed on fertility (fast-LHS mode realization) at the expense of *per capita* investment based on economic capacity (slow-LHS mode realization). Slow LHS (LHS: life history strategy) realization underpins a favourable ratio of economic capacity to number of offspring/fertility/accumulated population size and is thus supportive of favourable *per capita* wealth, i.e. low poverty levels. Depending on circumstances, either fast or slow LHS realization may be adaptive in terms of fitness maximization. Economic success and capacities, and thus poverty levels, may vary over time and space (due to *inter alia* global economic trends, war or internal conflict), but a pervasive global latitudinal pattern is revealed where poverty is dependent on a climate-linked association with temperature responsive fast-LHS realization prevalent in resident or ancestral populations (Table 2.3.4c).

Generally, tropical, warm subtropical and warm temperate climates cue fast-LHS expression and associated reproduction strategies, whereas cool/cold winter seasonality tends to cue for predominantly slow-LHS realization and associated reproduction strategies (Table 2.5.1.1a). As outlined in section 2.5.1.1 (Table 2.5.1.1a), under the peri-Arctic metabolic performance syndrome (as associated with peri-artic/temperate-type conditions), the combined tolerance capacity for both P (Production processes: growth and reproduction) and S metabolic performance (Survival: body size, energy storage, thermogenesis, metabolic maintenance: slow LHS realization) comes at the cost of comparatively high supporting BMR-settings. Conversely, at the cost of being constrained to narrow metabolic amplitudes, as linked to metabolic functionality strictly in relation and sensitive to resource levels (narrow optimality: resource level

tracking) and with ***high-temperature performance settings*** with low maintenance costs/low BMRs, the tropical metabolic performance mode combines resource-level responsive metabolic performance (capacity for peak performance under resource surplus conditions) with stress resistance (fast-LHS realization: r-reproduction strategy: Table 2.2.2a). The greater the extent of cold-adaptation (partially uncoupled OXPHOS mtDNA mutations re Wallace 2005), as required in increasingly colder, more northern regions, (a) the higher the predominance of slower LHS-mode expression (K-Selection reproduction strategy: Table 2.2.2a) and also (b) the lower any fast-slow LHS trade-off constraints (Table 2.3.3b). Fitness maximization may be pursued through fast-LHS (r-reproduction strategy: Table 2.2.2a) or slow-LHS (K-Selection reproduction strategy: Table 2.2.2a) realization. Early sexual maturity and early commencement of reproduction, as realized through fast-LHS expression, is advantageous through transferring the developmental lead into increased reproduction and is thus positively associated with fecundity, fertility and life time reproductive success, as indicated by the number of surviving children (emphasis on offspring quantity). Slow-LHS traits involve fewer children, greater energy investment per child (offspring quality) and supporting pychosocial traits include commitment to long-term relationships, long-term planning rather than focus on short-term gains, provisioning for the future of offspring through the accumulation of resources (2.2.2d).

Sinding (2009): The conclusion of analyses is that, absent effective programmes to enable individuals to manage their own fertility more effectively, virtually none of the Millenium Development Goals (United Nations Millenium Summit in 2000) can be achieved by the target date of 2015 in the majority of low income countries.
Nevertheless, poverty has been declining in most of the World's regions over the past two to three decades (World Bank: The proportion of the developing world's population living in extreme economic poverty has fallen from 52 % in 1981 to 26 % in 2005).
Poverty in East Asia. Poverty in this region, the world's poorest region in 1981, has fallen from nearly 80 % of the population to 18 %; largely owing to dramatic progress in poverty reduction in China. Between 1981 and 2005, the number of people in poverty has fallen by around 600 million in China alone. In the developing world outside of China, the poverty rate has fallen from 40 to 29 % over 1981-2005, although the total number of poor has remained unchanged at around 1.2 billion.
Poverty in South Asia. Has fallen from 60 to 40 % over 1981-2005; but this has not been enough to bring down the region's total number of poor, which stood at about 600 million in 2005.
Poverty in middle-income countries: Latin America, Middle East and North Africa. The poverty rate has fallen since 1981in Latin America, the Middle East and North Africa, but not enough to reduce the total number of the poor. Despite impressive

fertility declines over the last 30 years, Latin America as a whole has seen comparatively little reduction in poverty or improvement in income distribution.
Poverty in Sub-Saharan Africa. The poverty rate has shown no sustained decline over the whole period since 1981, starting and ending at around 50 %. In absolute terms, the number of poor has nearly doubled, from 200 million to 380 million in 2005. Whatever the reason, African policymakers are not hearing the message that the future of economic development in Africa depends in part on bringing down the extraordinarily high fertility of most Sub-Saharan states.

It is clear that poverty alleviation, in regions of the world where fitness maximization is pursued through high-temperature responsive fast-LHS expression, requires a two-pronged approach, involving both the enhancement of economic capacity ***and*** interventions to curb population growth (as similarly recognized by Sinding 2009). Without the latter, enhancement of economic growth on its own cannot realistically and sustainably result in poverty alleviation. It must however be kept in mind that, whilst materialistic Westerners consider poverty as highly undesirable, in other population groups of the world having few children is considered unsatisfactory. External interventions in order to achieve poverty alleviation through a two-pronged approach will accordingly be constrained by conscious or subconscious resistance by local populations.

h) Sociobiological dysfunctionality

Europe is mired down in a state termed the "second demographic transition"; characterized by psychosocial incoherence, manifesting in the decline of marriage, rising cohabitation, rising divorce rates and childnessless; progressive dissolution of gender role complementarity, increasingly replaced by scramble competition for power between the sexes (2.3.3e), as underpinned by an increasing loss of male performance vitality, associated with a compromised vitality/capacity of males to fulfil traditional male roles relating to protection and provisioning; as performed through patriarchy (Table 2.3.3m; Table 2.3.2b). Low levels of instinctual vitality for fitness maximization is evident (2.3.3e). In the associated state of psychosocial incoherence and win-lose competition between the sexes becoming increasingly evident, negative inter-gender behaviour (*inter alia* inter-gender harrassment), notably against women, is increasingly manifesting (following a change from win-win gender role complemetarity to win-lose competition for power during the SDT-phase). Smuts (1995), like feminists in general, attribute this to the persistence of patriarchy. This, however, is difficult to reconcile

with the historical pattern where patriarchy at the height of its expression (Middle Ages) was characterized by chivalry (warrior ethos) when women were notably respected and protected; in comparison and contrast with the current SDT (second demographic transition) stage where patriarchy is in dissolution (Table 2.3.3m).

Smuts (1995): Evidence from other primates of male sexual coercion and female resistence to it indicates that sexual conflicts of interest that underlie patriarchy predate the emergence of the human species. Humans, however, show more extensive male dominanceand male control of female sexuality than is shown by other primates (implicating an unusual degree of gender inequality). Feminist theory focuses on on issues of power: who has it, how they can get it, how it is used and what are its consequences. Many prominent feminist theorists argue that control of female sexuality lies at the heart of patriarchy (e.g. Lerner 1986, op. cit. Smuts 1995; MacKinnon 1987, op. cit. Smuts 1995). The central thesis of this article is that the origins of patriarchy lie far back in time, long before the development of agriculture, civilization, capitalism, or other similarly recent phenomena normally invoked by feminists to explain patriarchy (e.g. Lerner 1986, op. cit. Smuts 1995). For feminists, patriarchy is primarily an issue of male power over female sexuality.
Based on her analyses of relevant primate sociobiological features, Smuts (1995) concludes that patriarchy is the product of reproductive strategies typically shown by male primates, which in humans have undergone unusually effective elaboration.
Female and male mammals often have different reproductive interests, and these interests are often in conflict. Male interest in mate quantity combined with female interest in mate quality, creates a widespread conflict of interest between the sexes. The conflict is mitigated when males court females offering them the benefits females want from males such as food, protection or help in rearing young. (**AS: which would be applicable in the case of intact monogamous patriarchy**).
Evidence from non-human primates leads to four hypotheses regarding factors that could account for the evolution of patriarchy:
Hypothesis 1. Among ancestral homonids, female ability to resist male aggression was compromised by reduced social support from kin and female allies.
Hypothesis 2. Over the course of human evolution, male-male alliances became increasingly well-developed. These alliances were often directed against females, and they increased male power over females.
Hypothesis 3. Over the course of human evolution, and particularly since the advent of agriculture and animal husbandry, males gained control over resources that females need to survive and reproduce. This increased male ability to control and coerce females.
Hypothesis 4. Over the course of evolution, male socio-political arrangements increased the variance in male wealth and power and perpetuated family differentials across generations. As a result of increasingly unequal relationships among men, women became increasingly vulnerable to the will and whims of the few powerful men, and women's control over their own sexuality was greatly reduced. (**AS: Feminists are exceedingly concerned about males controlling female reproduction, but the sociobiological fact that female choice of the male partner for childrearing purposes is predominant in humans, despite the notion of the male being the 'hunter' (Knaul 1985), has escaped them**).

Furthermore, Hypothesis 5. In pursuing their material and reproductive interests, women often engage in behaviours that promote male resource control and male control over female sexuality. Thus women as well as men contribute to the perpetuation of patriarchy. Thus, with reference to patriarchy, Smuts (1995) concludes that:
Firstly, the ultimate goal of male control over females is reproduction: men coerce, constrain and dominate women in order to maintain control over female sexuality and the offspring women produce. Secondly, the ultimate sanction underlying male control over females is often: the use of physical force or violence to inflict costs on females who resist male control. So the ultimate goal is the control over female reproduction, and the ultimate sanction is to achieve this goal is violence. (**AS: As a feminist ideological construct, patriarchy is accordingly defined as a behavioural dispensation with the goal to control female reproduction, with violent means, if necessary. In the real world, however, intact patriarchy is a behavioural dispensation supporting fitness maximization for both males and females**).

Sociobiological behavioural dispensations, such as patriarchy, can only emerge and be sustained if and to the extent they contribute to fitness maximization of ***both males and females*** (supporting the genetic representation into future generations). For populations with a K-Selection reproduction strategy (Table 2.5.1.1a), the patriarchal monogamous family would represent such a behavioural dispensation (females harnessing male power for their fitness maximization versus challenging male power in the context of competition for power during the SDT-phase). The core element of patriarchy in this context is gender role complementarity, with males responsible for protection and provisioning in support of efficient female bearing and rearing of quality offspring.
Gender role complementarity, as manifesting in a win-win patriarchal value system underpinning male protection and provisioning roles (2.3.2c; Table 2.3.2b: Gender role specialization and complementarity: Energetics, reproductive ecology and human evolution), has changed towards an increasing preponderance of gender role competitiveness (for power) in parts of the population. Erosion of the patriarchal value system in low vitality males leading to male win-lose competitive behaviour (2.3.2). Generally, manifestations of declining gender role differentiation are evidenced (*vide* Knaul 1985).
Both male and female fitness is ensconced in monogamous patriarchal family units (female fitness benefits through the monopolization of male protection and provisioning and male fitness through the monopolization of the reproductive capacity of the attached female). Within the context of patriarchy, males are safe-guarding their mating contribution and functional role efforts in order to ensure that associated benefits actually accrue to their own genetic progeny through a defended family unit

(patriarchal family household); thus with interference competition supported by adequate levels of male competitive performance capacity. Female reproductive fitness is secured by keeping the monopolization of benefits derived from the particular male involved, intact (2.2.2e). The importance of biparental care (father absence as early stressor) for positive sociopsychological health outcomes in offspring has been documented (2.2.2c: Ellis et al. 2003; Quinlan 2003). In human females there are physiological and behavioural adaptations which are consistent with an evolutionary history involving male parental investment: food provisioning by males during pregnancy when females reduce their metabolic rates for efficiency of fat storage and during lactation women in foraging societies reduce their work effort and focus on high quality child care (Ellison 2001, op. cit. Kaplan & Lancaster 2003). Male protection of and provisioning to the female/family unit (effectively achieved with sympathetic ANS functionality) permits the mother to remain in a state of parasympathetic functionality underpinning reproductive and rearing success (2.3.2c). Congruent with the sensitivity of the regulation of female reproduction to energetic condition, high work loads of females and exposure to stress typically affect female fecundity and fertility negatively (e.g. Kaplan & Lancaster 2003). This is congruent with the critical importance of maternal energetics for reproductive success (2.3.2c; 2.3.2b; Table 2.3.2b: Ellison 2008; Jasienska 2003). Sympathetic overdominance in females, underpinning female competitive assertiveness, is energy-expensive and manifests at the expense of suppressed parasympathetic functionality (2.3.2a/b; Table 2.3.2a); resulting in compromised energy balance/body condition for female reproductive vitality; stress proneness: low response reaction thresholds; female win-lose competitiveness. Unresponsive parenting is positively associated with stress levels in children (as indicated by elevated cortisol levels) and children of single mothers tend to have elevated cortisol levels (op. cit. Quinlan 2003). In addition to more overt forms of pretection provided by males, the role of fathers in minimizing maternal stress during all reproductive/rearing phases is thus of crucial importance for parental reproductive success; both in terms of quantity and quality of offspring (refer also to 2.6a).

It is concluded that, in a state of persistent psycho-social incoherence, as characteristic of the current, advanced state of the SDT, recovery of normal reproductive competence able to sustain population sizes in Europe, is not to be expected.

i) Population policies

Hank (2001): Couples intending to have children or already have small children leave cities and tend to move to suburban belts representing semi-rural areas advantageous for families (*inter alia* in terms of quality housing conditions: Frick 1998, op. cit. Hank 2001). These suburban zones are important to focus family policies providing for children-favourable conditions (maintaining semi-rural character, geening, sufficient house spacing and appropriate house specifications).

(**AS: the importance of low population density stress zones. When subject to relatively lower population densities, disproportionate relative fertility advantages can result (2.3.3b: e.g. in low density refugia of higher status individuals**).

Kohler et al. (2006). The only viable long-term strategy to limit population ageing and decline in population sizes is to increase the levels of fertility. An increasing number of Eropean countries recognize their low birth rates as crises jeopardising the basic foundations and threatening the survival of their nations. McDonald (2000b, op. cit Kohler et al. 2006) presented a policy toolbox aiming to counteract low fertility. This includes ***financial incentives*** (periodic cash payments to parents for each child; lump sum payments or loans at the time of the birth of a baby; tax rebates, credits or reductions based on the presence of a child; free or subsidized services or goods, including education at all levels, some health services, public transport, and others; housing subsidies in various forms depending on the prence and number of children); ***work and family initiatives*** (maternity and paterny leave, subsidized child care, flexible working hours, gender equity in employment practices); ***broad social change supportive of children and parenting*** (employment initiatives that improve job prospects of young men and women, child-friendly environments: including traffic calming, safe neighbourhood policies, provision for children in places of entertainment and in shopping centers); ***gender equity*** (*inter alia* support of workers with family responsibilities irrespective of gender); marriage and relationship supports (including the provision of greater encouragement in the formation of relationships, and economic incentives to marry, e.g. housing assistence) and ***development of positive social attitudes towards children and parenting*** (including a clear message that people desiring children will be supported by society).
Policies which are aimed at reducing the pace of fertility postponement, or reversing the trend, have also been proposed (Lutz et al. 2003, op. cit. Kohler et al. 2006).

Kohler et al. (2006) however caution that even if some of the mentioned policies are effective, future declines in the number of women/couples in childbearing ages will limit the impact of any population policies in the short- and medium term future. The number of women in childbearing ages are projected to decline by 35 % for Europe between 2000-2040. The negative population momentum (Lutz et al. 2003, op. cit. Kohler et al. 2006), already built into the current population structure, fertility policies, even when effective on the individual level, implies that only limited effcts can be expected on slowing population ageing and reversing declines in population sizes.
Generally, there seems to be consensus among studies that population policies have only a moderate and long-term effect. Studies reviewed in Sleebos (2003, op. cit. Kohler et al. 2006) provide mixed conclusions regarding the effects of various policies on fertility behaviour. Kohler et al. (2006) conclude that policies increasing the compatibility between childbearing and female labour force participation and reducing uncertainty in early adulthood as a result of high unemployment and related factors, are the most promising.

Grant et al. (2006). European countries are faced with increasing welfare costs associated with an increasing population of the elderly and a declining work force: a big challenge in view Europe's Social Agenda involving full employment, economic growth and social cohesion. Based on a comprehensive literature review, Grant et al. (2006) identified some policy implication for member states of the European Union:

- Population ageing cannot be remedied through replacement immigration. Permitting large numbers of work-age immigrants into EU nations is neither feasible nor sustainable as a strategy to offset population ageing (UN 2000): (a) Levels of migration needed to offset population ageing and maintaining potential support rattios would be extremely large; (b) Any rejuvenation effect of migration is modest and unlikely to have a long-term effect and (c) The success of immigration strategies depends on the successful integration of immigrants, which is considered problematic with large contingents of migrants.
- Governmemt policies can slow declines in fertility rates. Family policies that involve employment policies allowing couples to combine family responsibilities with work appear to be the most effective (e.g. Sweden).

- No single policy works. No single policy intervention can reverse low fertility in all cases. Family policies may be necessary, but are not sufficient for affecting fertility levels.
- Political, economic and social contexts influence policy impacts.
- Population policies take effect slowly. Government policies intended to reverse fertility declines require a long-term focus and many years to implement. There is thus a disconnect between short-term priorities in line with electoral cycles (4-5 years) and longer term implementation of population policies. Politicians accordingly tend to prioritize short-term policy implementation related to socio-economic security reforms rather than, often politically contentious, population policy implementation.

Brewster & Rindfuss (2000).

Demeny (2011). Whereas substantial population increases in less developed countries are anticipated in coming decades; aggregate fertility levels inadequate for population replacement in developed countries, policies confronting such low fertility levels have/are receiving much attention in some European countries. Incentives to increase the willingness of couples to have children include differential taxation favouring familes with children, services such as free or subsidized day care centers for pre-school children provided by public programs or mandates imposed on the private sector. However, the net effect of family-friendly redistribution of incomes and provision of relevant services on the willingness of potential parents to have children remains unclear. Low fertility despite general material affluence in industrial economies is often linked to the double burden on women of raising children and pursuing successful carreers (working outside of their homes). Measures enhancing the compatibility between raising children and labour force participation seem effective in respect of couples having one child or even two. It is however unverified that such measures can sustainably increase the proportion of the number of women having more than two children. There is thus little indcation that such measures can achieve replacement level fertility. Continued prevalence of subreplacement fertility represents a clear threat to the continuing viability and survival of the involved countries as demographic collapse takes effect. Responsible European governments would consider such a situation as a crisis requiring adequate pronatal policy responses. Demeny

(2011) discussed options more appropriate to the severity of the situation. Once European governments embrace long-term horizons and realize that they are confronted with survival-threatening circumstances, more unconventional pro-natalist policies may become politically acceptable/unavoidable.

2.3.5 Sociobiological demographic trajectories during and beyond demographic transitions

a) Demographic trajectories under r- and K-selection

K-selection LHS-mode PM (plasicity)
Rising and falling demographic implosion
r-selection fast LHS-mode (robustness)
boom to bust demographic implosion
Regarding both trajectories we have an initial phase of social win-win harmony (expressed as ubuntu in Africa), followed by an extended phase of increasing populations and mounting population density stress (win-lose), then ultimately cumulating in demographic implosions.

Peri-Arctic metabolic performance syndrome (Table 2.5.1.1a): K-Selection reproduction strategy
Europe (cold winters): K-Selection rise-fall trajectory:
FDT-SDT-protracted demographic implosion

Subtropical metabolic performance syndrome (Table 2.5.1.1a): T (temperature)-responsive reproduction strategy
Latin America (warm summers, cool winters): Tranquility to exodus demographic trajectory. DOC LATIN-AMERICA-frank
Fast LHS realization: high early fertility/low economic capacity (2.3.4g)
Increasing population numbers and population density stress; increased fast LHS response; burgeoning population densities of/in especially lower SES classes; reinforcing progression along the tranquility-exodus demographic trajectory; general population increasingly subject to poverty and crime; exodus: attempts to escape circumstances of high crime and poverty through out-migration.

Fast-slow; 222d p 151; 222c Harshnes/unpredictability p 146/147; 222j SES p 190 present orientation

Tropical metabolic performance syndrome (Table 2.5.1.1a): r-Selection reproduction strategy
Sub-Saharan Africa (aseasonal, warm climate): boom to bust demographic trajectory.

Wealth-deficient countries are usually entangled in a demographically-driven poverty trap (2.3.4g); placing these countries on a socioeconomic-psychological boom to bust trajectory (2.3.5a). During initial phases along this trajectory (boom phase) levels of population density and resource competition are relatively low and psychosocial harmony prevails. With progression towards the bust phase, as the relation between population density stress and per capita wealth becomes successively more unfaviourable, competition for livelihood resources intensifies, poverty and psychosocial intolerance levels increase, increasing ideological polarization manifests, increased vulnerability to emerging disease epidemics, crime rates and civil unrest increase and the incidence of violent conflict escalates; often culminating in population displacements and civil wars (2.3.5a).
Scarce remaining resources increasingly monopolized by the more powerful
Power and resources concentrated by politicians (power/ resource monopolization capacity), not professionals (capacity for economic efficiency), resulting in further compromization of economic efficiency (as the bust stage is is approached).

Under conditions of low human population carrying capacities (supporting only relatively slow population increase rates), extended boom phases are sustained (protracted phases of slow population increase, accounting for critical resource availability/per capita discrepancies only being reached after relatively extended time periods). Colonialism, by establishing socioeconomic conditions resulting in increased human population carrying capacies and associated conditions of accelerated population increase rates, resulted in critical resource availability/per capita discrepancies being reached after relatively shorter time periods and maintained over longer time spans (chronic fixation of pre-bust circumstances and attenuation of demographic bust effects, i.e. population declines). The result of this is that populations exist in boom phases for relatively shorter durations in comparison with existence in

protracted pre-bust phases (colonialism → shorter duration in boom ('paradise') relative to bust ('paradise lost') phases: from 'paradise' to 'paradise lost'). Also, historically, large areas were uninhabited and population density build-ups were alleviated by people from inhabited areas migrating into such uninhabited areas as their population densities increased; thereby preventing population densities to increase along the demographic trajectory towards the bust phase. This left large areas in boom phases for extended periods.

Mabovula (2011): Core humanistic attributes of Ubuntu: being caring, humble, thoughtful, considerate, understanding, wise, generous, hospitable, socially mature, socially sensitive and virtuous: character attributes that veer away from confrontation towards conciliation. Khosa (2005, op. cit. Mabovula 2011) defined Ubuntu as "an African value system that means humanness or being human, a wordview characterised by such values as caring, sharing, compassion, communalism, communocracy and related predispositions". Ubuntu regulates the exercise of individual rights by emphasising sharing and co-responsibility and the mutual enjoyment of rights by all. It promotes good human relationships and enhances human value, trust and dignity. Ubuntu as based on four principles (Mbigi 1997, op. cit. Mabovula 2011): I) Morality which involves trust and credibility; II) Interdependence which concerns the sharing and caring aspect that is co-operation and participation; III) Spirit of man which refers to human dignity and mutual respect that insists that human activity should should be person-driven and humanness should be central; and IV) Totality, which pertains to continuous improvement of everything by every member.

Erosion of Ubuntu as communal value system.
Community members no longer trust each other. Lack of discipline, violence, crime, and aggressive behaviour in society become the accepted facts of life. Regardless of fluctuations and rates of incidence and categories, the erosion of traditional codes of humanism continues to create an ongoing challenge to African communities. A sudy conducted during 2004-2008 revealed that school children from different kinds of communities showed little respect for their principals in schools, parents, educators, elders, and friends. The prevailing worsening deterioration of Africa's social fabrics outlined above is endorsed by a study of Waliggo (2005, op. cit. Mabovula 2011) revealing that contemporary African society does not take the current economic immorality and crimes which involve fraud, embezzlement of public funds, corruption and abuse of office seriously.

b) Life history adaptations and demographic transitions

In response to prevailing/anticipated conditions/circumstances the body adopts particular LHS settings which support fitness maximization

Homozygosity

Homozygosity. Earlier advance to pM4 and pM5 ? North more or earlier. Homozygosity in general increased towards the north: reduced M-P trade-off constraints. Link to cold adaptation. (both fast-slow and P-M tradeoff costs ameliorated/buffered by homozygosity and cold adaptation. Explore homozygosity-cold adaptation link: both reduced trade-off intensity; but sensitivity to PIE loads disrupting trade-off amelioration).

Homozygosity – slow LHS association.

Low trade-off intensities of P vs M: supporting LHS-PM combination; implying absence of male vs female physiological/dimorphism and fast vs slow: underpinning fast-slow LHS trait combination; favouring LHS-PM modes

SAR LHS-M-P (matriarchal households/patriarchy combination; check Table 2.3.3m)

Endogamy reduced M-P trade-off.

273 Pronounced homozygosity has been reported to favour male longevity (Poulain et al. 2011). Mechanisms relating to the predominance of slow life history strategy-mode expression, indicative of slower rates of ageing, seem to be involved. Slow-LHS expression typically manifests in late female reproductive behaviour, slow somatic aging and longevity. Similarities observed between the spatial patterns of late fertility and longevity seem to be related to higher endogamy/consanguinity, i.e. homozygosity (Montesanto et al. 2008; Poulain et al. 2011; Lisa et al. 2015). High heterozygosity levels reflect an underlying inherent predisposition towards increased P-fast versus M-slow LHS-mode expression (Fast-LHS-mode realization: early life fertility realization, fast ageing); as increasingly more prevalent in southern European populations. Low heterozygosity, i.e. homozygosity, underpins an inherent predisposition for slower LHS-mode realization (later life fertility realization, slower ageing); as more prevalent in northern European populations (Table 2.3.3b).

K-selection: Plasticity; Density

Fast-LHS-setting in response to food resource abundance (food resource use) and coping with population density pressure (P capacity realization in a trade-off relationship with health/fertility: increased P-M trade-off constraints; LHS P > M to M > P)

K-selection: 1. Performance at carrying capacity; 2. Population density stress sensitive. Plasticity: use of scarce resource space at carrying capacity. pM4 tolerance to migrants; pM5 increasing intolerance to migrants.

K-Selection syndrome: how to deal with population density effects at carrying capacity. NW-S-E. (Plasticity scope increased physiological reactivity amplitude)
Homozygosity/cold adaptation/Table 2511a/PM reduced trade off/plasticity-resilience-off

Coping with population densities approaching or at carrying capacity. Slow LHS PM setting or fast LHS setting
From fast LHS P > M settingto fast LHS M > P setting (mortality down, life expectancy up, P vitality downas P-M trade off costs constraints increase)
To fast LHS M4 setting STRONG TRADE-OFF PHENOTYPES to slow LHS M(P) setting. Phenotypes: weak M-P trade-off
High SES slow LHS M(P↑)
Low SES slow LHS M(P↓)

Fast LHS setting for fast-P resilience in coping with population density and social stress (sympathetic ANS functionality) and for resource surplus utilization.
PIE up: P-M trade-off up. Fast LHS P > M, P up M down. Fast LHS M > P, P down, M up, mortality down, longevity up, life expectancy up

E reduced P-health trade-off, resilience; some sustaiuned vantage sensitivity? Sustained P-vitality, but restricted childbearing age range: fertility down (resilience costs)
NCS Plasticity PIE up non-PM; differential susceptibility trsde-offs. Pm up accentuated P health/fertility trade-off; as P down and M up (LHS M > P; M4) accentuated plasticity costs for M up in the form of P down; but relaxation under LHS M(P)5
N Association of highrr SES and low density refuge areas P > M to M(P); wider childbearing age span

C High Pm-types associated with high density stress (indusrializatio/urbanization); P-fertility trade-off. Career opportunities, especially for high SES Pm-types (competent and competitive), city-based: high sociospatial density stress: low TFRs.
Page 277 Geist

Plasticity vs resilience re slow LHS effects NS/WE. Resilience: Cold adaptation E(cold adaptation-H-types-anomy)-W; Heterozygosity-temperature S-N fast LHS.
Refer to pages 194-194.
S: From PM to P > M via fast LHS, P up/M (heterozygosity, temperature). GO TO SEASONALITY AND CHECK TEMPERATURE/LATITUDINAL POVERTY GRADIENT.
pM4-fast; P-M trade-off: fast for P up as M up postponement; fast-slow trade-off, early-later fertility: later fertility at cost of early fertility; but insufficient later fertility for recuperation. Resilience costs (associated with heterozygosity/less cold adaptation). Fixation on early P realization via fast LHS expression (resilience effect) restricting later life fertility. Narrowed childbearing age span.

E: Geared/fixed to coping with population densities at carrying capacity. PM (homozygosity, cold adaptation); PIE accumulation: Increasing P-M trade-off constraints; fixation on P-fast LHS capacity realization P > M/mP3. Resilience in coping with anomy/social/population density stress: P-early life performance capacity based resilience. P-fast LHS expression strong trade-off re M-later life fertility. When associated with postponement and no recuperation. Narrow childbearing age span. TFRs down. Reduced plasticity scope, but also reduced plasticity trade-off costs.

2.3.3b On the basis of ancestral migration patterns two divergent phenotype dispositions were derived: D-conditioned phenotypes shaped under conditions of dispersal and H-conditioned (territory-holding) phenotypes having arisen in sedentary, more densely packed populations. The former pertaining to western, central and northern European populations and the latter to eastern European (Slavic) populations; characteristically associated with inherent predispositions of plasticity/generalism supporting abilities to cope with diverse contingencies and robustness/resilience/specialism in coping with competition under conditions of population density pressure; respectively (as outlined above and summarized in Table 2.3.3b).

Ex p 281: 233b Generally NWS also under LHS- mode PM section

233b p 265+ cold adaptation 233b p 279-280-281

pM5. Sustaining some P-fast capacity (resilience) with reduced trade-off costs i.t.o. M (health/fertility). To variable degrees depending upon resilience capacity (P-fast LHS expression) N-E-C-S. Relatively high P-up/sustained and recupero/e (rel. low P); relatively high P-up/sustained and some recupero (C and E rel. high P), depending on P/M realization ratio.

Reduced P-M trade-off re offspring (prenatal P up cueing). Wider childbearing age span, depending on plasticity scope inversely related to resilience capacity (N > CE > S). N: P down, scramble competition extramarital births up versus P-fast based resilience up, interference competition, family-based fertility, low levels of extramarital fertility.

However, as PIE loadings accumulated during the course of the demographic transition, fast-slow LHS trade-off constraints (LHS-mode pM↑:4) are intensified, more so in individuals of countries subject to inherently faster LHS-modes towards the south/south-west of Europe; but less so in more cold-adapted northern European countries (more relaxed fast-slow LHS trade-off constraints).

Sort out plasticity gains and costs, N vs S, re homozygosity/cold adaptation
PIE up: M demands go up, shift towards slow-M LHS expression/requirements; P down, little PM capacity; f-P/s-M trade-off (reduced combination scope). Initially f-P > M. then s-M > P as DT unfolds. Unerpinning LHS with minimum P-M trade-off and the roles homozygosity, cold adaptation, autophagy/fasting and dietary factors.
Associations: Fast-P-LHS capacity/expression and heterozygosity with reduced plasticity gains and costs; and, slow-M LHS expression with homozygosity and cold adaptation with increased plasticity gains relative to plasticity costs (relaxed trade-off constraints; especially associated with LHS-mode PM).
S-EU Relying on early fast-P fertility. P capacity heterozygosity-based. PIE up, weakening P (shifting to slower-M LHS expression; intensified f-P vs s-M trade-off), but little capacity for fertilityreplacement at later ages.

C High plasticity trade-off costs re pop dens stress esp on P

S and E narrowed plasticity scope = resilience costs. 1975 pre-postponement

S vs E.

S T-linked fast LHS trade-off relationships; plasticity scope costs high-fast P (opportunistic, risk-taking, use of currently available opportunities, coping with immediate adversity) at the cost of M-slow LHS capacity (at cost of later life-maturity-competence, long-term strategic approach, wealth-creation capacity realization, risk

aversion). High fast-P to slow-M trade-off costs. Postponement (M up) brings down fertility; and also later life type P competencies (M up; P down). Intensified fast-P expression is accompanied by substantial loss of later life/M competencies (Latin American demographic trajectory).

E Restricted plasticity scope. Resilience costs. High performance restricted/constrained to fast P LHS expression; high increased slow LHS expression (later life fertility realization; postponement) at the cost of at the cost of early life fertility realization, but not P competence (resilience gains). Reduced P-M trade-off costs (resilence gains); but strong fast-slow LHS expression trade-off costs. Postponement brings down fertility, but not P-competence. Robustness of maintenance of P capacity in spite of shift to slower LHS expression.

In Dysgenics p336. Cross-talk with K-selection and dealing with population density stress

Under acute LHS trade-off constraints (not PM, but P-supporting fast LHS realization/expression subject to population density stress): Pm-type expression have health-fertility trade-off costs.

Cross talk to DYSGENICS

Post-fall low population density advantage for LHS PM based reproduction in post-fall populations subject to a K-selection reproduction strategy underpinned by LHS-PM type realization more pronounced under conditions of cold seasonality adaptation (latitude/altitude) Low population density enclaves/P-type association. P-types monopolizing space as resource in association with other livelihood resources (re-emergence of positive fertility-P-type association) Low density circumstances (relatively; increased positive sensitivity of fertility to low population density stress) P-type/fertility association only cold adaptation Role of cold adaptation versus advanced stage of adaptation

222e Minimum fast-slow LHS trade-off constraints support fitness maximization. According to the theory of evolution of organisms, including humans, are expected to maximize their fitness within relevant socioecological constraints (Voland 2000). Children produced at an early age contribute more to fitness of the female parents than children produced later in life (Stearns 1992, op. cit. Korpelainen 2003). As indicator of fitness, life time reproductive success (LRS) does not take variation in generation length into account. Thus, as an appropriate indicator of fitness λ includes rate measures sensitive to both reproductive quantity (LRS) and timing (parental age of reproductive events: McGraw & Caswell 1996, op. cit. Korpelainen 2003). Thus high fitness (λ) is achieved through the combination of early reproduction (fast-LHS mode expression) and high LRS (slow-LHS mode realization), as clarified by Korpelainen (2003).

LHS M(P)5 wider childbearing age span more so for high SES ? ! Reduced P-M trade-off

Post-SDT LHS M(P)5 High SES have adequate livelihood resources and monopolize space as resource (low population density enclaves/environments, low population density socio-economic settings); achieving disproportionate fertility advantages consistent with a steep negative fertility-population density relationship (fertility sensitive to negative feedback on fertility, as applicable in K-selected populations: ref): a little density relief is associated with relatively higher fertility advantages. Re-establishment of positive high SES-fertility association.
Low SES: resilience to socioeconomic stress /anomy via fast-P LHS fixation

233b In cold-adaptive mtDNA variants harbouring uncoupling adaptations, plasticity benefits are realized to a greater extent, involving a wider range of Pm versus Mp realization due to attenuated P-M LHS trade-off constraints. Wider adaptability amplitudes associated with reduced/attenuated LHS trade-off constraints have plasticity costs, particularly so as and when these trade-off constraints are intensified as a result of lowered vitality of functional energetic efficiency (due to PIE accumulation associated with uninterrupted food abundance and population density stress). The greater the extent of cold-adaptation (partially uncoupled OXPHOS mtDNA mutations re Wallace 2005), as required in increasingly colder, more northern regions, (a) the higher the predominance of slower LHS-mode expression and also (b)

the lower any fast-slow LHS trade-off constraints (Table 2.3.3b), particularly in healthy individuals (low PIE loadings; LHS-mode PM). However, as PIE loadings accumulated during the course of the demographic transition, fastP-slowM LHS trade-off constraints (fast LHS-mode pM↑:4 setting) are intensified, more so in individuals of countries subject to inherently faster LHS-modes towards the south/south-west of Europe; but less so in more cold-adapted northern European countries (more relaxed fast-slow LHS trade-off constraints).

Population density stress. Sensitivity of fertility to population density stress is highest in populations subject to the periarctic metabolic performance mode (Table 2.5.1.1a; 2.5.1.1b: K-Selection reproduction strategy). Inherent to the periarctic metabolic performance mode is a plasticity of fastP-slowM LHS adaptability, but associated plasticity costs (2.2.1d) involve a sensitivity of fertility to population density stress (vulnerability to negative impacts of population density stress on fertility). Attenuated trade-off constraints regarding fast-P versus slow-M LHS realization when subject to pronounced cold-adaptation, particularly prevalent at higher latitudes/altitudes (and conditions underpinning LHS-PM expression: pronounced cold seasonality and plant growth-curbing conditions: low-nutrient soils, aridity, low temperature growth: 2.5.1.2). Under conditions supporting LHS setting PM (Table 2.2.2b).

Facilitating wider childbearing age spans; also for P-types (of higher socio-economic status) and ***notably reduced plasticity costs under conditions of lower population density stress***.

When subject to relatively lower population densities, disproportionate relative fertility advantages can result (low density refugia of higher status individuals; northern *versus* southern Sweden). NWS cold adaptation/age range 233d incl. subsection on population density p259, 272, 275 Later age fertility at cost of earlier age fertility: accentuated fast-slow trade-off (more towards the south); when relaxed wider childbearing age span (more to the north). E persistently lower mean ages at first child (Table 2.3.3j).

1. LHS PM-slow LHS setting

Minimal P-M trade-off constraints are applicable in individuals subject to the LHS-mode PM; which is prevalent under conditions of balanced feast-famine alternation (2.2.2e; Table 2.2.2b).

2. LHS P > M(1)-fast LHS setting

Differential susceptibility applies as the efficiency of the endogenous energetic functionality declines due the the impact of patho-information-engram load accumulation (2.1.2). As a result, plasticity underpinning high P-LHS-mode expression (relating to *inter alia* capacity for interference competition and early reproductive performance) then also involves higher vulnerability to negative experiences/adversity, manifesting in higher P *versus* health trade-off constraints (costs of plasticity: 2.2.1d).

3. LHS M > P(2)-fast LHS setting

(**AS:** ***This is furthermore consistent with LHS-mode pM > Pm expression (high maintenance to performance investment ratio supporting longevity; associated with autumn births***).

Under conditions of sustained resource abundance, the build-up of patho-information-engram loads (accentuation of Pm-pM trade-off) results in a progressive shift from the LHS-mode Pm > pM to the LHS-mode pM > Pm (from fast-type to slow-type life history strategy: from early to late fertility realization; ***from early to later life performance***: lower mortality; relatively longer lifespans).

Spring-borns are accordingly metabolically cued towards high performance rates, especially also for high rates of reproduction (**LHS-mode Pm > pM; Pm-types**), whereas autumn-borns have greater survival capacities, reflected in better health (through somatic maintenance) and longer life span (**LHS-mode pM > Pm: Mp-types**).

4. LHS Pm↑(3)-fast LHS setting

This LHS dispensation is applicable to Eastern European populations (2.3.3b/c).

As higher plasticity costs are constrained through resilience, resilience costs are incurred; manifesting in, *inter alia*, an associated narrowed plasticity scope for fast versus slow LHS-mode expression (2.2.1d). This implies that the capacity for early life fertility realization is at the expense of later life fertility realization; that is, resilience costs are manifesting through, *inter alia*, a narrowed childbearing age span.

5. LHS M(4)-fast to slow LHS setting

Pregnancy at older maternal age; involving spring/S prenatal P cueing under a slow maternal LHS setting. Optimization shift to slow LHS setting: towards P-M optimization (reduced P-M trade-off costs); broader PM combination scope. M(P) or P(M) , ie some P-M combination achieved/supported by slw LHS setting. For positive P-fertility relationships, a health-P trade-off should be absent/weak.

LHS optimization shift to slower LHS setting supporting reduced M-P trade-off costs and later age functionality (recuperation; wider childbearing age span: earlier and recuperation). Especially under conditions of lower population density stress. But producing Mp-type, low baseline fertility offspring (Gloria-Bottini). Mp-type predominance. Low P vitality males.

6. LHS pM(5)-slow LHS setting slow M4

P-vitality-compromized PM (LHS-mode M ≥ P). Low baseline fertility as still underPIE load effects. LHS-mode setting MP; with PIE erasure both P and M capacities restored; fertility up.

c) Rise and fall of civilizations: Surviving the fall ?

Post-disintegration survival (back reference to 3.1, beginning)
Prerequisite conditons:
I) Non-replacement of gene pool
II) Substantive persistence of authentic gene pool
III) Extended time periods with post-SDT conditions; conditions of adversity and relative lower population densities re-emergence of positive selection

2.4 Conceptual framework of Systems-Ecological Healing

Medical Disclaimer
All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

2.4.1 Recursion-healing

Recursion-healing in the context of Systemsecological Healing (SEH) is a transgenerational project. It involves various phases, each with its own phase-specific considerations (pre-reproductive adult phase; pregnancy, lactation, infancy and childhood: 2.6a; adult phase: 2.6b).

Procursion impacts (traumatic psychological or physical insults, toxins, acute diseases, infections), if not completely overcome/healed during the acute phase by the defensive systems of the body, are layed down as patho-information-engrams in the biocybernetic system of the body. When too overwhelming at the time of impact, survival is ensured by allaying the acute response to the impacts (resulting in up-loading of impact-linked patho-information-engrams). At a later stage, when the body has regained sufficient vitality, these patho-information-engrams can then be subjected to healing processing in the context of their re-exposure and acute reconfrontation resulting in their deletion from the biocybernetic system (**recursion-healing**).

REFERENCE TO 212a

Als epigenetische Information vererbt zur Vorbereitung der Nachkommen für eine Umwelt mit relevanten Prokursionsimpakten. Eine Löschung der (epigenetischen) Patho-information-engramme durch Rekursionsheilungsprozesse in der Form akuter Erkrankungen.

Biocybernetic system: genome (genetic information), epigenetic information, modifying the expression of genetic information, interacting with information received reflecting environmental conditions/stress (including procursive patho-information-engrams: as yet undeleted unprocessed imprinted stress impacts).

Recursive healing mechanisms (exposure of pathoinformation-engrams and reconfrontation with the immune system/healing processes in order delete/erase the patho-engraminformation from the biocybernetic system)

Ultimate/primary causality, proximate/secondary causality, symptoms
Main interfaces: fasting (autophagy), inflammation (fever); proximate interfaces acid-bsase equilibrium, gut health and sleep.

Revitalisation of genealogical vitality
Minimisierung von Stresseinwirkungen physischer und psychischer Art (Prokursionsneutralisierung) und Pathogrammlöschung

Ungewöhnliche Indikationsbreite (Fieber, Fasten, Darmgesundheit, Säure-Basen-Regulation): Schlüsselelemente der ursächlich wirkenden Rekursionsheilung.

Nach alter medizinischer Weisheit kann ein chronischer Zustand nur über eine akute Reaktion permanent gelöscht werden (Pischinger 1989; Kellner 1984 a,b).
Reckeweg
Unüberwundene Traumata (physische oder psychische Stresseinwirkungen) werden als Pathoinformations-Engramme eingelagert und wirken funktionsstörend im Körperfunktionssteuerungssystem. Diese Pathoinformations-Engramme können nur gelöscht werden durch eine Rekonfrontation/Exponierung an erfolgreich überwindende, akute Immuninteraktionen (Fasten/autophagy, Fieber). Kluger
Prokursionsimpakte = wenn nicht überwunden, werden als Pathogramme eingelagert zur späteren Verarbeitung (Überlebenswichtig zur Zeiten der Impakte). Als epigenetische Information vererbt zur Vorbereitung der Nachkommen für eine Umwelt mit relevanten vorgezeichneten Prokursionsimpakten. Eine Löschung der (epigenetischen) Patho-Information-Engramme durch Rekursionsheilungsprozesse in der Form akuter Erkrankungen (Entzündungen).

Bach (2002): role of infections.
Microbiota and health (Dethlefsen et al. 2007) GUT-dethlefsen
Als Ausgangsposition haben wir eine Patho-Information-Engrammbelastung die sich in jüngeren Jahren nicht unbedingt schon durch Krankheitserscheinungen manifestiert.

Subclinical dysfunctionalities. Rekursionsheilung muss aber angestrebt werden so früh wie möglich derweil jugendliche Vitalität noch vorhanden ist und bevor die körperliche Funktionseffizienz zunehmend kompromittiert ist durch fortschreitende Prokursionsimpakte. Im Rahmen einer Rekursionsheilung können drei Komponente identifiziert werden.

2.4.2 Supporting recursive healing

- **Unterstützung körperlicher Funktionseffizienz**

  Funktionskatalyse (Mennerich 1979). Catalysing the functionality of PIE load-compromised metabolic processes supports recursive healing; whereas symptom suppression represents procursive impacts, thereby blocking acute/subacute healing processes, leading into further chronification.

  Intermittancy principle The PIE-related functional insufficiencies are exposed through PIE-specific symptoms (of the most recently deposited PIE). Functional catalysis of symptom-indicated insufficiencies results in regulated uncomprimized functionality which may lead to erasure of the PIE. This may require **repeated intermittent catalysis**. After successful PIE erasure, the next now uppermost PIE-layer will become exposed, revealed in turn by its PIE-specific symptoms (related to the associated functional insufficiencies). The next functional catalysis can now proceed in the context of recursive healing. Wilson (2014)

  Efficient catalysis of functionality requires a tension gradient between dysfunctionality (manifested by exposed symptoms) and the healthy, regulated state. After some time of induced catalysis this tension gradient is diminished and catalysis needs to be changed or interrupted for continued efficiency of catalysis. Multiple catalysts applied dynamically are required for synergy (*vide* Mennerich 1979) within the context of anabolic (tonification) and catabolic (regulation; autophagy) metabolic states.

  Oxygen therapy (Weiss 1990): re-injection of suitably oxygenated blood. NB additional to fasting for hetero-protein removal.

  Natural Allopathic Medicine (Sircus 2014: Treatment Essentials). Alkaline water/alkalinity and oxygen status; potassium and sodium bicarbonate (Sircus) Natural Allopathic Medicine (Sircus 2014); oxygen therapy (Sircus 2015)

Catalism of metabolic functionality ()

INTEGRATE MENNERICH

Supplementation: Therapeutic doses (relatively high: Sircus 2014), ensure proper absorption and avoid overdosing. Clement (2010)

ADAPTOGENS CHECK ALL

Wilson (2014)

Howes (2006) HOWES-cardiovascular-disease

Howes (2006) ANTIOXIDANTS-howes; Howes (2011) HOWES-mythology

Lichtenstein & Russel (2005) SUPPLEMENTS-lichtenstein

Ubiquinol-coenzyme Q10

Therapeutic supplementation (Sircus 2014). Natural allopathic medicine

Gedgaudas (2011) comprehensively deals with the topic of supplementation and consulting her book in terms of this and other issues of healthy living is recommended. Reasons for magnesium deficiencies (Table). Clement (2010)

MS DIET-supplementatio-bjelkovic ANTIOXIDANTS-howes For example, caution is required in the dosing of pyridoxine as relatively low doses have been implicated to result in irreversible neurological damage (op. cit. Anderson (2008)

ADS Nemeroff (2004): Emerging literature suggests that traumatic experiences early in life increase the risk of mood and anxiety disorders in genetically predisposed persons. Long-lived alterations in the corticotropin-releasing factor (CRF) system and stress responses underpin this vulnerability.Women with histories of abuse and current depression exhibit the greatest dysfunctionalities in the hypothalamic-pituitary response system. Surrogate parenting/anti-depressant treatment.

TCM, homoeopathy

Adrenal fatigue AFS Adrenal fatigue, neurotransmitter imbalance and sleep disturbances (Head & Kelly 2009) Beishuizen & Thijs (2003) ENDOTOXIN-beishuizen NB

Anxiety disorders syndrome ADS (Scott 2011) EPIE load manifestation (subclinical-clinical): fungal infections candida

Fungal infections

Stomach acid deficiency (Wright & Lenard 2001) bone broth

Detoxification

Darmgesundheit, Säure-Basen Dynamik

Azidose-Ausleitung (Magensäure, Magnesium)

Ernährung

Stressmanagement

Ausheilung anstatt Symptomunterdrückung (fever, rest). Avoidance of influenza vaccinations.

- **Minimisierung prokursiver Auswirkungen**

  Abwehr/Ausschaltung ernährungsbedingter und psychischer Stresseinwirkungen (Lebensumgebung)

  Ernährung, Darmgesundheit.

- **Unterstützung bzw. Anwendung aktiver Rekursionsprozesse**

  Fieber, Fasten (extended fasting), Ausheilung anstelle Unterdrückung von akuten/subakuten Krankheiten (Epigenetische Entrümpelung).

  Infektionen (Bach 2002)

  Daily intermittent fasting.

2.4.3 Synthesis: Systems-Ecological Healing

2.5 Recursion-promoting lifestyle imperatives

2.5.1 Health-conforming lifestyles and nutrition

2.5.1.1 Life history strategies: context and nutrition

a) Metabolic performance syndromes (peri-arctic, subtropical, tropical).

Life history theory focuses on trade-off relationships in the allocation of finite energy resources to either maintenance/survival (S: basal metabolic rate BMR, thermoregulation, energy storage, immune function and physical activity) or productive purposes (P: growth and reproduction) for maximum fitness under disparate environmental circumstances (spatiotemporal variability of climate, water and nutrient availabilities). These trade-off relationships shape demographic patterns subject to metabolic trade-off constraints. Factors associated with high absolute energy requirements for daily maintenance are large body mass, high degrees of muscularity, exposure to pronounced cold stress (relatively high basal metabolic rates (BMRs), consumption of high meat/protein diets and high levels of physical activity (Snodgrass & Leonard 2009). Body size favours fasting endurance under conditions of seasonality (Lindstedt and Boyce 1985); representing a condition of combined P_t (sustained productivity) and S_t (costly maintenance) metabolic competence; as for periarctic populations (Table 2.5.1.1a). As adaptation to severe cold stress, northern populations have elevated basal metabolic rates compared to lower latitude populations. BMRs independent of body size are relatively depressed in tropical populations and elevated in northern groups (Leonard et al. 2002); in congruence with a strong negative association between BMR and mean annual temperature (Leonard et al. 2005, op. cit. Snodgrass & Leonard 2009). These considerations are congruent with those outlined by Wallace (2005) in the context of mitochondrial DNA mutations and lineages (regional haplogroups).

Wallace (2005): In addition to having to adapt to changing caloric availability due to seasonal changes, ancient human hunter-gatherers had to adapt to the rigours of different climatic zones. This was achieved by the acquisition of mtDNA mutations which partially uncoupled OXPHOS (oxidative phosphorylation) which resulted in persistently increased mitochondrial heat production. Phylogeographic studies of human mtDNAs (mitochondrial DNAs) revealed a strong correlation between mtDNA lineages and the geographic origin of indigenous populations. The regional groups of mtDNA lineages represent groups of related individual mtDNA sequences known as haplogroups. The various regional haplogroups were generated by the accumulation of sequential mtDNA mutations on radiating maternal lineages. The human mtDNA tree

is rooted in Africa, and has specific branches which developed under different selective pressures associated with different climatic zones (Cann et al. 1987, op. cit. Wallace 2005; Merriwhether 1991, op. cit. Wallace 2005; Wallace et al. 1999, op. cit. Wallace 2005). African mtDNA, the most diverse and ancient (overall age of about 150 000-200 000 years before present), fall into four major haplogroups: L0 (oldest), L1, L2 and L3 (youngst). In north-eastern Africa, two mtDNA lineages, M and N, arose from L3 about 65 000 years before present (These were the only mtDNA linages succeeding in leaving sub-Saharan Africa and radiating into Eurasia, resulting in all of the Eurasian mtDNAs). In Europe, haplogroup L3 gave rise to to haplogroups I, J and K; and haplogroup N to haplogroups H, T, U, V, W and X. Europeans separated from Africans about 40 000-50 000 years before present. Of relevance here is that functional mtDNA variants that founded specific mtDNA lineages, affect, *inter alia*, mitochondrial physiological functions.

The dynamics of energetic balance in response to regional differences is explained by Wallace (2005).

Wallace (2005): Mitochondria are at the intersection between environmental factors such as calorie availability and cold and the human capacity to cope energetically with environmental challenges in different regions of the globe. Our ancestors had to adapt to two classes of environmental changes: I) short term changes in the availability of calories and climate associated with seasonal variation, and II) long term changes in the nature of calories and average annual temperatures as defined by latitude and geographic zones in which they lived.
Humans adapted to the more general regional differences through the fixation of functional mutations in their mtDNAs which changed the coupling efficiency of OXPHOS (oxidative phosphorylation); shifting the the energetic balance from predominantly ATP (adenosine triphosphate) production in the tropics to increased heat production in the arctic. The occurrence of fundctional mtDNAs variants allowed for the shifting of the energetic balance in certain individuals sufficiently that they could move into and survive in more northern environments from which their warm-adapted predecessors were excluded. However, adaptive mtDNA mutation are subject to trade-offs. In the tropics, tightly coupled mitochondria maximized the efficiency of physical work and minimized heat production (AS: low basal metabolic rates: Table **2.5.1.1a**: tropical zones). Mutations which partially uncoupled OXPHOS decreased work efficiency, but provided essential heat for surviving chronic cold (**AS: high basal metabolic rates:** Table **2.5.1.1a**: Peri-Arctic: Subarctic and cold temperate zones).

Fundamental trade-off relationships exist between metabolic response modes geared for optimal performance coping with **spatiotemporally unpredictably dispersed resources** operating at relatively high temperatures (tropical-type conditions), as against those having to optimally utilize **seasonally fluctuating spatiotemporally clumped resources** by sustaining performance under strongly variable, often relatively low temperatures. The combined tolerance capacity for both P (Production processes: growth and reproduction) and S metabolic performance (Survival: body size, energy storage, thermogenesis, metabolic maintenance) comes at the cost of comparatively

high supporting BMR-settings (Peri-artic/temperate-type conditions). Conversely, at the cost of being constrained to narrow metabolic amplitudes, as linked to metabolic functionality strictly in relation and sensitive to resource levels (narrow optimality: resource level tracking) and with high-temperature performance settings with low maintenance costs/low BMRs, the tropical metabolic performance mode combines **resource-level responsive** metabolic performance (Pr: capacity for peak performance under resource surplus conditions) with **stress resistance** (Sr: persistence under resource deficit conditions and reduced P versus S trade-off constraints). The partial resource-level independence of the peri-arctic metabolic performance mode is based on on a **higher physiological capacity of adjustability** (wide metabolic amplitude and broad resource optimality). This involves **sustainability of performance** over time (Pt) in the face of fluctuating resource and temperature levels. The associated enhanced **stress tolerance** (sustained resource use efficiency at variable and also relatively low temperatures) is at the cost of incurring relatively higher levels of maintenance respiration costs/relatively high basal metabolic rates (BMRs). Thus, the underpinning phenotypic/metabolic plasticity is energetically costly (DeWitt et al. 1998). The peri-arctic/tropical metabolic performance mode dichotomy accordingly involves a trade-off between the capacity for sustained metabolic performance under conditions of cold climate seasonality (the former) and the capacity for combined high peak performance and stress resistance (metabolic efficiency also at relatively low resource levels) under conditions of relatively seasonally sustained elevated temperatures (Metabolic performance trade-off model: Table 2.5.1.1a). This model is in congruence with basic principles as outlined by Gilchrist (1995): in constant environments performance specialists with narrow preference ranges are the favoured phenotype; whereas in environments with considerable variation selection favours broad performance breadths, i.e. tolerance generalists.

Gilchrist (1995): The results of the performance and tolerance models suggest that, for most patterns of environmental variation, organisms should be performance specialists and tolerance generalists.
In constant environments and environments in which there is significant within-generation variation, specialists with narrow preference ranges are the favoured phenotype. In environments in which there is considerable among-generation but little within-generation variation, generalists with broad preference ranges are favoured. The buffering of internal operative conditions from external environmental fluctuations allows the evolution of specialized physiologies, presumably at some significant fitness benefit. Although the physiology of such organisms might in fact evolve to allow

activity over a broad environmental range, fitness such as growth and reproduction are often restricted to a narrow preferred range of conditions even in the most variable environments (Andrewartha & Birch 1954, op. cit. Gilchrist 1995). Realized fitness in a fluctuating environment depends on both tolerance probability of survival and performance capacity of an individual to grow, mate and reproduce under various conditions (Huey & Kingsolver1989, op. cit. Gilchrist 1995). Generally, temporal variation selects for generalists. The tolerance curve function (describing survival rate along a continuous environmental gradient) should evolve to span the range of conditions an organism is likely to experience within a generation.
The optimal performance curve differs dramatically from the optimal tolerance curve in a changing environment. Under the assumption of a constant area beneath the performance curve, a trade-off between maximal performance and performance breadth is implicated (Levins & MacArthur 1966, op. cit. Gilchrist 1995).
Natural selection favours increased efficiency during even limited times of optimal conditions rather than extending the range of conditions that support fitness-enhancing activity. The same specialist phenotype, characterized by a narrow Tbr, is favoured in both constant and in environments with with substantial within- and among-generation variation. In a variable environment, specialization is made possible by the existence of some period of suitable conditions for mating or some other fitness-related activities during the organism's lifetime. Specialists are favoured if such a time window exists nd if specizalization on those conditions provides enough of an increase in efficiency during those times. Selection favours broad performance breadths only in environments characterized by considerable among-generation but little within-generation variation.

Table 2.5.1.1a	**Metabolic Performance Syndromes (Periarctic-Subtropical-Tropical)** according to the **Metabolic Performance Trade-off Model**
Latitudinal gradients in metabolic functionality. Among the most productive genotypes, the most stress tolerant had the most **negative $\delta^{15}N$ values** regarding both drought and nitrogen starvation stresses (Robinson et al. 2000). Globally, foliar $\delta^{15}N$ was found to increase with mean annual temperature (MAT) across sites with mean annual temperatures ≥ -0.5°C (Craine et al. 2009). Correlation between MAT and growing season temperature and length (nearness to the equator) was shown by (Reich and Oleksyn 2004). Cold temperature metabolic activity (high latitudes, higher altitudes, winter rainfall activity) is associated with low $\delta^{15}N$; indexing **stress tolerance** (periartic metabolic performance; high $\delta^{15}N$: stress resistance as associated with tropical-type metabolic performance). Following the results of Codron et al. (2005), seasonal shifts in plant $\delta^{15}N$ corresponded positively with seasonal summer rainfall (concurrently high temperature and water availability); whereas winter rainfall functionality (low temperature growth) is associated with lower $\delta^{15}N$ values (Craine et al. 2009), indicative of more sustained, stress tolerant metabolic performance (Robinson et al. 2000); reminiscent of periartic metabolic performance. Increasing $\delta^{15}N$ values are accordingly interpreted indexing resource-responsive, high temperature-water metabolic functionality (tropical-type metabolic performance mode). Low $\delta^{15}N$	

values correspondingly indicate sustained, stress tolerant peri-arctic metabolic functionality (under conditions of low temperature and pronounced sesonality). $\delta^{15}N$ seems to index the capacity/realization for peak high temperature metabolic performance when combined with sufficient water availability; such as activity under high temperature-water surplus conditions (summer rainfall; tropics).

Genetic differentiation or phenotypic plasticity. Epigenetic inheritance systems enable environmentally induced phenotypes to be inherited over generations (Pál 1998). Frequencies of epigenetic variants are determined by genetically-based plasticity and efficiency of transmission (Pál 1998). Following Geist (1978), selection for canalization (evolved **robustness** of final outcome to pertubations occurring to a developmental process) is expected whenever organisms or mechanisms are **required to perform a constant function.** Robustness: the property of the system to produce relatively invariant output in the presence of perturbation (Masel & Siegal 2009). Phenotype redundancy for physiological processes is accordingly expected in animals from stable environments (tropical forests). Highly canalized organs are virtually a direct expression of the genes and variability in such organs/functions reflects primarily genetic, not environmental variability (Geist 1978). Tissues or body parts having high growth priority are likely to have phenotypic redundancy since they develop during ontogeny almost without being influenced by the ontogenetic environment. **Plasticity** of phenotypic development is gained at the expense of phenotype redundancy, and *vice versa*. Since phenotype redundancy (robustness) permits high reproductive fitness in a stable environment (tropical/subtropical species), it permits lower viable population sizes for species from stable environments than for species that have been selected for plasticity (species from temperate/artic regions). Thus, the periarctic metabolic performance mode underpins **phenotypic plasticity**, whereas the tropical metabolic performance mode is associated with **genetic differentiation** into narrowly specialized niches.
STRESS-ellis-2006-NB

The latitudinal decline in species diversity is a ubiquitous phenomenon (Hillebrand 2004); but a conclusive explanatory mechanism for the latitudinal gradient of increasing species diversity from temperate zones to the tropics (Hillebrand 2004) has yet to emerge. The metabolic performance trade-off model is in alignment with and can contribute towards an explanation of the latitudinal species diversity gradient. Species-specific occupation of narrower niches in the tropics, rather than broad niche occupation by fewer species with intra-specific plasticity, provides for higher niche carrying capacities and hence species diversity in the tropics.

(Each of the three here differentiated metabolic performance modes and associated life history strategies is characterized by evolutionary superiority under the conditions of their selection. Any differences in value systems associated with particular strategies are to be respected. Value judgements would be inappropriate)

	Metabolic Performance Syndromes		
Metabolic performance mode/tactic	**Peri-Arctic: Subarctic and cold temperate zones (cold winters: 36° - 40° N/> 40°)**	**Subtropical (warm summers, cool winters)**	**Tropical (aseasonal warm climate)**

Temperature and seasonality regime	**Pronounced low-temperature seasonality**	**Pronounced seasonality: high summer, low winter temperatures**	**Weak or no seasonality: sustained relatively high temperatures**
Resource availability gime	**Spatiotemporally clumped: variable, but seasonal superabundance** (pronounced seasonality)	**Spatiotemporally clumped: seasonally fluctuating** (pronounced seasonality)	**Spatiotemporally dispersed: non- or weakly seasonal** (non- or weakly seasonal)
Productivity (P): **P (growth, reproduction) = Pr x Pt** **Pt = productivity mainly achieved through sustained productivity over time at a given productivity rate** **Pr = productivity mainly achieved through relatively high productivity rates, but over shorter periods**	**Pt through time, partly uncoupled from resource availability and enhanced St capacity (Stress tolerance: size, storage, health, longevity); adaptability to resource level fluctuations with high costs of high BMR settings**	**Trade-off: Size through growth rate P_r at reduced St (size, longevity, health)**	**Pr through metabolic rates being linked to current resource availability and stress resistance (Sr) due to capacity to scale down BMR in the face of low resource availabilities (survival)**
Productivity resource-level buffered (Pt) or resource-level tracking (Pr)	**PtSt generalist plasticity** **Pt: Sustained P-efficiency (resource-level buffered)**	**PrSt flexible adaptability**	**PrSr specialist robustness** **Pr: capacity for opportunistic resource-tracking performance with P rates in congruence with resource availability levels (high to low)**
Stress tolerance versus stress resistance **Stress tolerance (St): capacity for sustained metabolic functionality under conditions of variably fluctuating resource levels.** **Stress resistance (Sr): capacity for the downscaling of maintenance requirements relative to productivity, especially at low resource availability levels**	Stress tolerance (S_t): Resource use efficiency through broad metabolic amplitudinal adaptability. Relatively high BMR-maintenance settings sustain activity over broader resource and temperature optima.	Flexibility of metabolic performance for both cold winter (St) and warm summer (Pr productivity) seasonality.	Stress resistance (S_r): Low productivity outside of narrow optimum range. Coupling of energy requirements for activity with resource availability and relatively high temperatures and decoupling from maintenance respiration settings (Low BMR-maintenance settings)
Metabolic performance trade-off relationships	Efficiency of metabolic performance: resource use	Combination of Pr and St: metabolic flexibility in coping with both	Opportunistic peak metabolic performance (P_r) under resource

	efficiency for productive processes (P_t) and resource use efficiency for survival capacities (S_t: size, energy storage, longevity), traded off against relatively high maintenance costs sustaining plasticity of metabolic performance (high BMR settings) (requires relatively high levels of sustained per capita resource availability)	warm/high resource summers (Pr) and cold/low resource winters (St) Increased Pr vs St capacity trade-off (opportunistic flexibility): Combinations of high Pr realization and St capacity (Stress tolerance to cope with low temperature seasonality) vs Pr capacity for warm season performance	surplus conditions and stress resistance (S_r) to cope with resource deficits Opportunistic maximum resource use of spatiotemporal resource surpluses (resource tracking)
Resource use tactic	Sustained metabolic performance and resource use at variable/ fluctuating resource levels	Seasonally opportunistic maximum resource use rates (Pr in summer) and stress tolerance (St) for coping under low temperature conditions (winter)	Opportunistic maximum resource use of spatiotemporal resource surpluses (resource tracking)
Metabolic settings	Combination of sustained metabolic performance settings (Pt resource-level buffered) and stress tolerance (St: sustained metabolic performance over time facing resource level and temperature fluctuations	Settings for seasonally peak metabolic performance rates (Pr in summer) traded off against St capacity settings geared for performance under low temperatures (winter)	Combination of capacity for metabolic performance narrowly-linked to resource levels (resource level tracking) and stress resistance (Sr capacity: survival/persistence through stress resistance: resource level-dependant down-regulation capacity
Stress tolerance (broad resource level optima) versus stress resistance (narrow resource level optimality)	Tolerance: Pt-St; tolerance of metabolic efficiency over time, in spite of resource level fluctuations within a broad optimality range; increased productivity relative to costs at relatively high resource levels Resource use efficient metabolic performance (stress tolerance) with	Accentuated Pr vs St trade-off High Gr (growth rate) realization (settings) is at the cost of reduced St capacity.	Resistance: Pr-Sr: resource-level responsive P, with efficiency of productivity within narrow optimality ranges through the capacity to function at relatively high P rates relative to S costs at relatively low resource levels (steeper downregulation of S costs relative to P

	broad resource-level optimality is associated with relatively high maintenance costs		energy demands with declining resource levels). Resource use tracking at narrow resource level optimality incurs lower maintenance costs (stress resistance) i.e. facilitates survival capacities under conditions of resource limitations
Dynamics of resource monopolization (Table 3.1.2a): K-Selection *versus* r-Selection	K-Selection Stress tolerance Long-term wealth accumulation (of plenitude/reserves)		r-Selection Stress resistance Opportunistic consumption in the present
Reproduction strategies. **Reproduction at various levels of resource availability**	K-Selection reproduction strategy (Table 3.1.2a). Stress tolerance mode (St) relatively resource-costly (relatively high BMRs). Reproduction only possible above a relatively high level of resource availability Relatively high reproduction-resource level threshold (RRT high) Reproduction resource level sensitive (relatively high nutritional and space requirements for successful reproduction)	T-responsive reproduction strategy. Flexible utilization of temperature as resource: high temperature use through fast (life history strategy) LHS expression: early and high reproduction. Under lower temperature conditions: shift towards slower LHS expression: later and lower reproductive rates.	r-Selection reproduction strategy (Table 3.1.2a). Stress resistance mode (Sr) incurs relatively low resource costs (relatively low BMRs) Reproduction possible even at relatively low levels of resource availability Lower reproduction-resource level threshold (RRT low) Reproduction resource level insensitive (relatively low nutrition and space requirements for successful reproduction)
Negative feedback sensitivity of reprodfuction to population density stress	High	Relatively high and low at high or low metabolic functionality	Low

b) Resource-level sensitivities of reproductive strategies associated with divergent metabolic performance modes.

Under the **adaptive resource re-allocation hypothesis** dietary restriction (famine) reduces rates of intrinsic aging due to activated autophagy effects, but at the cost of reproductive output (Adler & Bonduriansky 2014); thus resulting in fertility-longevity trade-off constraints. According to evolutionary theory selection is expected to strongly favour reproduction early in life, even at the cost of healthy aging and reduced longevity. Adler & Bonduriansky (2014) thus presented an alternative framework to the **adaptive resource re-allocation** hypothesis where dietary restriction, inducing autophagy and increasing apoptosis, is interpreted to be part of a suite of facultative physiological responses that enables organisms to maximize immediate reproductive output even under conditions of reduced resource availability, as well as in times of resource surplus (reduced trade-off constraints between P, reproduction and M, maintenance via autophagy; as underpinned by LHS-mode PM). A baseline level of nutrients must be available before reproduction is possible. According to the interpretation of Adler & Bonduriansky (2014), responses to dietary restriction under the **nutrient-recycling, efficient resource use mode** lower this baseline, making reproduction more attainable under conditions of relative nutritional constraints. Thus, the organism makes more efficient use of incomimg resources, but with a slower conversion rate that is more than sufficient to accommodate the lower resource intake rate under dietary restriction (energy use efficiency).

Processes such as autophagy and apoptosis could accordingly be considered mechanisms of **differential resource allocation**, as under dietary restriction, stored resources are recycled and put to use for survival or reproduction. This form of differential allocations differs fundamentally from that envisaged under the **adaptive resource re-allocation hypothesis** because it does not involve sacrificing reproduction for the sake of somatic maintenance (relaxed P versus M trade-off constraints). Responses to nutrient availability entail trade-offs. Expressions of autophagy and apoptosis (as under nutrient restrictions) are inversely correlated with nutrient availability, with resulting inhibitory effects on cell growth rate, reproductive rate and environmental stress tolerance (wound healing, cold tolerance, immune function). Under the **adaptive resource re-allocation hypothesis** such trade-off constraints are postulated to be pronounced. Since the stress tolerance capacity (plasticity) of the periartic metabolic performance mode is relatively resource-costly (relatively high BMRs), reproduction is only possible above a relatively high level of resource availability (relatively high reproduction-resource level threshold; high RRT; Table

2.5.1.1a: Reproduction and various levels of resource availability). Reproduction is thus resource level sensitive (relatively high nutritional and space requirements for successful reproduction). The adaptive resource re-allocation explanatory framework is accordingly taken to apply in conjunction with the periarctic metabolic performance mode. Adler & Buriansky (2014) presented an alternative, evolutionary more plausible hypothesis, i. e. that of a highly conserved physiological response to DR (dietary resriction) where the up-regulation of autophagy and apoptosis represents a **nutrient-recycling, efficient resource use mode** that enables organisms to maximize immediate reproductive output under conditions of resource scarcity (amounting to a relaxation of the production *versus* survival trade-off under resource constraints). The tropical metabolic performance mode (Table 2.5.1.1a: Reproduction and various levels of resource availability) involves lower reproduction-resource level thresholds (RRT low), implying that reproduction is relatively resource level insensitive (successful reproduction can be sustained with relatively ***low nutritional and space resource requirements***). Thus, rather than representing mutually exclusive alternatives, the **adaptive resource re-allocation** explanatory framework is congruent with the periarctic metabolic performance mode (high reproduction-resource level thresholds), whereas the explanatory framework of Adler & Buriansky (2014), involving **nutrient-recycling efficient resource use** (low reproduction-resource level thresholds**)**, fits in with the tropical metabolic performance mode.

From the above trade-off patterns, two scenarios are established:

- Prevalence of the **nutrient-recycling, efficient resource use mode**. Tropical metabolic performance mode: BMR/Pr-costs under resource scarcity lower than Periarctic BMR/Pt-costs (Table 2.5.1.1a); supporting early breeding and sustained reproduction at relatively low resource availability levels: **reproduction relatively resource-level insensitive** (r-Selection reproduction strategy).
- Prevalence of the **adaptive resource re-allocation** feast-responsive resource use mode. Periarctic metabolic performance mode: BMR/Pt-costs under resource scarcity relatively higher than tropical BMR/Pr-costs (Table 2.5.1.1a); later breeding; sustained reproduction requires relatively higher resource availability levels. ***Reproduction is thus relatively resource-level sensitive both in respect of nutrition and space availability***. Under the K-Selection

reproduction strategy, reproductive success is accordingly sensitive to population density stress ().

However, depending on circumstances, relating to environmental resource availabilities favouring either LHS-mode PM (Table 2.2.2b) as opposed to LHS-modes P > M(1), M > P(2) and M(4) with increased plasticity trade-off constraints; and codetermind by inherent LHS-settings of haplosubgroup-types (Table 2.3.3e) either the **differential nutrient-recycling efficient resource use** mode or the **adaptive resource re-allocation feast-responsive resource use** mode may apply within the realm of the peri-arctic metabolic performance mode (2.2.2f).

2.5.1.2 Traditional healthy-living (THL) population groups

Life style, diet and environmental factors of traditional healthy living (THL) populations prominently known for health and longevity (also known as *Blue Zone* populations) were investigated through a review of relevant literature in order to identify those factors underpinning associated positive health outcomes. From a perspective of diet two main groups of THL populations were identified. In the diets of populations from the **periartic realm** (Table 2.5.1.1a), high protein-fat sources (some meat, but mainly butter, high fat milk products such as goat milk, yoghurt and sheep cheese) and carbohydrates (whole grain breads; starch-rich carbohydrates ≥ nutrient-dense carbohydrates) featured prominently. The THL populations Burusho-Hunza in the Hindukush-Karakorum Mountains (Table 2.5.1.2a), in the Caucasus Mountains and on the islands of Ikaria (Greece) and Sardinia, Italy (Table 2.4.1.2b) are linked to this group. In comparison, THL populations from the **subtropical** realm (Table 2.5.1.1a) have diets emphasising salads, vegetables and fruit. Vegetables are relatively low in carbohydrate content, but nutrient-dense. The diet can be characterized as one of moderately high carbohydrate (nutrient-dense carbohydrates ≥ starch-rich carbohydrates), low animal-derived protein-fat content (Table 2.5.1.2c). THL populations linked to this group include those on Okinawa Island (Japan), Nicoya Peninsula (Costa Rica) and Vilcabamba in the Ecuadorian Andes (Table 2.5.1.2c).

Table 2.5.1.2a Health and Longevity of Traditionally Healthy Living Populations: Burusho-tribes in Hunzaland (Karakorum; northern Pakistan) and Nuristani tribes (Kafiristan; Hindukush; Afghanistan and Pakistan): Periarctic Realm
Tribes living in remote and partly isolated, high mountain areas of the Hindukush and Karakorum. The Hindu Kush (mainly south of the main ridge) is largely inhabited by Nuristanis (recently/partly islamized; formerly Kafiristan). Ethno-linguistic tribes of the Hindukush were identified *inter alia* as Kata, Ashkun, Vasi, Kalasha, Kalasha-Chitral, Mumo and Kom (Strand 1973). Tribes according to Voigt (1933): Western Kafiristan: Kulam, Ramguli; Central: Ashkun, Kti, Wei, Pressun; Eastern: Kashtan, Kam, Madugal, Katir. Ujfalvy (1884) recognized that the Hindukush Nuristani are in close affiliation with the Burusho (Hunza, Nager, Dardus, Baltis, Jassin, Jeschkun) and Biddulph (1880) derived that the Burusho had originally descended from the Yuetshi (Yüe-tschi). By implication, both Hindukush tribes and the Burusho (Karakorum) were considered genetic affiliates descended from the Yuetshi (Voigt 1933). Both Kalasha and Burusho represented genetic isolates (Rosenberg et al. 2002). The Paleolithic Yuetshi ancestry prominantly showed European/Siberian genetic affiliation (Li et al. 2015). Comparison with genetic data of ancient hunter-gatherers/European farmers revealed that the Kalash share genetic drift with Paleolithic Siberian hunter-gatherers, suggesting the Kalash to represent a genetically drifted ancient northern Eurasian population that also contributed to and was linked to European and Near Eastern ancestries (Ayub et al. 2015). In the Pakistani eastern Hindukush the Kho represent the predominant population, speaking the Indo-Iranian language Khowar (e.g. Ishkomanis).
Remoteness and partial isolation in the high mountain ranges of the Hindukush and Karakorum. Hunza-Valley: *ca* 2600 m above sea level. Hindu Kush (Encyclopaedia Iranica, ISSN 2330-4804): Has risen since the late Tertiary period. Consists mainly of metamorphic rocks (shist, gneiss, marble, etc.), but also some intrusives (granite, diorite, etc.) of varying age and size (volcanic activity). Lower-lying areas on the southern side of the mountain are on the fringe of the Indian summer monsoon. Above 1300-2300 (rain in winter and spring): sclerophyllous forests (*Quercus* and *Olea*) and higher up (3300 m) with cedars, *Picea*, *Abies*, *Pinus* and junipers. Inner valleys of Hindu Kush have an arid vegetation (rain shadow).
Shah (1984): Ophiolite belts indicated by the occurrence of ultramafic, rocks, pillow lavas, greenschists, pyroclasts and basaltic flows. Northeastern Pakistan. i.a. Karakorum. Petterson (2010): Geologie. Kafiristan: mountains of metamorphic rocks. Zanchi and Gaetani (2011): describing the geology of the Karakorum mountain range. Gansser (1980): Rakaposhi 7800 m: highest ophiolitic mountain in the world).
Voigt (1933): The fair-haired and blue-eyed type, which is more or less distinctive in all Kafiri-tribes, and dolichocephaly, indicate their affiliation to the north-European group of the Indo-Germans. Mixed zones occur. Close affiliation with the Burushko-tribes (Burushko: Hunza, Nager, Dardus, Baltis, Jassin, Jeschkun) is widespread (Ujfalvy 1884). Biddulph (1880) recognized the Burushko-tribes as originating from ancestral Yüe-tschi (prominantly with European/Siberian genetic affiliation: Li et al. 2015), a classification also supported by Voigt (1933). Accordingly, we have a close affilation between the Hunza and Kafiri tribes; both originating from/belonging to the Yüe-tschi ancestral ethnic entity. The neighbourly connection between these ancestral groups was disrupted by Islamic-Iranian tribes which had successfully inserted themselves into the ancestral tribal complex in a wedge-like manner via the more easily accessible river valleys (Voigt 1933).
The Hunza (between the mountain ranges Hindukush in the west and Karakorum in the east; historically a kingdom; currently part of Pakistan) are known for their extraordinary good health, the basis of which has been investigated repeatedly (Taylor 1964). The distinctive characteristics of the Hunza, their lifestyle, as their ethnicity, were largely preserved through their existence in remote mountain valleys (Wrench 1938). Accompanyng the good health status we find a striking social harmony (Taylor 1964; Schaefer 1979). Such health status is attributed primarily to their specific diet and seasonal fasting (Wrench 1938). Wallach and Lan (1996): Hunza farm soils were/are maintained by organic agricultural practices (most of the original valley consisted of bare rock with a soil bed being placed on crafted stone terraces and watered through constructed aquaducts; the water, glacial milk, originated mainly from the Rakaposhi mountains, was used for irrigation and drinking purposes).
Nutrition. Voigt (1933): The diet of the Kafiri was characterized by modesty (frugality). Flatbread and milk products were the main dietary components. At higher altitudes, millet and barley is used for making

flatbreads; at lowerwarmer sites, maize and wheat is used. Milk products are of particular importance (raw milk, butter, goats cheese). Fruit (mainly from planted trees: mulberries, apricots, and apples), as well as from wild-growing species are used in the fresh or dried condition as side dish. Meat from domestic animals (beef, goats) or hunted game is used infrequently. The meat (including the organs and fat) is roasted on an open fire and consumed in a half-raw state.

Schaefer (1979): **Hunza**: chapatti flatbread (barley, wheat, buckwheat, millet). Fruit (especially apricots, apricot oil *Oil of Life*, sun-dried apricots in winter), soured milk products, such as cottage cheeses/quark, ghi, salads, nuts. Meat at special occasions. Glacial milk (glacial water); for drinking well before or after meals, irrigation of fields and for lifestock.

Hunza eat 2 meals a day. Meals are not large and menus do not often vary (Wrench 1938, Taylor 1964): Hunza eat mainly stone ground grain (chapatti), leafy green vegetables, potatoes and other root vegetables, fresh milk and buttermilk, clarified butter and cheese, fruit (mainly apricots and mulberries: fresh and sun-dried), meat on rare occasions (omnivorous diet).Vegetables are mostly eaten raw with skin (Wrench 1938, Rodale 1949). Wallach and Lan (1996): Basic diet consists of grains (whole grain and sprouts), vegetables (raw or steamed), fruits (fresh, dried or served in gelatin, based on goat and mutton tendon and cartilage), meat as available (generally all parts of mutton, goat, yak, beef, poulty) and dairy products are a staple (whole milk, soured milk, yoghurt, cheese, butter). Fat sources include whole milk, butter, ghee, apricot oil and animal fats.

Different summer and winter diet. Summer: harvesting season for grains, fruits and vegetables from gardens; vegetables were consumed raw. Very little meat was consumed in summer. Original winter diet: Meat from sheep, goats and domesticated yaks and milk products (high-fat milk, buttermilk, yoghurt, butter, cheese). All parts of the animals were consumed. The fat of bone marrow was used for cooking. Indigenous wildlife provided early Hunza hunters with meat (e.g. markhor and Marco Polo sheep). Sun-dried fruit and stored grain.

Health.

The populations are generally in good health; with a relative low incidence of diseases (Voigt 1933, Wrench 1938). Stress-free up-bringing of progeny; generally low stress levels (Schaefer 1979). Hunza: Excellent body constitution, longevity, endurance, vitality in youth and older ages, general absence of disease (McCarison op. cit. Wrench 1938). Two meals per day; the first being at noon (Redfern 2009). Breastfeeding up to 2 to 4 years. Drinking and irrigation water derived from mineral-rich glacial water from the Rakaposhi mountains (Gansser 1980: Rakaposhi 7800 m: highest ophiolitic mountain in the world).

Rodale (1949): Remarkable health and endurance attributed to diet, full breast feeding and vigorous exercise of their bodies. McCarrison: Nutrition and National Health op cit Rodale 1949). Diet considered as most important (McCarison op cit Rodale 1949). Redfern (2009). Lists groups of people known for their health and longevity living in high mountain ranges/extinct volcanic islands associated with the availability of pure alkaline water (*inter alia* Hunza northwest Pakistan, Japanese of Okinawa islands, Vilcabambas in Ecuadorian Andes). Alkaline water produces more oxygen in the body; reducing tissue acidity. Such alkaline water has a different viscosity, surfice tension and high colloidal mineral content (high alkalinity with a high amount of high active hydrogen, with a negative redox potential). Consuming alkaline water, the body increases its ability to absorb water because of its low surface tension. Wastes and toxins are flushed out easier (Drs Henri Coanda and Patrick Flanagan op. cit. Redfern 2009). Our body needs water with a low surface tension. If too high, waste removal is unefficient (*re* Nobel Prize Winner 1912 Alexis Carrel op. cit. Redfern 2009). Water: highly alkaline, high content of active hydrogen (hydrogen with an extra electron), negative redox potential and high content of colloidal minerals.

Fasting.

At the end of winter when the food resources are exhausted, fasting is undertaken (Schaefer 1979). Seasonal fasting: Late spring before the new harvests have been gathered the Hunzas go on an enforced fast (Wrench 1938, Taylor 1964). Undernourished in weeks preceding the first summer harvest.

Exercise. Active daiy life routine: much labour performed daily as they climb the hillsides to their fields (Wrench 1938, Taylor 1964, Schaefer 1979).

The Ishkomani (speaking mainly Khowar: Indo-Aryan language) inhabit a valley just west of the Hunza. The Ishkomani are characteristically of smaller body size, of poorer body build, lower industriousness, lacking thoroughness in agriculture and suffering from a greater incidence of diseases (Wrench (1938). The Nagiris, on the southern side of the Hunza river, opposite to the Hunza on the northern side of the river bank, are of good body build in general, but do not achieve the extraordinary vitality of the Hunza (Wrench (1938). Compared to the Hunza, the Nagiri lack the bodily and mental excellence. The latter are not held in high esteem as load carriers in the mountains, occupy rather

miserable houses and were poor agriculturalists (Wrench (1938). Originally, Nagir was settled by the Hunza a few centuries ago, but subsequently Kashmiris penetrated the area. Accordingly, the fair-skinned Hunza can be differentiated from the smaller, darker-skinned Nagiris, although both speak Burushaski. (Wrench 1938). The Hunza are strong mountain people and typically more fair-skinned than the people native to the north-indian plains (of different tribal ethnicity). Both Ishkomani and Nagiri originated from relatively recent migrations from further south (Subtropical realm: Table 2.3.1.1a) into the Burusho-Hunza population complex (Peri-arctic realm: Table 2.4.1.1a).

Table 2.5.1.2b Periarctic Realm: Health and Longevity of Traditionally Healthy Living Populations

1. Kaukasus (upper slopes of the Greater Caucasus): Abkhasia, Georgien (Ost-Europa)

Abkhasia: Original ethnic Abkhasians living in the Caucasus mountains known for their healthy aging and longevity. Between Georgia and Russia, Caucasus mountains. Predominance of oceanic lithosphere of the Greater Caucasus mountains (Adamia et al. 2011; Manafi et al. 2013; also Gamkrelitze 1991). Georgian people living on high Caucasus mountain slopes at about 2400 m elevation on small farm plots surrounded by high peaks. Longevity and health noteworthy. They raise farm animals and grow hay, vegetables and some grain. No fruit due to high elevation and no food imports. They ate meat, butter and high-fat yoghurt with every meal. Diet: lots of meat, saturated fats, butter and lard; a small amount of bread made from whole grain, and seasonal vegetables. Much exercise/activity. Daily involvement in work/labour (Pitskhelauri 1982).
In the mountain regions of western Georgia, a milk-meat diet predominates (greater life expectancy in western regions; diet of the long-lived in eastern regions contained much raw vegetable salads/fresh greens). Meat such as boiled chickens and beef, and occasionionally mutton, is generally eaten. Fats of Greek walnuts. As source of animal protein: cheese (amino acids, Ca) and sour milk. Meat, butter, high-fat yoghurt. Small amounts of bread made from whole grain; and a few seasonal, freshly-collected vegetables (relatively low carbohydrate diet). Habit of undereating: never eat to satiety.

This is similar to the **traditional Bulgarian diet and lifestyle** (Wendt 1985). According to the Centre of Gerontology and Geriatrics (Sofia) more than 80 % of the currently living Bulgarians aged 90 to 100 years married early (18-23 years) and their partners gave birth to numerous children. About 70 % of centenarians had never experienced any serious disease and never made use of medical services. They all had been physically active throughout their lives. Their diets were characterized by moderation and low intakes of animal proteins and fat. Their most important dietary items included bread, potatoes, beans, cabbage, tomatoes, onions, paprika peppers, fruit, sheep's milk and many other dairy products; mainly sour milk and yoghurt.

2. Ikaria Insel (Griechenland)

Die Insel Ikaria war schon in historischen Zeiten isoliert; unter anderem durch die Abwesenheit geeigneter Häfen). Ophiolotische Gesteinsmischungen, unverändert durch neuere Metamorphismen, bezeugen von einer ozeanischen Krustenformation in der Spätkreidezeit (Late Cretaceous) für die Cycladischen Inseln von Griechenland, u a. Ikaria (Pe-Piper & Photiades 2006).
The Ikarians live relatively long in good health. The percentage of those over the age of 90 years significantly exceeds the European average (Panagiotakos et al. 2011). Whereas the ratio of men to women over the age of 90 years is 1 to 4 in most developed countries, this ratio is 1 to 1 in Ikaria Buettner (2012) describes the lifestyle and diet of the Ikarians as follows: The Ikarians grow crops in their own family gardens on relatively barren, stony soils. They cultivate crops for their own use, including vegetables, herbs for tea and grapes for wine. Their daily work in the garden provides the family with freshly picked, locally grown, organic products of high quality. A relaxed lifestyle predominates; involving rising late and naps in the afternoon (siesta). This routine secures a leisurely afternoon. Breakfast: goat milk yoghurt, bread (whole-grain sourdough breads: low glycemic index; providing the nutritional advantages of unprocessed grains) and honey. Wine, herb teas or coffee. Lunch: beans, potatoes, fresh vegetables from the garden, prepared with olive oil. Locally caught fish. Limited consumption of meat (of pigs raised in the family garden). Light dinner: bread, goat milk

(raw), vegetables, and a variety of herbs (from family garden or wild herbs: anti-oxidants). Herb teas are consumed daily.

This represents the traditional Mediterranean diet with associated health benefits as reviewd by Psaltopoulou et al. (2013; Sofi et al. 2010). The diet is free of imported, commercially produced and other refined nutritional items.
Buettner (2012) lists the core elements of the health advantages of the Ikarian lifestyle and diet: goats milk, mountain living (activity), Mediterranean-type diet (vegetables, fruit, whole grains, beans, potatoes, and olive oil: fresh and not overheated), daily intake of herb teas, Siesta (afternoon naps), occasional fasting (calorie restriction)and a active, harmonious social life. Of these crucial elements, much daily activity, healthy nutrition, an active-harmonious social life and siesta were highlighted by Panagiotakos et al. (2011).

3. Sardinien (Italien)

Cold rainy winters, especially at higher altitudes, a more continental version of the Mediterranean climate. Geology: Gaggero et al. (2007): ophiolitic rocks. Poulain et al. (2011): A Sardinian longevity hotspot was identified in the province of Ogliastra (high altitude province; ancestral ethnic refuge), notably in the village of Villagrande, 700 m above sea level. Agropastoral activities and a traditional life style are still prevalent (Poulain et al. 2011; Poulain et al. 2013); had not changed much since the time of Christ (Francalacci op cit. Buettner 2012). For developed countries it has been widely documented that females live longer than males. This female advantage in survival (Longevity gender gap) results from lower female death rates throughout the lifespan (op. cit. Poulain et al. 2011). Such cumulating effects result in a greater proportion of females surviving at more advanced ages. There are generally more than 4 times as many female centenarians than males (male/female ratio 4:1). Not so in the genetically homogeneous population of Villagrande (Ogliastria), where the percentage survival rates between 1970 and 2000 for the 1890-1919 birth cohort were similar for male and females; but considerably higher than for Sardinia in general and Italy (Poulain et al. 2013). An increased level of homozygosity has been reported to favour male longevity. The population of Villagrande was characterized by a high level of endogamy until World War II. Endogamy seems to apply generally to *Blue Zone* populations (Poulain et al. 2011). Mechanisms relating to the predominance of slow life history strategy-mode expression, indicative of slower rates of ageing, seem to be involved. Reduced size dimorphism between males and females in Blue zone populations and an inverse relationship between body height and longevity (Samaras et al. 2003). Shorter height for men on average in Villagrande than in the whole of Sardinia (Salaris et al. 2012). Late female reproductive behaviour and longevity and slow somatic aging for both men and women promoted by the same genetic variants (K-RS). Similarities observed between the spatial patterns of late fertility and longevity seems related to higher endogamy (Poulain et al. 2011). Spatial analyses of Sardinian populations by Lisa et al. (2015) revealed a positive association between consanguinity and late fertility. Laughlin et al. (2008) revealed an association between sustained age-specific testosterone levels in males, indicative of slow rates of ageing, and reproductive capacity at advance ages. Astolfi et al. (2009): Tendency towards delayed maternal reproduction (more so than Europe and mainland Italy). Association between life longevity and reproductive longevity. In Sardinia areas of reproductive longevity exist (higher incidence of late maternity and combined with low costs in terms of perinatal deaths). Geographic context of small, isolated mountainous villages (inland refuge also referred to as Barbagia). Consanguity (within kinship breeding) and high inbreeding coefficients in inner, central mountainous areas. Increased incidence of homozygosity in genetic traits conferring protection against pathology associated with ageing (Montesanto et al. 2008): geographic isolation and consequent inbreeding may bolster male longevity (in association with relatively smaller male body size). Correlation between population homozygosity and human longevity (Altukhov & Sheremet'eva 2000, op. cit. Montesanto et al. 2008). Telomere length is strongly inherited, longer in women and linked to survival (op. cit. Poulain et al. 2011). Inbreeding contributes to male longevity and equalizes female and male life span at old ages under harsh environmental conditions (Montesanto et al. 2008). Study identified some inner central areas of Sardinia with late and successful maternity; corresponding remarkably well with those characterized by a high frequencies of centenarians (Poulain et al. 2011; Poulain et al. 2013). Caramelli et al. (2007): Studied genetic variations of ancient (Nuragic) Sardinians who had lived in the Late Bronze Age and Iron Age. The Nuragic samples showed a remarkable low genetic diversity comparable to that recorded for ancient Iberians. Matches with two modern Sardininan population supporting a clear genealogical continuity from the Late Bronze Age up to current times. Sardinians are clearly part of a European genetic

cluster, but differ sharply from their European and Italian neighbours. Although people of different provenance reached Sardinia over time, strong isolating factors (Mediteranian Sea and mountain ranges, cultural barriers) enhanced the evolutionary role of genetic drift. Genetic closeness was found between the Nuragic people from modern and ancient Ogliastra and ancient Iberia (genealogical continuity with Bronze Age inhabitants). This is in agreement with the results by Contu et al. (2008) suggesting a pre-Neolithic settlement of the country, with very little subsequent gene flow from outside populations.

Central highlands of Sardinia (Buettner 2012): Every day hikes by Sardinian shephards; hard working throughout life as farmers or shepherds. Afternoon nap. Diet: fava beans, pecorino cheese, bread and meat as affordable. Daily consumption of Sardinian wine. Drinking red wine from Ogliastra was claimed to hand have a positive effect on longevity due to its higher content of anti-oxidants (flavonoids). They ate what they produced on their land: mostly bread, cheese and vegetables (fava beans, zucchini, tomatoes, potatoes, eggplant). Meat generally only once weekly. Sheep and goat milk products contributed most of the protein. The diet was lean and largely plant-based with an emphasis on beans, whole grain breads (wheat flat bread high in fibre and complex carbohydrate, barley bread: low glycemic index, high in protein, magnesium and fibre; sourdough bread: whole wheat with live lactobacilli: low glycemic index) and garden vegetables. Flavenoid-rich Cannonau wine used daily. Goats milk from locally grazing goats. Pecorino cheese made from grass-fed sheep (high in omega-3 fatty acids). The healthy traditional Meditteranean diet is relatively high in fat and lower in carbohydrate content. Health benefits associated with the Mediterranean diet were reviewed by Psaltopoulou et al. (2013). Strong family ties and reverence for the elders, harmonious social life (reverence for the elderly).

Table 2.5.1.2c Subtropical Realm: Health and Longevity of Traditionally Healthy Living Populations

1. Okinawa Insel (Japan)

Redfern (2009),

Subtropical climate. Centenarians: Prodigious gardeners going into the fields every morning and returning with greens and tubers in the afternoons. Can grow vegetables all year round due to the islands comparatively tropical climate (semitropical vegetation). Balance of both animal and plant protein (eat every part of pig). Long life expectancies and low disability rate (Sho 2001). Okinawan centenarians eat meat only during infrequent ceremonial occasions. Ryukyu Islands, between North Pacific and East China Sea. Key ingredients of the Okinawan diet: Sweet potato breakfast, lunch and dinner; soy (tofu: soy bean-curd) and seaweed are used everyday, herbaceous plants and teas. Fish and pork eaten infrequently (Sho 2001). Okinawa has stingy soils. Vegetables from the garden: daikon, bitter melon, garlic, onions, peppers, tomatoes and some fish and tofu. All day long she nurses a pot of hot, green tea. Before each meal she said *hara hachi bu* (Confucian inspired adage, meaning 'Eat until you are 80 % full'). Afternoon napping. Early, light dinner.

Willcox et al. (2009): Residents of Okinawa are known for their long average life expectancy, high numbers of centenarians and low risk of age-associated diseases. The longevity advantage is thought to be related to a healthy life style, especially the traditional diet, which is low in calories, yet nutritionally dense with regard to vitamins, minerals and phytonutrients (antioxidants and flavonoids). Traditional Okinawan diet: high in vegetable and fruit content, but reduced in meat, refined grains, saturated fat, sugar, salt, and full-fat dairy products. Relatively low fat intake and high carbohydrate intake (anti-oxidant rich, but calorie poor: orange-yellow root vegetables, such as sweet potatoes) and green leafy vegetables. Typical Western diet: Overconsumption of of foods that are calorie dense, nutritionally poor, highly processed and rapidly absorbable may lead to systemic inflammation, reduced insulin sensitivity and a cluster of metabolic abnormalities, including obesity, hypertension, dyslipidemia and gucose intolerance (known as metabolic syndrome). High glycemic food intake may lead to chronically high levels of oxidative stress. Traditional diet pattern of the traditional Okinawan diet: high consumption of vegetables (orange-yellow root vegetables: sweet potatoes; green leafy vegetables) and legumes (mainly of soy origin), moderate consumption of fish products, low consumption of meat and dairy products, moderate alcohol intake, low calorie intake, rich in omega-3 fats (fish, soy oil), high monounsaturated-to-saturated-fat ratio and emphasis on low-GI carbohydrates (staple carbohydrate sweet potato, *Ipomea batatas*, anti-oxidant rich, low-GI; vitamin-rich, relatively high magnesium content; considered a folk remedy in Japan regarding anemia, hypertension and diabetes). Apart from sweet potato, the Okinawan diet includes a variety of health-promoting items, such as soy products (tofu, miso soup) wich are relatively high in healthy fats and protein; Goya (*Momordica charantia*), seaweeds (nutrient-dense: high in protein, magnesium, iron,

calcium and carotenoids) and traditional herbs and spices with medicinal properties (e.g. turmeric, *Curcuma longa*; Calabrese et al. 2007, Mancuso et al. 2007, Anand et al. 2008; Rubinsztein et al. 2011: curcumin a pro-autophagic component). CR and healthy aging: Lane et al. (1997).
Willcox et al. (2006): An extended average and maximum lifespan and an associated lower incidence of chronic disease of the Okinawans is attributed to mild, but prolonged caloric restriction for about half of their adult lives.
Willcox et al. (2007a): The Okinawan population appeared to be in relative energy deficit consistent wth CR until 1960. Consistent with adaptation to long-term energy deficit the BMI of adult Okinawans remained stable at a very lean level until the 1960s. Diet 1949: high intake of vegetables (mainly sweet potatoes and soy, a principal protein), anti-oxidant vitamins, relatively high magnesium intake. Relatively high DHEA values in elderly males and women. CR induces reductions in risk for chronic diseases and increases the age of onset of chronic diseases: higher average and maximum ages in Okinawan population. The apparent increase of maximum life span is suggestive of slower aging in Okinawans. Mortality due to age-related disease was much lower. CR status at lower ages of the elderly. The Okinawan come from an island population with restricted gene flow. Low BMI of the Okinawan population until the 1960s is consistent with a long-term adaptive response to limited energy availability and periodic energy deficits. Low caloric intake coupled with high activity levels appeared to have contributed to a CR phenotype in older Okinawans. This phenotypes includes life-long low BMI, relatively high levels of DHEA at older ages, reduced mortality from age-associated diseases, and extended average and maximum survival.
Willcox et al. (2007b): Elderly Okinawans exhibit several phenotypic features of CR: low BMI, low prevalence of chronic diseases and exceptional longevity. Elderly Okinawans had lower caloric intake than Americans, and apparently been calorically restricted (10-15 %) at younger ages relative to their estimated energy requirements Okinawans also had significantly higher plasma DHEA, testosterone and estrogen levels as septuagenarians as against non-CR Americans of comparable /similar chronological age. Lane et al. (1997): Many hormones decline with age. Sex hormones and their precursor hormone DHEA (dehydroepiandrosterone) appear to decline more slowly in CR monkeys/humans (link between CR and indicator of healthy aging). Association between longevity and DHEA (S) levels. The higher the DHEAS levels at 20 years of age (< 40: Americans > Okinawans) the faster the decline to lower levels at 60-75 (Americans) than in Okinawans (higher levels > 60-85 on CR). (Table diet/metabolism-delayed maturation=longevity).

2. Nicoya (Costa Rica)

Ocean floor rocks (ophiolites) are geologically predominating on the Nicoya Peninsula (Kuijpers 1980). Hard water percolating from bedrock (high calcium and magnesium content). Descendants of the Chorotega Indian tribe lived in relative isolation on the peninsula for the last four centuries (Buettner 2012). Rosero-Bixby et al. (2013): Mortality by cardiovascular diseases in men as the main and only origin of the Nicoya advantage (not in females). Survival ratio of people age 60 is 15% higher for Nicoya men and 6 % higher for females than the rest of Costa Rica. The period probability becoming of becoming a centenarian for a 60-year old man residing in Nicoya is 4.8 %. This probability is four times that of Costa Rican males, more than double that of Okinawa. Nicoya women have a slightly lower probability than males: 4.3 % (less than half than the exceptionally high % for Okinawan women: 9.3 %). Nicoya residents show significantly lower levels in the following markers of cardio-vascular risk: triglicerides, fasting glucose, HbA1c for males and cholesterol, waist circumference, BMI, and diastolic blood pressure (marginally) for both sexes together. Elderly Nicoyans are taller than Costa Ricans. Elderly people of Nicoya, both males and females, have lower levels of functional disabilities and cognitive deterioration (healthier aging process). The longer telomeres and higher DHEAS (dehydroepiandrostesterone sulphate) levels in Nicoya suggests a slower ageing process (). Diet (Buettner 2012): Nicoyans eat corn-based tortillas (also specially prepared maize dough), beans, garden vegetables, abundance of fruit (mostly garden-grown), protein (mostly of animal origin: pork, beef, fish, chicken) and light cheese. High-level glycemic index foods are consumed at significantly lower rates in Nicoya. This reflects on the lower consumption of processed or refined foods (greater adherence to traditional diet; rice, beans and animal protein). Nicoyans drink significantly less milk than Costa Ricans. The Nicoya advantage can be statistically explained by lower cardio-vascular mortality and disappears in out-migrants. Nicoyans are leaner and taller and have fewer disabilities (physical and mental). Elderly Nicoyans, especially males, have a clear cohort survival advantage. A daily rhythm of hard physical work before noon and leasurely afternoons with naps (Buettner 2012).

3. Vilcabamba (Ecuadorian Andes)

The Andean range represents one of three main morphostructural regions of Ecuador. The Andean uplift and present distribution of terrains are related to active subduction of oceanic Nazca Plate (volcanic zone) beneath the continental South America Plate (Eguez et al. 2003).
Robinson (2012). Die Bewohner des abgelegenen Vilcabamba Tales in den Ekuadorischen Anden ragen hervor durch überdurchschnittliche Gesundheit und Langlebigkeit. Die Gesundheitsvorteile der traditionellen Lebensweise verschwinden in Teilen der Bevölkerung die sich einer modernen, eingeführten Ernährungsweise zugewendet haben. Das mineralreiche Gletscherwasser wird als ein wichtiger Faktor für den Gesundheitszustand der Vilcabambanos betrachtet (humic and ionized-charged water: pH 7.2, total solids 262 mg, hydrogen-bicarbonate 136.4 (52 %), Ca 40.8 (15.6 %), Mg 79.3 (30.3 %), chlorides 10.8). (siehe auch Redfern 2009). Ernährung: natural organic food intake. Low caloric intake (best for longevity: 1400-1600 cal vs 3800 in USA; caloric restriction with optimal nutrition: diets limiting excessive carbohydrates, proteins, while optimizing fat and fat-soluble nutrients. Nutrient-dense diets with fewer calories, restricting sugar and starches, while maintaining an adequate protein intake). Locally-grown fresh fruit and vegetables (high anti-oxidant content). Combinations of oranges/potatoes or tomatoes/broccoli: vitamin C. Much use of avocado. Raw or lightly cooked food. Uncooked seeds are added to soups and stews (notably Quinoa seeds: contain essential amino acids and quantities of Ca, P and iron, high protein content). Quinoa, *Chenopodium quinoa*: originated in Andean regions, e.g. Ecuador. Tolerant of dry soil and high altitudes. A grain crop grown for its edible seeds. Leaves are eaten as leaf vegetables. To sustain energy during forced marches at high altitudes Incan armies used war balls consisting of a mixture of quinoa and fat. Centenarians of Vilcabamba have almost always had a diet that was 70-75 % uncooked, with an emphasis on salads, vegetables and locally grown fruits. Their use of natural, organic, unpasteurized yoghurt from goats and cows provide the beneficial probiotics that might be heated out of the food. Tägliche harte Arbeitsleistung.

Common factors, pertaining to the investigated seven traditionally healthy living populations (THL populations; Tables 2.5.1.2abc), possibly related to their favourable health performance, include nutrition, transgenerational biocybernetic alignment, food being fresh and locally-grown, foods produced under growth rate curbing conditions, availability of ample base minerals (especially magnesium) associated with a balanced acid-base metabolism, daily healthy physical activity, dietary restriction and feast and famine nutritional alternation (daily intermittent fasting, seasonal fasting, extended fasting). All THL populations were characterized by a sound family life and social harmony in general.

I) Nutrition. Macronutrient composition of diets varied among THL populations, but two main groups could be differentiated, relating to peri-artic (Table 2.5.1.2a: Hunza-Nuristani; Table 2.5.1.2b: Caucasus, Ikaria, Sardinia) and subtropical realms (Table 2.5.1.2c: Okinawa, Nicoya, Vilcabamba) respectively (Table 2.5.1.1a: realm-linked metabolic performance modes). All THL populations had in common the absence of refined, commercially processed and grown food items. In an investigation involving a different set of THL populations, Price (1939) compared health outcomes of traditional dietary regimes with those of Western diets (consisting of commercially

produced food items: refined flour products, sugar, polished rice, marmelades, tin food, plant fats). Determination of food nutrient concentrations revealed that traditional diets contained significantly higher nutrient concentrations: calcium 5.2 times higher (2.1-7.5), phosphor 5.4 times higher (2.2-8.2), Magnesium 14.3 times higher (1.3-28.8), Eisen 14.3 times higher (1.5-28.5), more than ten times higher of fat soluble vitamins and also higher concentrations of water soluble vitamin concentrations (THL populations studied: indigenous eskimoes, Indians of northern Canada, residents of Loetschental in Switzerland, the Gallic of the Hebrides, indigenous Australians, Maori in New Zealand, Melanesians, Polinesians, Indians of coastal Peru, and in the Andes of Peru, livestock husbandmen of central Africa and agricultural tribes of central Africa). In all comparisons better health was recorded in the populations with traditional dietary life styles. Poorer health outcomes of the Western diet was attributed to the predominance of refined/processed foods (replacement of nutrient-rich nutritional items) and progressive nutrient impoverishment of soils subject to commercial agriculture. MS DIET-Bulgarian food wisdom

ISSUE OF DAIRY VERSUS MEAT PROTEIN INTAKE Wendt

MS MILK-garrel

MS MILK-Ghadiriam

MS HYPERURICEMIA-MILK-min

MS DAIRY-choi

II) Bio-Cybernetic alignment. THL populations are/were typically isolated in population refugia (in mountains/ islands/ peninsulas) and through endogamy (Tables 2.5.1.1abc). The associated remoteness also favoured the transgenerational continuation of group-specific and site-specific traditional lifestyles and dietary practices. For example, for European-type people, the Peri-artic metabolic performance mode (Table 2.5.1.1a) underpins metabolic competence for seasonal, cold climate regions (high latitude-altitude-winter rainfall regions: temperature-constrained plant growth). Human populations, having historically existed over many generations in specific regions with particular challenges in respect of metabolic performance requirements (e. g. Table 2.5.1.1a) posed by the edaphoclimatic environment and associated nutritional requirements and availabilities, were subject to positive genomic selection to form regionally adaptive polymorphisms (Stover 2007). Interacting with the environment, epigenetic adaptive states arise, but the genetic system specifies the

limiting conditions, that is, the possible epigenetic states of the genotypes (Pál 1998). Under genomic and environmental spatiotemporally sustained conditions, **transgenerational genetic-epigenetic alignment** with the environment (including biogenic information: Table 2.5.1.2d) is sustained, with survival advantages in specific geographic regions, as manifested in health and longevity of THL populations (Tables 2.5.1.2 abc). The Ishkoman and Nagiri (genetically from the subtropical realm), having relatively recently migrated into the area of the Burusho-Hunza-Nuristani population complex (of Euro-Siberian origin, living under periarctic conditions), do not exhibit physical excellence and health performance of the Hunza-Burusho people, although having lived for some time in close proximity to these (Table 2.5.1.2a). Whether genetic-epigenetic discordance is causally involved here, as implicated, would require further verification.

III) Fresh and locally-grown

Traditional healthy living populations typically provide for the daily availability of locally-grown fresh food items. The importance of fresh vegetables and fruit in the diet is generally accepted (Milton 2000) and locally grown in home-linked gardens provides for the ready availability of such food items in alignment with seasonal rhythmicity. Local rearing of domestic live stock is also practised. Biogenic information contained in such produce reflects *subtle organizing energy fields* (Table 2.5.1.2d) arising from interactions of the food organisms with the local environment. An alignment of the genetic-epigenetic and biogenic information systems is accordingly sustained. Fresh and local postnatal diets are considered of importance through the establishment and maintenance of human gut microbiomes (Turner & Thomson 2013), sustaining biocybernetic alignment. These gut microbiomes play important roles in respect of digestion, immune function and nutrient production (Guarner & Malagelada 2003). Local environments and diets seem to result in the development of differentiated and distinct intestinal biomes in human populations (Turner & Thomson 2013) and the disruption of such coevolved mutualisms between human populations and gut microbiota is expected to contribute towards the increasing incidence of chronic and degenerative diseases (Dethlefsen et al. 2007).

Table 2.5.1.2d	**(Life Force Model of Nutrition: Biogenic content of food)** **Konzept: Lebenskraftmodell in der Ernährung**

Biogenischer Nährstoffinhalt **(*vide* Robinson 2012)**
Dr. Edmund Bordeaux Szekely characterized nutritional components according to their energetic and physiological effects (**biogenic potency**) rather than their biochemical composition (calories, proteins, carbohydrates, fats). Nutritional components with high biogenic potency are raw and sprouted seeds, nuts, grains and grasses. Sprouting results in improved nutrient composition and easier digestion. **Such food components with high biogenic potency contain a vital-energetic *blueprint* (life force) and serve revitalisation and bodily regeneration** of the consumer.
This *blueprint* (*Vibrierende Universalenergie*, morphogenetic fields, cosmic energy, Orgonenergy *vide* Wilhelm Reich). All these are designations for an ordered un-manifested state from which manifestation arise in the material, planetary universe. Albert Einstein emphasized repeatedly that matter arises from a pre-existing energy field (op cit Robinson 2012). Wilhelm Reich represented the idea that matter is generated from orgon energy. Morphogenetic fields (*vide* Rupert Sheldrake) represent potential structures of developing systems before its materialisation in physical form (Sheldrake 2009).
The concept of subtle organizing energy fields (SOEF, Subtil Organisierende Energiefelder) is built on a synthes is of both intuitive and scientific knowledge and relates to previous life force models with the interaction of humans, plants and foods.
The existence of *subtle organizing energy fields* is based on the assumption that all living systems are surrounded and penetrated by an energy pattern which determines functionality on all levels (functionality steering/control; Funktionssteuerung). These fields already exist prior to incarnation as information templates (blue prints) for biological structure and functions (refer also to Quantum Physics: Laszlo). When SOEFs are energized they become more structured and form clearer templates for improved total system functioning of organisms (health promoting). The electrical potential of our cells and tissues is enhanced by living nutrients which increase the electrical potential within the cells, between cells and in the boundary zone between cells. When cells have sufficient electrical potential they can effectively detoxify, therewith maintaining their capacities for nutrient uptake and oxygen delivery.
The Krebs Szent-Görgyi cycle (citrus cycle) determines how energy is being produced in our bodies. This energy is transferred as energy-rich electrons and provided to the body in diverse oxidative steps (Albert Szent-Görgyi: Nobel Prize 1937; Hans Adolf Krebs: Nobel Prize 1957).
Life force model of nutrition (proposed by Stan Funk vide Robinson 2012): This paradigm implies a dynamic interaction between the *subtle organizing energy fields* of plants, ingested as food, with the *subtle organizing energy fields* of the human organism. According to this holistic model, plants contain nutrients as well as energy (life force). With the intake of live plant material the energy of the *subtle organizing energy fields* is transferred to the *subtle organizing energy fields* of the human body (Energy fields as information carriers).
When cooked or processed plant material loses the integrity of their *subtle organizing energy fields*. Fresh, raw and unprocessed food materials strengthen our *subtle organizing energy fields*. In this context it is important to note that natural enzymes (metabolic catalysts) are destroyed through heating (notably above 109 °F: 42.8°C). Also through microwaving (Vallejo et al. 2003).

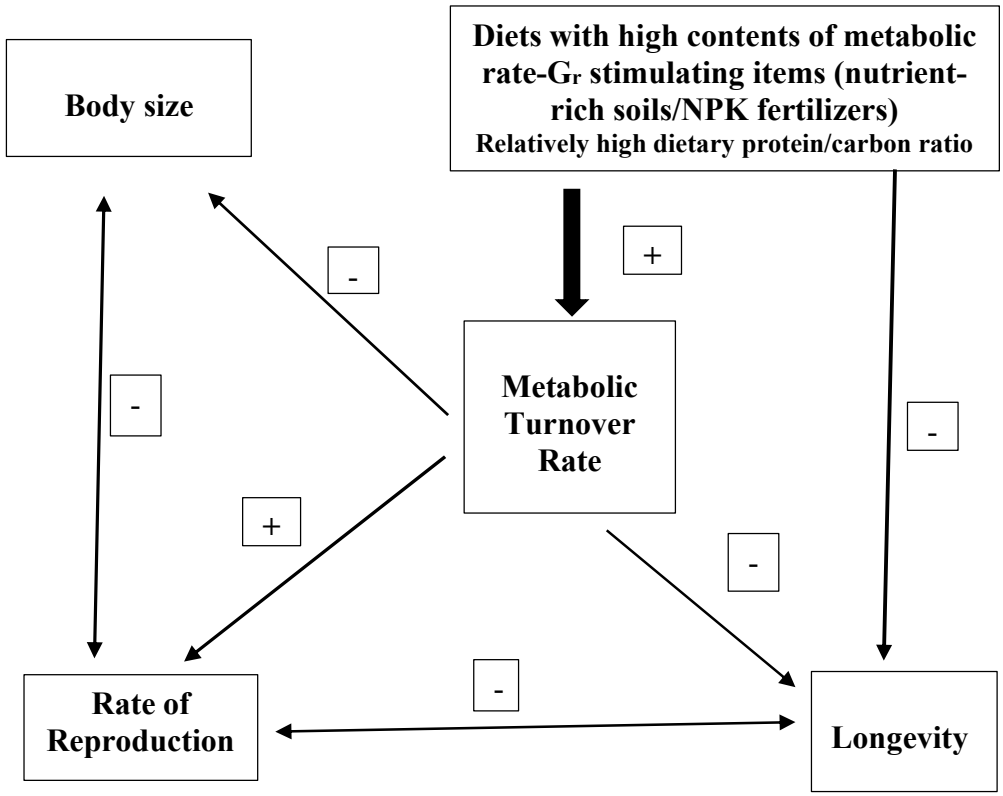
IV) Plant growth rate curbing conditions.

Curbed plant growth due to low temperatures (altitude), nutrient-poor soils in terms of nitrogen, phosphorus and potassium (but possibly mineral-rich) and aridity is typically encountered in environments of THL populations. Congruent with this, higher accumulated nutrient concentrations of plants at higher altitudes (Bano et al. 2009) are reported (cold acclimation of plants). Under such conditions plants are growth efficient (growth tolerance permitting sustained growth) traded off against the capacity for opportunistically high peak growth (resource tracking growth). Nutrient dilution

through high carbon growth is minimized when the metabolism of plants is geared to slow rather than high growth realization. Slow growth realization in plants serving as food items is supportive of a combination of life history features, involving longevity, larger body size and slower rates of reproduction in their consumers (Table 2.5.1.2e).

Table 2.5.1.2e Nutrition and interactive life history features (both inter- and intra-specific)
Diät und interaktive lebensgeschichtliche Strategien (inter und intraspezifisch)

(Life history features *vide* McNab 1980; Eisenberg 1983; McNab 1983; Clutton-Brock and Harvey 1983)



Arrow points show direction of effect and plus (+) or minus (-) signs in square boxes indicate whether effects are positive or negative, respectively.
G_r: growth rate versus G_t: curbed but sustained growth (vide Table 2.5.1.1a).
Reproduction (reproductive rate) *versus* somatic investment (size, storage, longevity) trade-off relationships.

Inherent metabolic turnover LHS settings of species, variants or phenotypic predispositions: high metabolic turnover HMT-low life expectancy *versus* low metabolic turnover LMT-high life expectancy combinations.

In contrast to plant growth-curbing environmental circumstances (high mountains, nutrient poor soils derived from nutrient-poor geological substrates, semi-aridity) usually associated with THL populations promoting low metabolic turnover settings (size, longevity), artificial fertilization has the opposite effect. In pursuit of maximum yields through artificial fertilization (NPK: nitrogen, phosphorus, potassium) quality production (of food with nutrient-physiological quality) is sacrificed (Vogtmamm 1985). Artificial fertilization has *inter alia* been linked to increased levels of health-harming levels of nitrate/nitrites, reduced vitamin C concentrations and increased calcium to magnesium levels (op. cit. Vogtmann 1985). Vogtmann (1985) concludes that biological production systems are superior in providing crop plants with a more balanced nutrient supply. Furthermore, artificial fertilization boosts Gr (growth rate-based) metabolism (high metabolic turnover growth) and associated nutrient compositions in crop plants, inducing high metabolic turnover metabolism (Table 2.5.1.2e) in consumers (propensity towards reduced body size, shorter life span and higher reproductive turnover rates). This would be expected to compromise health and longevity, particularly so in the case of populations of the peri-artic realm (Table 2.5.1.1a: peri-arctic metabolic performance mode).

Rusch (1985)

It is noteworthy that THL populations from the peri-artic realm seem to derive significant health benefits from milk products of goats and sheep (Tables 2.5.1.2a and 2.5.1.2b). The importance of the health-promoting dietary role of milk products from goats and sheep is widely reported, notably in the context of THL populations living in the peri-arctic realm (Tables 2.5.1.2a/b), wheras bovine dairy products are considered problematic (2.5.1.3). Cattle (Bovinae) are geared to feed on high-growth grasses (resource surplus plant growth: water, temperature, nutrients), whereas sheep and goats generally subsist on plants subject to curbed growth conditions (arid, low temperatures, nutrient-poor). Metabolic performance modes of goats and sheep (as feeding on curbed growth plants) are in alignment with the metabolism of their consumers, supporting the combination the combination of large body size/energy storage, longevity and a K-selected reproductive strategy (Table 2.5.1.2e). This is in alignment with the periarctic metabolic performance syndrome (Table 2.5.1.1a). Dietary items from sheep and goats are accordingly expected to be health-promoting particularly for Caucasians. Bovine dairy products, also dependant on the environmental conditions under which the cows

were raised (especially when artificially fed or grass-fed on fertilized pastures), are expected to be less beneficial in this context (high growth rate underpinning high metabolic turnover: association with smaller body size and/or reduced life span, higher reproduve rates, but less investment in energy storage: Table 2.5.1.2e), as they are biocybernetically at discord with the periarctic metabolic performance mode (Table 2.5.1.1a).

V) Base minerals and acid-base metabolism

The association of ophiolites and related geological substrates with THL environments is remarkable. Ophiolites represent oceanic lithosphere, referring to cross-sections of the oceanic crust/lithosphere which had been emplaced on land. Ophiolites and their association with mountain belts suggests that their formation and emplacement are related to oceanic closure and continental collision (Mason 1985). Ophiolites in ophiolitic belts occur as curvilinear zones of mafic-ultramafic rock assemblages (with associated metamorphic and sedimentary rocks), representing relics of different stages of the evolution of ancient ocean basins (Dilek 2003). Following Gamkrelidze (1991), ophiolite nappes are formed as a result of squeezing out of the oceanic type-crust and the occurrence of bilateral or unilateral obduction, occurring simultaneously with oceanic crust subduction. Ophiolitic environments are characteristically associated with alkaline and mineral-rich (glacial) water and soils supporting vegetation adapted to nutrient-poor conditions; thus underlying nutrient-constrained vegetation, but with relatively high magnesium to calcium levels (Angelone et al. 1991). As also recognized by Redfern (2009), traditional healthy living (THL) population groups, typically known for their health and longevity, consistently inhabit high mountain ranges/extinct volcanic islands/peninsulas associated with the availability of pure alkaline water (Tables 2.5.1.2 abc). Alkaline water produces more oxygen in the body; reducing tissue acidity. Such alkaline water has a different viscosity and surfice tension (high alkalinity with a high amount of high active hydrogen, with a negative redox potential). By consuming alkaline water, the body increases its ability to absorb water because of its low surface tension. Wastes and toxins are flushed out easier (Drs Henri Coanda and Patrick Flanagan op. cit. Redfern 2009). Our body needs water with a low surface tension (hard water). If too high, waste removal is inefficient (*re* Nobel Prize Winner 1912 Alexis Carrel, op. cit. Redfern 2009). The central role of magnesium in human health has been summarized in Table 2.5.1.3b (The Magnesium Factor) and the

importance of a balanced acid-base metabolism for health (Jentschura & Lohkämper 2014) was dealt with in Section 2.1.2 (Table 2.1.2c).

VI) Longevity and calorie restriction.

Avoidance of over-eating generally applied to THL populations, but the extent of caloric restriction was variable and unquantified. This would have supported efficient functioning of the digestive system, a key factor in the maintenance of health (**2.1.2**; Rauch 1986). Dietary restriction, that is dietary reduction in food intake without malnutrition, has been found to extend life spans in various organisms and promote healthy aging (Fontana et al. 2010). Profound health benefits of dietary restriction have been reported in humans (2.5.1.4), as associated with low prevalence of obesity, insulin resistance, inflammation, oxidative stress, left ventricular diastolic dysfunction and reduced risk factors for cardiovascular disease (reduced cholesterol, C-reactive protein, blood pressure and intima-media thickness of the carotid arteries). Protein restriction alone may provide some benefits in this regard (Fontana et al. 2010). An extended average and maximum lifespan and an associated lower incidence of chronic disease of the Okinawans is attributed to mild, but prolonged caloric restriction for about half of their adult lives (Willcox et al. 2006). Extreme dietary restriction can however have negative effects on health (Hershlag 2015; Dirks & Leeuwenburgh 2006; Fontana et al. 2010) and certainly on reproductive performance; especially in females. A lifestyle involving substantial or uninterrupted dietary/carbohydrate restriction may be associated with loss of fat and muscle mass, of libido, menstrual irregularities, infertility, bone thinning and osteoporosis, cold sensitivity, loss of strength and negative psychological conditions (Dirks & Leeuwenburgh 2006). Willcox et al. (2007a) reported on a relatively high prevalence of delayed menstruation and deficient lactation, consistent with low caloric intake and/or low body fat levels in Okinawan women. Solon-Biet et al. (2015) CR-solonbiet-macronutrients

Nevertheless, moderate dietary restriction (DR) significantly increases lifespan. Generally, DR has less effect in extending lifespan in males. The proportion of protein intake was more important for life extension via DR than the degree of caloric restriction (Nakagawa et al. 2012). Life extending effects seemed to have peaked at 30 % of the percentage of total food energy coming from protein in relation to the other macronutrients nutrients (carbohydrates and fat). The key determinant of the

relationship between diet and longevity thus seems to be the balance of protein to non-protein ingested. This ratio also affects total energy intake, metabolism, immunity and the likelihood of developing obesity and associated metabolic disorders (Simpson & Raubenheimer 2009). It was the balance of carbohydrates (C) to protein (P) ingested which was strongly correlated with longevity. However, overconsumption of energy on low percentage protein diets in humans (protein appetite drives energy overconsumption) promotes obesity and associated metabolic disorders (Simpson & Raubenheimer 2009). Increased longevity in calorically restricted primates was associated with a reduction in the incidence of diabetes, cancer and cardiovascular disease relative to *ad libitum* fed controls. Even when a fixed diet is nutritionally balanced, when integrated across the entire lifespan, changes in requirenments at a finer time scale will result in accumulated damage from short-term nutrient excess, which may be ameliorated by modest diet restriction (Simpson & Raubenheimer 2009). Nakagawa et al. (2012) emphasize that dietary restriction effects are not to be expected if the protein proportion is < 20 and > 40 %. For the role of macronutrient balance in health and longevity refer also to Solon-Biet et al. (2015). These results are congruent with the patterns of nutrition and life history features in Table 2.5.1.2e. This is also congruent with relatively lower meat-protein intakes in THL populations, but with higher dairy product protein intakes (generally non-bovid), notably of THL populations of the periarctic realm (Tables 2.5.1.2ab).

VII) Daily intermittent fasting. Not to be confused with alternate day fasting. Hershlag 2015 (vide Maimonides): Intermittent fasting, consisting of a daily regimen of two meals per day, involves four components: late breakfast/midday meal as first meal (1), early dinner (2), exercise/physical activity before meals (3) and post-meal rest/ afternoon naps (4). From available records it can be derived that three or all four of these components feature in the daily lifestyles of THL populations (Tables 2.5.1.2abc). Daily intermittent fasting has many health-promoting benefits: avoidance of concurrently high levels of cortisol and insulin during the circadian rhythm, enabling efficient burning of fat, increased deep sleep, assisting in limiting calorie intake and facilitation of autophagy (Table 2.5.1.5d: Daily intermittent fasting).

Autophagy counteracts disease states through cellular self-digestion and autophagic dysfunction is associated with cancer, neurodegeneration, microbial infection and ageing (Mizushima et al. 2008). Daily intermittent fasting can be implemented without

unduely interrupting daily routine, unlike extended fasting, providing some of the benefits of feast-famine alternations to which we seem metabolically adapted.

VIII) Extended fasting.

Ancestral diets varied widely in composition and quality due to factors related to geography, food availability, seasonality and climate (Garn & Leonard 1989); but were generally subject to conditions of alternating feast and famine. THL populations were typically subject to or subjected themselves to fasting, seasonally or under religious protocol. Self digestion (autophagy) is the central mechanism involved (Terman 2006). The findings on autophagy of *inter alia* Bergamini et al. (2007) and Masiero et al. (2009) support the view that regular cycles of feast and famine, also as inducer of thrifty gene expression (Chakravarthy et al. 2004), are important for efficient metabolic functioning. The fundamental advantages accruing through fasting towards health and transgenerational health are strongly supported by empirical knowledge and scientific research (2.1.2; Table 2.1.2d: Fahrner 1985).

Referring to alternate day fasting, Anson et al. (2003) implicate alternating periods of anabolism and catabolism as playing a mechanistic role in triggering increases in cellular stress resistance and the repair of biomolecules and cells resulting from a cellular stress response induced by the fasted state. During phases of limited carbohydrate supply, ß-hydroxybutyrate levels increase in various tissues, including the brain. Mice on the intermittent fasting regime (but sustained calorie intake), rather than those on a daily lowered calorie intake, had larger adipose reserves and a greater ketonic response (ketones are products of fat breakdown for energy). Ketogenesis and ß-hydroxybutyrate have been identified as cytoprotective/neuroprotective in rodent models; supporting the notion that intermittent fasting can enhance health (Anson et al. 2003). Autophagy inhibition is associated with accumulation of abnormal mitochondria, sarcoplasmic reticulum distention, disorganization of sarcomere and formation of aberrant concentric membranous structures. Muscle loss was exacerbated during fasting. Results suggest that the inhibition of autophagous function contributes to myofiber degeneration and weakness in muscle disorders and that autophagy flux plays an important role in preserving muscle mass and the maintenance of myofiber integrity (Masiero et al. 2009).

IX) Lifestyle factors. Regular physical activity (all-muscle workout of diverse, natural movement patterns increasing metabolic rates) was characteristic of all THL populations. Warburton et al. (2006) reviewed the then available literature on health benefits of exercise, confirming the effectiveness of regular physical activity in primary and secondary prevention of chronic diseases and premature death. Furthermore, social harmony and associated minimal stress levels and sound family lives applied to all THL populations, indicating health-promoting circumstances in themselves (especially during gestation, lactation and childrearing). This harmony and the absence of stress during gestation and lactation, supported through crucial life stages by extended full breast feeding generally encountered in such populations, as well as harmonious mothering (2.6a), were a key elements in maintaining transgenerational health. It should however be realized that social harmony was not only health-promoting at any given time, but primarily also the result of healthy constitutions of members of the relevant populations on the basis of transgenerationally low patho-information engram loadings () and the absence of population density stress (*vide* Knaul 1985). Bio-cybernetic continuity in THL populations.

Altukhov & Sheremet'eva (2000 op. cit. Montesanto et al. 2008), for example, found that an increase in population homozygosity resulted in an increase in life expectancy (also Takata et al. 1987, op. cit. Montesanto et al. 2008; Bonafe et al. 2001 op. cit. Montesanto et al. 2008; Cardelli et al. 2006 op. cit. Montesanto et al. 2008). Population inbreeding (homozygosity) contributes to male longevity and tends to equalise male and female lifespan at old ages in comparatively harsh environments (Montesanto et al. 2008) and this effect is seemingly involved in endogamous THL populations in general (Cockerham & Yamori 2001, op. cit. Montesanto et al. 2008; Willcox et al. 2007, op. cit. Montesanto et al. 2008; Poulain et al. 2011). The similarities between observed the spatial pattern of late fertility and high longevity could be related to higher endogamy.
Montesanto et al. (2012); an association also revealed by analyses in respect of Sardinia by Lisa et al. (2015).

Homozygosity is associated with relatively lower peak performance, which ameliorates any performance-maintenance trade-off (LHS-mode PM: allowing for the combination of relatively high performance and maintenance capacities: Section **2.2e**). In contrast,

the secular increase on body height as observed in developed countries during the past 150 years is being attributed to improving living conditions and nutrition, as well as growing heterozygosis (Wolanski 1980, Terrenato & Ulizzi 1983, op. cit. Salaris et al. 2012). Such conditions, notably including increased heterozygosis boost LHS-mode Pm > pM performance: high fertility but at the expense of longevity and health (**2.2e**).

The currently observed health-supporting factors applicable to THL populations are characteristic of a lifestyle sustained over many generations; implying very low levels of or the absence of transgenerationally Patho-Information-Engram load accumulation.

2.5.1.3 Health and nutrition

a) Ancestral nutrition. Hominin diets would expectedly have varied according to geographic locale, climate and specifics of ecologic niche occupation (Cordain 2007; Turner & Thomson 2013). Available evidence suggests that animal foods played a significant role in the diets of hominin species (Cordain 2007). The increased reliance on animal foods formed the basis for enhanced encephalization and concomittant behavioural sophistication of hominids (Cordain 2007; Milton 1999). Brain metabolism is energetically costly (Leonard et al. 2003). Development and maintenance of relatively large human brains accordingly requires high quality diets (relatively rich in energy and other nutrients: energy and nutrient-dense). High body fatness in infancy represents a ready supply of energy to feed the developing brain when intake is limited (Cunane & Crawford 2003). Improvements of dietary quality in this context also involved the incorporation of more animal foods into the diet. Particularly in zones with pronounced winters (as for paleolithic cold climate populations) hunting became essential for survival (Geist 1978). For Caucasians, with a metabolism adapted to cope with seasonally cold climates, the nutritional regime is accordingly designed for an omnivore hunter-gatherer diet in alignment with the peri-arctic metabolic performance syndrome (Table: temperate and subarctic environments).

Milton (2000): Likely macronutrient intakes from plant and animal foods in the diets of recent hunter-gatherers (largely 20th century) were estimated by Cordain et al. (2000). They concluded that most such societies derived more than half of their subsistence energy from animal foods and since wild plant foods have relatively low

carbohydrate contents, protein intake was elevated at the expense of carbohydrate. However, the wide range of dietary behaviours does not fall into one standard macronutrient pattern that contempory humans could emulate for better health. Using data from the *Ethnographic Atlas*, Lee (1968, op. cit. Milton 2000) found that gathered vegetable foods were the primary source of subsistence for most of the hunter-gatherer societies examined, whereas an emphasis on hunting occurred only in the highest latitudes. Data on modern-day hunter-gatherers as well as hunter-gatherer-agriculturalists who consumed traditional diets indicate that such societies are largly free of diseases of civilization regardless of whether a high percentage of dietary energy is supplied by wild animal food, wild plant foods or domesticated plant foods taken primarily from a single cultivar (Ho et al. 1972, op. cit. Milton 2000; Truswell 1977, op. cit. Milton 2000; Neel 1977, op. cit. Milton 2000). Modern human nutritional requirements (e.g. the need for a dietary source of vitamin C), features of the modern human gut (hastrated colon), and the modern human pattern of digestive kinetics (similar to that of great apes) suggest an ancestral past in which tropical plant foods formed the basis of the daily diet, with perhaps some opportunistic intake of animal matter. However, consumption of animal matter to satisfy requirements for protein and many essential micronutrients would free up space in the gut for carbohydrate-rich plant foods and allow for their use as fuel for the increasingly large human brain (Milton 1999). In natural environments, energy-dense, highly digestible foods of any type are generally rare. When available, such foods often serve not so much to serve that day's energy demands but rather to provide fat stores for use as energy during times of low food availability or, in women, to help meet the extra energy demands of reproduction. Humans have large brains and it is thus of particular importance that they are adept at storing excess dietary energy as fat because ketones (derived from fat) can serve as an alternative fuel for the brain.

b) Macrocomposition of diets. Two main forms of diet are being promoted: a low carbohydrate, high protein/fat diet (Banting diet: Noakes et al. 2014; Paleo diet: Cordain 2011; Sanfilippo 2012) and a low protein/fat diet, with relatively high carbohydrate content (e. g. Weiss 1990: protein: 5-10 %, fat: 20 %, carbohydrates: 70-80 %; also intervalfasting diet according to Bracht 2018). Jentschura & Lohkämper (2014) emphasise that a healthy diet needs to be net base yielding (thus predominantly vegetarian). Further interpretation of broadly-based, relevant scientific contributions suggests that a balanced Paleo diet, with some modifications, would best meet health requirements under modern conditions for periarctic populations (Table).

The analysis of Cordain et al. (2000) showed that, whenever it was ecological possible, hunter-gatherers consumed high amounts (45-65% of energy) of animal food (meat and fat). This reliance on animal-based foods, in conjunction with the relatively low carbohydrate content of wild plant foods, resulted in macronutrient consumption ratios of animal-protein (19-35 % of energy), which were higher in comparison with contemporary Western diets, at the expense of carbohydrates (22-40 % of energy),

which were lower than those of contemporary Western diets. On the other hand, Milton (2000) emphasised a diet consisting of a variety of fruit and vegetables, with a slow transit of food particles through the digestive tract, as health-maintaining in hunter-gatherers. Diets of worldwide hunter-gatherers were characterized by a 30-35% carbohydrate content (of total energy intake), decreasing at latitudes beyond 40° north of the equator as meat/fat became increasingly important and available. However, for most hunter-gatherer societies, carbohydrate intakes were typically lower than those of modern Western diets (Ströhle & Hahn 2011). Cordain et al. (2000) estimated plausible percentages of carbohydrate energy intake of historical hunter-gatherer populations as ranging between 22% and 40 %. The relatively high reliance on animal-based foods in hunter-gatherer diets (protein: 19-35 % energy; carbohydrate: 22-40 % energy; fat: 28-58 % energy) was found to be non-atherogenic (largely free of cardiovascular disease; Cordain et al. 2002a). With increasing latitude, plant food availability became seasonally limitited, thus requiring an increasing inclusion of animal food (Cordain et al. 2000). In order to prevent protein toxicity (hyperammonemia and hyperaminoacidemia) an increasingly greater inclusion of fat or carbohydrate in the diet would be required. Simply increasing the plant-animal subsistence ratio by world-wide hunter-gatherers was constrained by considerations of optimal foraging. For hunter-gatherers, animal foods are associated with a higher ratio of energy capture to expenditure than the pursuit of plant-based foods. Calculated plausible percentages of total energy (not exceeding protein toxicity levels) were 19-35 % for dietary protein, 22-40 % for carbohydrate and 28-58 % for fat.

The protein to non-protein energy intake ratio affects lifespan, total energy intake, metabolism, immunity and the risk of developing obesity and related metabolic disorders (Simpson & Raubenheimer 2009). Fung et al. (2010) found that animal-based low-carbohydrate diets were associated with negative health outcomes (higher risk of overall mortality), whereas vegetable-based low-carbohydrate diets were associated with lower risk of all-cause and cardiovascular disease mortality. These findings are not surprising since protein cannot be appropriately processed without sufficient calories from fat and/or carbohydrates. Inadequately processed proteins result in various disease states (Wendt 1985). The findings of Fung et al. (2010) can furthermore be explained with reference to animal-based low-carbohydrate diets probably lacking proper catabolism-anabolism balance and rhythmicity, have insufficiency of

vegetables/fruit contents and likely to be acid rather than net base yielding (Plaskett 2003).

Speth & Spielmann (1983) investigated energy and protein metabolism of hunter-gatherers subject to periarctic metabolic performance constraints (Table **2.5.1.1a**; subarctic and cool temperate environments). Under conditions of marginal caloric intakes, when *lean* meat became the principal source of energy, protein-induced elevated metabolic rates increased caloric requirements and protein catabolism. To counteract the associated loss in body condition hunter-gatherers selectively targeted prey animals with high fat contents and were seeking out carbohydrate-rich foods for the accumulation of body fat stores. The protein-sparing effect of fat and carbohydrate intake was higher for carbohydrates than for fat. This is in agreement with Wendt (1985) who stressed that sufficient energy from carbohydrates and fat is necessary for adequate protein digestion. In general, the importance of vegetables/fruit (carbohydrates) in the diet is widely accepted, especially the uncooked proportion thereof (Rimm 2002; Leenders et al. 2013; Stefler et al. 2016).

High protein intake has been implicated to be damaging to renal function (e.g. Wakefield et al. 2011). Martin et al. (2005) reviewed the evidence concerning the link between high dietary protein intake and compromised renal function. It emerged that excessive protein intake remains a concern in pre-existing renal disease, but the surveyed literature lacked evidence demonstrating a link between protein intake as causative agent in renal pathology. No significant evidence was found for detrimental effects of high protein intakes on kidney function in healthy individuals. However, protein intake has negative health implications if the protein is not processed efficiently by the body (Wendt 1985).

Wendt (1985) contributed a comprehensive explanatory framework dealing with disease ethiology of insufficiency of processing of protein and associated disease states. The body responds to an influx of excess protein with a raised basal metabolic rate, deposition in basal membranes and eventually with protein excretion through the kidneys. The extent of elevation of the metabolic rate is determined by the quantity of aminoacids introduced through the diet and which need to be de-aminated. ***In the presence of sufficient energy from carbohydrates and fat, a larger proportion of the aminoacids can be used to build protein and the metabolic turnover rate is correspondingly reduced*** (promotion of an anabolic metabolic state through the combination of protein and carbohydrates in the same meal is good for the build-up of

body condition). However, overconsumption of protein and when the protein is not fully processed, is likely to result in elevated blood pressure, raised blood sugar levels, elevated erythrocyte and haemoglobin values, kidney damage with albuminurea and thickened basal membranes. Wendt (1985) realized that not only does the body provide for storage of carbohydrates and fat, but also for proteins (in basal membranes). Endothelial cells and pericytes build up and reduce the thickness of the basal membrane, normally keeping its thickness within physiological limits. However, as excess and insufficiently degraded protein is deposited onto basal membranes, the capillary-membrane permeability is progressively reduced. When protein storage in basal membranes takes on pathological forms (overfilling of protein stores) due to insufficiency of protein degradation processes, pathological thickening of capillary basal membranes takes place and their permeability is reduced (hypoporopathies). These hypoporopathies are involved in the pathogenesis of a variety of disease states such as type 2 diabetes, high blood pressure, arteriosclerosis, microangiopathy, retinopathy, gout, pregnancy gestosis and others. Protein antigens also induce hypoporopathies, even at low protein intakes (autoimmune diseases). According to Wendt (1985) about 25 % of individuals of Western populations can be expected to have inherited limited protein degradation capabilities and even normal, moderate protein consumption represents pathological protein overconsumption (protein mast). For these, Wendt (1985) proposes a vegetarian diet, although he recognises the costs thereof in terms of metabolic performance. In individuals with efficient protein processing, a relatively elevated protein intake is beneficial for body growth during adolescence, enhanced reproductive success, heightened joyfulness, spirit for enterprise and cognitive performance in adults. Activites requiring more willpower are less easily performed by individuals under conditions of dietary protein deficit (Wendt 1985) and Wilson (2014) noted that animal protein was a necessary part of the dietary recovery protocol for adrenal fatigue. The crucial importance of protein, particularly in the context of metabolic performance of periarctic people is furthermore documented elsewere (Table 2.5.1.5e). Given the health advantages of protein in the diet, intermittent phases of protein fasting (and other measures: 2.1.2; Table 2.5.1.5e) are preferable to a vegetarian diet in order to address problems of insufficiency in the capacity of protein processing. Extended full fasting is more effective in addressing metabolic hyperproteinaemia, but requires spatiotemporal interruption of the normal work routine; which is not required for protein fasting. Protein fasting takes a few

weeks and involves a diet totally lacking any protein ingredients (any animal-derived items, including egg-based products and all forms of dairy products). Also avoided should be sources of plant-based proteins which are difficult to digest (especially peas, lentils, beans and soya). Complete protein starvation of the body then results in the removal of pathophysiological protein deposits. Protein fasting should not be confused with procedures for intestinal sanitation/cleansing (Darmsanierung), which require different approaches (Rauch 1986; Table). Furthermore, protein fasting is not effective in cases of para- and hetero-proteinaemia, inflammatory or autoimmune processes of which the protein depositions on basal membranes are ongoing and cannot be removed through protein fasting alone. Under such conditions extended full fasting would be required (**2.1.2**; Table **2.1.2h**) in order to fundamentally clear underlying patho-information-engrams. In addition to the 25 % of the population with impaired protein digestion capacity, a further 50 % have only moderate capacities for full protein degradation. Protein degradation processing capabilities accordingly vary widely in populations. Given the progressive increase in patho-information-engram loadings, the issue of efficient protein processing should be considered an issue for everybody. Measures to ensure/facilitate complete/effective protein processing/ digestion are accordingly paramount (Table **2.5.1.3a**). **Daily intermittent fasting and annual extended fasting is required to fully clear hypoporopathies, also including the clearance of underlying patho-information-engrams at the epigenetic level. Bouts of intermittant protein fasting would further assist in this context.**

Table 2.5.1.3a Efficient Metabolic Protein Processing/Digestion
Efficient protein digestion requires sufficient functional metabolic potency (vitality) which is frequently compromised by specific patho-information-engram loadings (2.1.3.2), notably manifesting in adrenal fatigue/insufficiency (yang deficiency; a state of depressed metabolic turnover capacity). Following Wilson (2014) important elements in treating this condition entail stress minimization, healthy sleep and naps, the combination of protein (***animal*** protein as source of yang energy), unrefined carbohydrates and fat at every meal (notably also for breakfast), dietary supplementations (especially pantothenic acid and magnesium) and herbals to balance HPA axis functionality (for more details refer to 2.3.2 ***Adrenal fatigue***). Animal protein as metabolic rate enhancer of up to 30 % following a meal, with diminishing effect lasting for 12 hours (Guyton & Hall, Reed & Hill, op.cit. Snodgrass & Leonard 2009), is indispensable for effective (protein) digestion; as supported by caloric energy from carbohydrate and fat ( ).

Often the epigenetic Impaired Protein Metabolism syndrome (IPM) applies and special measures are then required; such as intermittent protein fasting and other therapeutic measures (**2.1.3.2**; **2.1.3.3**).

Inadequate protein digestion and processing cause diseases of reduced capillary membrane permeability (Wendt 1985).

1. **Eating in a leisurely state of mind** (little mental distraction; in parasympathetic mode of the autonomous nervous system (parasympathetic rest and digestive mode). Consciously tasting in order to cue digestive processes. When in stressed sympathetic mode (fight-flight mode) during food intake body reacts under the assumption that digestive efficiency is insufficient (low parasympathetic competence) and may react allergically to incomimg food items; resulting in compromised digestion. ***A strong feeling of hunger should preceed main meals*** (Wendt 1985).
2. **Intake moderation** (Avoid overfilling of the stomach. Overfilled stomachs result in inadequate digestive processing in the stomach and generally to intestinal functional insufficiency, notably in respect of protein digestion, toxic fermentation in the duodenum and putrefaction in the colon).
3. **Complete chewing** (slow and extended chewing: efficient oral digestion: Jentschura & Lohkämper 2014; Insalivation as initiation of good protein digestion in the stomach. **Significance of stomach acid** (Adequate stomach acid levels are essential for the complete digestion of nutrients, especially protein; only little fluid intake during meals in order to avoid stomach acid dilution). (**Wright and Lenard 2001**)
4. **Warm meals are better digested than cold meals**.
5. **Daily rhythm of meals and rest.** Of particular importance is to delay breakfast until when a feeling of hunger has set in (otherwise poor digestion and absorption must be anticipated). A ***strong feeling of hunger*** should have emerged before meals. This supports efficient digestive processing, especially also of proteins. The hunger-regulating hormone ghrelin initiates stomach acid secretion, which is of particular importance for protein digestion, but also for the full digestive process (Wright & Leonard 2001). Furthermore of importance is resting for half to one hour after the midday meal. The evening meal (a relatively light meal) should be well before going to sleep, when metabolic turnover and thus digestion is reduced (Jentschura und Lohkämper 2014).
6. Sustain a dynamic anabolic-catabolic balance through a balanced diet in respect of all three macronutrients protein, fat and carbohydrates. (Plant proteins are poorly digestible: gluten, phytates, etc. (Sanfilippo 2012). Animal-derived proteins are better digested in combination with fats; bone broth: fat and minerals. No pork: contains sutoxine (Reckeweg 1986). Avoidance/minimization of a*nti-nutrients (*Sanfilippo 2012: refined foods, legumes, sugar, antibiotics, alcohol; soya: contain trypsin inhibitors which disrupt protein digestion (Sanfilippo 2012). With stomach acid deficiency supplementation with apple cider vinegar may be indicated, taken with meals (Wright & Lenard 2001). Supplementation with minerals of plant origin (vegetable juices) is furthermore then recommended in order to facilitate the metabolism of dissolved acids and the excretion of metaboilic toxins (Jentschura & Lohkämper 2014). No alkanising supplemets should be taken within half an hour before meals and within one hour thereafter. Such should preferably be taken at times of the day in alignmement with the daily base rhythm (Jentschura & Lohkämper 2014: Table 2.1.2e). Magnesium supplementation is essential (Section 2.5.1.3h; Table 2.5.1.3b)
7. **Bedeutung vollständiger Proteinverdauung**. Hoher Stoffwechselumsatz erforderlich für effiziente Proteinverdauung; nicht gedämpft durch Antibiotika (Einnahme oder im Fleisch). Proteine müssen vollständig verdaut werden um u. a. körpereigen von Nutzen zu sein, ansonsten sind sie äusserst gesundheitsschädigend (Wendt 1985). Unvollständig verdautes Eiweiss = Fremdeiweiss: induziert Immunrespons = chronische Entzündungsprozesse und autoimmuninduzierend). ***Wendt (1985) furthermore emphasized that sufficient energy from carbohydrates and fat in the same meal is necessary for adequate protein digestion.***
8. A vitally important dietary ingredient for effective protein digestion is bone broth, taken daily (Table **2.5.1.5e**).

Wendt (1985): (Aderlass) Bloodletting for males and postmenopausal females. AS: for all. Minimizing the metabolic incentment for protein storage. Protein fasting re Wendt (1985).

References: Davis 1972, Wendt 1985, Rauch 1986, Jentschura & Lohkämper 2014, Sanfilippo 2012, Reckeweg 1986, Wright & Lenard (2001)

In terms of macronutrient composition, it is here concluded that a healthy diet is required to support a dynamic anabolic-catabolic balance, allowing for amplitudinally pulsating anabolic-catabolic metabolic states. The animal-protein component underpins elevated rates of metabolic turnover performance catabolic processes, whereas the vegetable-carbohydrate component supports anabolic metabolic processes (at lower metabolic rates), notably energy storage in the form of fat. Both metabolic states are required for the maintenance of body condition (Table) and health. Fat intakes, providing high caloric density substances, buffer against overconsumption of either proteins or carbohydrates in pursuit of calorie intake as needed; thereby also facilitating rhythmicity of anabolic-catabolic metabolic states and processes (which would be impeded under caloric over- or underconsumption). A life style which supports recursive healing must provide for alternate states of metabolic catabolism (autophagy) and anabolism (body condition-building), mutualy reinforcing one another.

c) Acid versus net base yielding diets. African Paleolothic hunter-gatherers consumed near-neutral to net base producing diets, which differed from populations which had colonized higher latitude environments *ca* 46000-7000 years ago (Stroehle et al. 2010). Upper Paleolithic Europeans then consumed a predominantly animal-based diet (plant to animal food ratios around ≤ 26: ≥65: Cordain et al. 2000), which would be generally net acid-producing; reflecting reduced bicarbonate and increased endogenous organic acid production (Stroehle et al. 2010). They calculated that with animal fat densities of between 3-10 % the diets of hunter-gatherers would have been net acid-producing at latitudes > 40° and net base producing < 40° (in the model including 20 % animal fat densities these latitudes were < 50° and > 50° respectively). Hunter-gatherer diets with 15 % animal fat densites tended to be net base-producing at latitudes 41-50°. This highlights the importance of animal fat densities for the achievement of net base-producing diets in populations functioning according to the periarctic metabolic performance syndrome (*vide* Table). According to Sebastian et al. (2002), a shift towards net acid producing diets can result due to the displacement of high-bicarbonate-yielding plant foods of the preagricultural diet (base-rich plant food groups: roots, tubers, leafy green vegetables, vegetable fruit, fruit) by cereal grains and energy dense, nutrient-poor foods (separated fats, refined sugars, vegetable oils)

characteristic of contemporary diets. Sebastian et al. (2002) emphasized that the net base producing effect of replacing cereal grains and energy-dense with non-grain plant food groups was achieved without changing the amounts of net acid-producing animal foods (meat, cheese, milk, yoghurt, eggs) in the diet. This implies that a net base-producing diet is compatible with substantial animal-protein sources included in the diet.

Extrapolation from available knowledge furthermore suggest that potential health benefits may accrue from a life-long dietary net base load, *inter alia*, in respect of osteoporosis (Sebastian et al., 1994; Bushinsky 2001), muscle wasting (Ballmer et al. 1995) and slowing of age- or disease related chronic renal insufficiency (Goraya & Wesson 2013; Kraut & Madias 2016; Raphael 2016). According to Raphael (2016) acidosis is associated with demineralization and protein catabolism in patients with chronic kidney disease, effects which could be ameliorated with alkaline treatment.
Chronic metabolic acidosis stimulates protein degradation, down-regulates albumin synthesis and induces a state of sustained negative nitrogen balance in humans (Ballmer et al. 1995). The findings of Wiederkehr & Krapf (2001) show that metabolic acidosis is characterised by decreased body bicarbonate stores and is known to induce endocrine and metabolic disturbances (nitrogen wasting, depression of protein metabolism, growth hormone insensitivity = a mild form of hypothyroidism and hyperglucocorticoidism, negative calcium balance = resorption from bones, hypophosphataenemia). Metabolic acidosis is accordingly an important factor in wasting syndromes, particularly also associated with many illnesses. Chronic metabolic acidosis notably increases glucocorticoid (mediator in acidosis-induced protein catabolism) activity in normal human subjects (Sicuro et al, op. cit. Wiederkehr & Krapf 2001). JentschuraTABLE

d) Low carbohydrate diets. Paoli et al. (2013a) reviewed the therapeutic uses of very-low-carbohydrate (ketonic diets) diets. Ketogenic diets involve a reduction in carbohydrate intake and relatively increased proportions of protein and fat. The authors emphasize that ketosis is a completely physiological process clearly to be differentiated from pathological diabetic ketoacitosis. Normally insulin activates enzymatic pathways for the storage of carbohydrates as fat. Under conditions of reduced carbohydrate availability (drastically reduced carbohydrate consumption: < 50g/day; fasting) glucose reserves become insufficient for fat oxidation via the Krebs cycle and for the

supply of glucose to the central nervous system (CNS). Ketone bodies are then used as source of energy in tissues, most importantly also by the CNS. During the associated fasting states autophagy is activated, producing multiple and decisive health-regenerative benefits (2.1.2; Table-fasting; Table-IF). Paoli et al. (2013a) reviewed the evidence for positive effects of low-carbohydrate-diets in the treatment of weight loss, cardiovascular disease, type 2 diabetes and epilepsy (op. cit. Paoli et al. (2013a); as well as emerging evidence of potentially treatment-supportive roles in cases of acne, cancer, polycystic ovary syndrome and multiple neurological disorders (headache, neurotrauma, Alzheimer's and Parkinson's disease, sleep disorders, brain cancer, autism and multiple sclerosis; op. cit. Paoli et al. (2013a). There is strong supporting evidence that ketogenic diets are effective in weight-loss therapy. Paoli et al. (2013a) list several factors involved in the weight loss effect of very-low-carbohydrate diets: a) Reduction in appetite due to higher satiety effects of proteins, effects on appetite control hormones and to a possible direct appetite-suppressing effect of ketone bodies. b) Reduction in lipogenesis and increased lipolysis (greater metabolic efficiency in consuming fats). c) Increased metabolic costs of gluconeogenesis and the thermic effect of proteins. However, long-term weight loss and maintenance was optimally achieved with a long-term Meditteranean diet coupled with brief periods of a metabolism enhancing ketogenic diet (Paoli et al. 2013b). However, prolonged and uninterrupted metabolic states of carbohydrate deprivation are counterproductive (Plaskett 2003; Hershlag 2015). Persistent ketosis leads to acidosis and associated negative effects on renal function, bone mineral and nitrogen balance and negative effects on the nervous system (Plaskett 2003). It also prevents the build-up and maintenance of body condition; which may compromise female reproductive success; particularly in the case of non-obesic body condition types (Table 2.5.1.5c).

e) Grain cereals. It is undisputed that without cereal grains there could not have been an agricultural revolution allowing for increased human population concentrations and associated societal stratification leading to the development of technological and industrial progress. Neither could present-day human populations be sustained. However, Cordain (1999) refers to significant evidence that cereal grains (grass seeds), were generally less consumed in preagricultural periods, and implicates that such represent suboptimal food items for humans since the human genetic make-up and physiology is apparently not fully adapted for the efficient processing of high levels of

cereal grain consumption (Cordain 1999). Whenever cereal-based diets were first adopted as staple food, replacing primarily animal-based/fresh-vegetable/fruit diets of hunter-gatherers, poorer health outcomes resulted. These included a reduction in stature, increased infant mortality, reduced lifespan, an increased incidence of of infectious diseases, iron deficiency anemia, osteomalacia, porotic hyperostosis and other bone mineral disorders, an increased incidence of dental caries and enamel defects (op. cit. Cordain 1999). Cereal grain consumption as a predominant dietary source of carbohydrate and proteins is a relatively recent phenomenon (adoption thereof 5500-10000 years ago) and it is contended by Cordain (1999) that there is considerable genetic discordance between the cereal grain staple and foods humans were adapted to genetically. Following from this, Cordain (1999) outlined health challenges associated with and attributed to grain cereals: lacking some nutrients essential for human health (which becomes a problem when grains form a substantial part of the diet by *inter alia* displacing antioxidant-rich fruit and vegetables), low bioavailability of various vitamins (e.g. vitamin B_6) and minerals, and the inability of humans to overcome associated cereal grain antinutrients (such as phytates, alpha-amylase inhibitors, alcylresorcinols, protease inhibitors, lectins and others). Certain cereal peptides seem to interact with the immune system resulting in a variety of autoimmune-related diseases. For example, dietary antigens from milk, grain and legume as food sources contain peptides which mimic those found in joint tissue of arthritis patients. Cordain (1999) discusses varies autoimmune diseases where cereal grain antigens are implicated to be involved: celiac diseases, dermatitis herpetiformis, insulin-dependant diabetes mellitus, rheumatoid arthritis, IgA nephropathy, aphthous stomatitis, multiple sclerosis and various psychological/neurological illnesses (such as epilepsy, autism, schizophrenia). Revealingly, most of the listed conditions may occur simultaneously with celiac disease.

According to Cordain (1999), the human digestive system is inherently unadapted to deal with grass seeds (grains), resulting in poor health outcomes as a result of their consumption. On further consideration, however, this notion appears invalid (Turner & Thomson 2013) and negative health outcomes are rather associated with refined grain product consumption; whereas whole grain intake is associated with health benefits (refer to *inter alia* to Slavin 2004; Espeseto & Giugliano 2006; Fardet 2010; below).

Slavin (2004): Coarse bran delays gastric emptying and accelerates small bowel transit. The coarse nature of whole grains as compared with refined grains has unique physiological effects beyond composition differences between whole and refined grains (McIntyre et al. 1997, op. cit. Slavin 2004). Plasma insulin responses increased stepwise, with whole grains less than cracked grains less than coarse flour less than fine flower. Oat-based meals evoked smaller glucose and insulin responses than wheat or maize-based meals (Heaton et al. 1988, op. cit. Slavin 2004). Wholegrain products are relatively high in antioxidant activity (e.g. soluble antioxidants include phenolic acids, flavonoids and tocopherols). The total antioxidant activity of wholegrain products is considered similar to that of fruit and vegetables on a per serving basis (Miller 2001, op. cit. Slavin 2004).

Antinutrients found in grains include digestive enzyme (protease, amylase) inhibitors, phytic acid, haemagglutinins, and phenolics and tannins. However, protease inhibitors, phytic acid, phenolics and saponins have been shown to reduce the risk of cancer of the colon and breast in animals. Phytic acid, lectins, phenolics, amylase inhibitotrs and saponins have also been shown to lower plasma glucose, insulin and/or plasma cholestrerol and triacylglycerols (Slavin et al. 1999, op. cit. Slavin 2004). Food consumption patterns that include whole grains appear protective for cardiovascular disease. The intake of refined diets which do not include whole grains were associated withn higher serum cholesterol levels and lower intakes of micronutrients (Van Dam et al. 2003, op. cit. Slavin 2004).

Furthermore, whole grains are an excellent source of dietary fibre, resistant starch and oligosaccharides, which are fermented by intestinal microflora to short-chain fatty acids, such as acetate, butyrate, and propionate. Short-chain fatty acids have been shown to lower serum cholesterol (Hara et al. 1999, op. cit. Slavin 2004). Pereira et al. (2002, op. cit. Slavin 2004) investigated the effect of substitution of whole grain for refined grain on insulin sensitivity. Fasting insulin levels were 10 % lower after 6 weeks on the whole grain diet. This suggests that a change in insulin sensitivity may be responsible for the reduction in insulin levels and the risk of type 2 diabetes reported in epidemiological (population) studies. There is substantial evidence that whole grains as commonly consumedreduce the risk of cancer. In a meta-analysis of whole-grain intake and cancer, whole grains were found to be protective in the majority of cases (Jacobs et al. 1998a, op. cit. Slavin 2004). Epidemiological studies have reported that higher serum insulin levels are associated with an increased risk of colon, breast and possibly other cancers. The reduction of these insulin levels by whole grains may be an indirect way in which the reduction in cancer risk occurs. Whole grains also contain several antinutrients, such as protease inhibitors, phytic acid, phenolics and saponins, which until recently were thought to have only negative nutritional consequences. Some of these antinutrient compounds may act as cancer inhibitors by preventing the formation of carcinogens and by blocking the interaction of carcinogens and cells. Other potential mechanisms linking whole grains to a reduced cancer risk include large-bowel effects, antioxidants, alterations in blood glucose levels, weight loss, hormonal effects, and the influence of numerous biological active compounds.

Preliminary studies suggest an association between whole-grain intake and the regulation of body weight (Pereira 2002, op. cit. Slavin 2004). Whole grains were inversely associated with BMI and waist:hip ratio at baseline and 7 years later (Pereira et al. 1998, op. cit. Slavin 2004). Whole grains are a good source of fibre; and individuals with the highest dietary fibre intake gained approximately less 3.6 kg less in weight than did those with lowest intake. Similar results were found for the waist:hip ratio (Ludwig et al.1999, op. cit. Slavin 2004). Regarding all-cause mortality, Liu et al.

(2003a, op. cit. Slavin 2004) reported that both total mortality and CVD-specific mortality were inversely associated with whole grain but not refined grain breakfast cereal intake.
Whole grains are rich in many components, including dietary fibre, starch, fat, antioxidant nutrients, minerals, nutrients, lignans and pheolic compounds that have been linked to the reduced risk of CHD, cancer, diabetes, obesity and other chronic diseases. Most of the protective components are found in the germ and bran, which are reduced in the grain-refining process.

Espeseto & Giugliano (2006): Evidence suggests that whole-grain intake confers protection against the metabolic syndrome, associated inflammation and cardiovascular disease. Higher fiber content of whole-grain food items was found to be associated with a reduced likelihood elevated C-reactive protein (CRP: a marker of inflammation) regardlessof age and BMI (King et al. 2003, op. cit. Espeseto & Giugliano 2006). High intakes of cereal fiber were furthermore associated with higher plasma concentrations of adiponectin (an insulin-sensitizing adipocytokine). The increased consumption of foods rich in refined grains and poor in natural antioxidants and fiber is implicated to cause an activation of the innate immune system (excessive production of proinflammatory cytokines associated with a reduced production of anti-inflammatory cyokines). The thus favoured inflammatory milieu is implicated to result in a predisposition of the metabolic syndrome.

Fardet (2010): Epidemiological studies have clearly shown that whole grain cereals can protect against obesity, diabetes, cardiovascular disease and cancers. The specific effects of food structure (increased satiety, reduced transit time and glycaemic response), fiber (improved faecal bulking and satiety, viscosity and short-chain fatty acid production, and/or reduced glycaemic response), and Mg (better glycaemic homeostasis through increased insulin secretion) together with the antioxidant and anti-carcinogenic properties of numerous bioactive compounds, especially those in bran and germ (minerals, trace elements, vitamins, carotenoids, polyphenols and alkylresorcinols), are today well-recognized mechanisms in this protection. The involvement of polyphenols in cell signalling and gene regulation, and of sulphur compounds, lignin and phytic acids should be considered in antioxidant protection. Whole grain wheat is also a rich source of methyl donors and lipotropes (methionine, betaine, choline, inositol and folates) that may be involved in cardiovascular and/or hepatic protection, lipid metabolism and DNA methylation. Potential protective effects of bound phenolic acids within the colon, of the B-complex vitamins on the nervous system and mental health, of oligosaccharides as prebiotics, of compounds associated with skeleton health, and of other compounds such as α-linolenic acid, policosanol, melatonin, phytosterols and *para*-aminobenzoic acid also deserve to be studied in more depth.

Such positive health effects () are consistent with notable whole grain consumption by traditionally healthy living (THL) populations, especially those of the Peri-arctic realm (2.5.1.2; Tables 2.5.1.2a/b)

f) Bovine dairy products. Dietary proteins in cow milk cross react with beta-cell antigens, therefore being suspected to represent environmental etiologic agents.

Exposure to cow milk triggers a cellular and humeral anti-ß caseine immune response cross-reacting with a beta-cell antigen (Cavallo et al. 1996). Many traditional healthy living (THL) populations gain their protein requirements predominantly from dairy products rather than meat, especially as age progresses. Efficient protein processing of dairy protein for such populations, as implicated by Wendt (1985), is however likely to be based on their robust health to begin with (patho-information-engram loadings low or absent).

For new-borns, which still have weak protein digestive capacities, milkproteins are readily digestible, not so meat proteins (Wendt 1985). Also in adults, depending on the efficiency of their protein metabolisms, milk protein is better digestible than meat protein. This suggests that protein from dairy products is less likely to result in health problems in this context and is consistent with long-living THL populations often meeting their protein requirements from dairy products; especially those living in periarctic environments (Section **2.5.1.2**).

Dairy product intake has an inverse relationship with uric acid. According to a study by Choi et al. (2005c), higher levels of meat and seafood consumption were associated with higher serum levels of uric acid, whereas dairy consumption was inversely associated with serum uric acid levels. Individuals consuming yogurt at least every other day had lower serum uric acid levels than those who did not (Choi et al. 2005). The implicated mechanism for the inverse relationship between dairy product consumption and serum uric acid levels involve the uricosuric effect of milk-forming proteins lactalbumin and casein (Ghadirian et al. 1995).

Wright & Lenard 2001). In infants, an allergy to cow's milk may cause gastroesophageal reflux (Miloco et al., op. cit. Wright & Lenard 2001; Staiano et al. 1995 DL MILK INTOLERANCE-staiano; Iacono et al., op. cit. Wright & Lenard 2001) and be involved in type 1 diabetes in some infants (Paronen et al. 2000 DL AUTOIMMUNITY-paronen RE BREASTFEEDING. Investigators found impaired gastric acid secretion in cow-milk intolerant infants also leading to atrophic gastritis (Kokkonen et al., op. cit. Wright & Lenard 2001).

MS AUTOIMMUNE-cavallo Staiano et al. 1995 DL MILK INTOLERANCE-staiano; Generally, according to Wendt (1985) proteins from dairy products are more efficiently metabolically processed than meat proteins. DL DIET-dairy protein DL DIET-bendtsen-dairy protein ALSO CHECK DAIRY ISSUE OF LACTASE PERSISTENCE CH Lactase (an enzyme) is is necessary fo the complete digestion of

whole milk; it breaks down lactose, a milk sugar. Lacking lactase results in the symptoms of lactose intolerance.

DL DAIRY-vesa-lactose

MS MILK-garrel

MS MILK-Ghadiriam

MS DAIRY-choi 2005c

Biocybernetic disalignment

By excluding such antigens, relief of symptoms is often achieved (impoved immune system functioning). Curing of relevant disease conditions however generally requires involving ultimate causality at the epigenetic level (reduction of patho-information-engram loading through autophagia and acute immunological interactions, as during fever and inflammatory states). Internal ref

g) Fructose. Lustig (2010) fructose: Fructose consumption linked to rising rates of obesity, type 2 diabetes and metabolic syndrome. Obesity has been equated with addiction. Examined fructose and its fermentation product ethanol. 1. Hepathic fructose metabolism is similar to ethanol as both serve as substrates for de novo lipogenesis and in the process both promote hepatic insulin resistance, dyslipedemia and hepatic steatosis. 2. Fructolisation of proteins with resultant superoxide formation can result in hepatic inflammation similar to acetaldehyde, an intermediary metabolite of ethanol. 3. Fructose creates habituation and possibly dependence also paralleling ethanol. Fructose induces alterations in both hepatic metabolism and central nervous system energy signalling, leading to vicious cycle of excessive consumption and disease consistent with metabolic syndrome. Gedgaudas (2011).

Hershlag (2015): Relative to other carbohydrates, fructose-enriched meals have a poor ghrelin suppression capacity, thereby promoting increased caloric intake, weight gain and obesity under conditions of chronic consumption. Leptin strengthens the immune system and suppressed levels thereof under prolonged calorie restriction can lead to illness. Elliott et al. 2002. DL FRUCTOSE-quyang DL FRUCTOSE-tappy MS FRUCTOSE-KIDNEY-gersch DL FRUCTOSE-Johnson-2007 MS DIET-schwarz-thermogenesis

BRING IN ROLE OF POLYPHENOLS COUNTERACTING NEGATIVE FRUCTOSE EFFCTS

Gersch, M. S., Mu, W., Cirillo, P., Reungjui, S., Zhang, L., Roncal, C., Sautin, Y. Y., Johnson, R. J. & Nakagawa, T. (2007). Fructose, but not dextrose, accelerates the progression of chronic kidney disease. *American Journal of Physiology. Renal Physiology* 293 (4): F1256-F1261.

Johnson et al. (2007): Excessive caloric intake and physical inactivity are implicated as important factors driving the obesity epidemic. But, also fructose has the unique ability to induce an increase in uric acid, thereby representing a mechanism by which fructose can cause cardiorenal disease. Elliott et al. (2002) identified the fructose content of sugar as a critical component associated with obesity and heart disease. (sucrose is a disaccharide consisting of 50% of fructose and 50% of glucose). Clinical studies confirmed that sucrose (and particularly fructose) can induce weight gain and features of metabolic syndrome. Diets enriched with sucrose (Cohen et al., op. cit. Johnson et al. 2007) or fructose (Faeh et al. 2005 **DL EPI-galloukalani-metabolic syndrome**) were found to cause impaired glucose intolerance and insulin resistance. Fructose, but not dextrose accelerates the progression of chronic kidney disease (Gersch et al. 2007). Mice fed fructose-sweetened water gain more weight than mice given the same calories in starch; with the implication that fructose may slow the basal metabolic rate (DL FRUCTOSE-jurgens-adiosity). Fructose is the only sugar that raises uric acid concentrations ().
Nakagawa et al. (2006) found that lowering uric acid concentrations could counteract features of metabolic syndrome induced by fructose (including weight gain, hypertriacylglycerolemia, hyperinsulinemia, insulin resistance, and hypertension). The negative effects of uric acid are seemingly in contrast to its positive role as, *inter alia*, an important antioxidant (Ames et al. 1981). Existing studies have implicated uric acid as independant risk factor/predictor of hypertension, obesity, hyperinsulinemia and renal disease (op. cit. Johnson et al. 2007). The mechanism implicated in uric acid having these effects involves a reduction in the concentrations of endothelial nitric oxide. Impaired production of endothelial nitric oxide results in dysfunctionalities characteristic of the metabolic syndrome.

URIC ACID-nakagawa-fructose Nakagawa et al. (2006)
The increased incidence of metabolic syndrome corresponds with both elevated uric acid and fructose intake. Fructose raises uric acid levels, which in turn inhibit nitric oxide bioavailability. Insulin requires nitric oxide in order to promote glucose uptake. The authors accordingly hypothesised that fructose-induced hyperuricemia may have a causal role in the pathogenesis of metabolic syndrome. The authors found that fructose, but not dextrose, induced hyperuricemia, hyperinsulinemia and hypertriglyceridemia (components of the metabolic syndrome). In rats fed a high fructose diet, the lowering of uric acid with either allopurinol (a xanthine oxidase inhibitor) or benzbromarone (a uricosuric agent) prevented or reversed features of the metabolic syndrome. Allopurinol prophylactically prevented fructose-induced hyperinsulinemia, systolic hypertension, hypertriglyceridemia and weight gain. Uric acid inhibited endothelial function in a dose-dependant manner. (Johnson is a consultant for pharmaceutical firms).

DL URATE-zgaga-sugar Zgaga et al. (2012).
Sugar-sweetened beverage consumption was positively sssociated with urate. Dairy, calcium and lactose intakes were inversely associated with urate. Energy-adjusted fructose intake was not associated with urate (other studies finding a positive association often had much higher fructose intake levels). Meat intake was associated with plasma urate concentration, but not seafood intake in general or shell fish in particular. Skimmed milk and low calorie yoghurt were negatively associated with urate; whereas the intake of semi-skimmed, full-fat milk, low-fat and full-fat yoghurt were not. Our results do not support the hypothesis that fructose is the causal agent underlying the association between sugar-sweetened beverages and urate. See also Livesey (2009) DL URIC ACID-livesey

From the considerations presented in this and previous sections a central principle in the context of nutrition is now being stated: for efficiency of metabolic processes they must function in a *state of dynamic balance.* This implies anabolic-catabolic, base-acid, sufficiency-deficit food intake, balanced macronutrient intake, fasting, protein intake-protein fasting states must be in sequential alternation according to some schedule in order to achieve health and the promotion of recursion healing.

Katabolismus/Anabolismus: def. + Fasting/CR/Starvation

h) Calcium *versus* magnesium

Laires et al. 2004; Laires & Monteiro 2008; Kim et al. 2010 3x in ref

Cavicchia et al. (2009)

Table 2.5.1.3b The Magnesium Factor	
Magnesium is involved in numerous regulatory and biochemical systems and the impact of low levels (hypomagnesemia) spans all areas of health and medical practice (Dean 2014). Magnesium ions stabilize structures of proteins, nucleic acids, and cell membranes by binding to the surfaces of macromolecules and promote **catalytic activities** of proteins, enzymes and ribozymes. Magnesium insufficiency is of particular relevance in societies subject to many social, dietary and environmental stressors, resulting in sympathetic nervous system dominance (Gedgaudas 2011). Prevalent epigenetic high patho-information-engram loadings are associated with metabolic functional insufficiencies and low fight-flight reaction thresholds (2.1.2); predisposing towards dominance of the sympathetic mode of functionality of the autonomous nervous system. We were however designed for predominance of functional efficiency in the parasympathetic state (*inter alia* Gedgaudas 2011). **Magnesium** is of critical importance for the healthy functioning of both the sympathetic and **parasympathetic nervous systems**, **especially the latter** (Gedgaudas 2011; Dean 2014).	
Factors predisposing towards magnesium deficiencies (Dean 2014) • Stress: Adrenaline and cortisol, being byproducts of of the fight/flight response, are associated with decreased magnesium levels. Stress causes magnesium deficiency and such deficiencies tend to magnify stress reactions. • Low magnesium diets (processed foods) and drinking water (soft water). Low nutrient densities of agricultural products due to growth-accelerating modern	A

farming practices on increasingly mineral-deficient soils. Refined sugar causes accelerated magnesium excretion and nutrient-poor dietary components dilute nutrient concentrations of the food intake. • Relative overconsumption of calcium through high intake of dairy products. • Alcohol overconsumption and other addictions. • Medications causing magnesium deficiencies (also Ca supplements). • Aging and associated illnesses. Digestive disorders. The natural processes of aging, as *inter alia* associated with reduced stomach acid levels compromizing magnesium absorption. • Digestive and genetic disorders. **Note: With modern-day sources of nutritional items and the prevalence of functional inefficiencies due to generally high patho-information-engram loadings, certainly Caucasians are expected to generally suffer from hypomagnesemia.**	
Sircus (2014a): ***Medical treatments of any kind are likely to be less effective or ineffective when magnesium deficiencies are left untreated***. Magnesium deficiencies are consequential in the ethiology of all major diseases, including cancer, diabetes, neurological disorders and stroke. Gedgaudas (2011) provides a comprehensive list of disorders commonly associated with magnesium deficiencies; including ADHD, anxiety disorders, autism, chronic fatigue syndrome, crooked teeth or narrow jaw (in children from magnesium-deficient mothers), gut disorders (including allergies), heart disease, migraines, myopia, osteoporosis, stroke and thyroid disorders.	
Migraine, insomnia, depression and chronic fatigue: associated with magnesium deficiency (Vink & Nechifor 2011). Yablon & Mauskop (in Vink & Nechifor 2011) described the role of magnesium in the pathogenesis of headaches (migraines, tension-type headaches and cluster headaches). Sun-Edelstein & Mauskop (2009) suggest that magnesium deficiency may play a central role in the pathogenesis of migraine headaches by promoting cortical spreading depression, alterations of neurotransmitter release and the hyperaggregation of platelets. Studies pertaining to the therapeutic role of magnesium supplementation were reviewed and positive results found regarding the treatment of migraine headaches, menstrually related migraine, pediatric migraine and other neurological disorders. The authors recommend daily treatment with 400 mg of chelated magnesium or slow-release magnesium in patients with suspected hypomagnesemia (*inter alia* migraine headaches, premenstrual syndrome, cold extremities and muscle cramps). Lowered brain cytosolic Mg^{2+} levels seem to be secondary to bioenergetics deficits in the brain of patients suffering from various forms of migraines, stroke migraine and cluster headache (Iotti & Malucelli, in Vink & Nechifor 2011). Treatment with oral CoQ10 (Coenzyme Q_{10} 150mg/day for 6 months) increased cytosolic Mg^{2+}; which was attributed to the improved efficiency of mitochondrial energy production. Thus, magnesium functionality is closely linked to cell bioenergetics and ion transport systems (Barbiroli et al. 1999). Mauskop & Varughese (2012) recommend that all migraine patient should be treated with magnesium. Deranged magnesium homeostasis is implicated in the pathogenesis of *inter alia* various types of migraine (Lodi et al. 1997). From the findings of their study on migraine patients, Lodi et al. (2001) conclude that the reduction in free Mg^{2+} in tissues with mitochondrial dysfunction (low brain cytosolic magnesium) is secondary to the associated bioenergetics deficit. Hence the combined supplementation with Mg-Vit B6 and coenzyme Q_{10} is indicated.	A
Physiological role of magnesium. H.R. Evers: The mitochondrion generates the energy for the cells to use. Energy is derived from oxidative reduction of cellular respiration.The problem arises when the cell is low in magnesium relative to calcium. Adenosine triphosphate, the energy currency, is magnesium dependant. Low levels of available magnesium inhibit the generation of energy and the low levels of energy inhibit the calcium pump. The mitochondria become calcified (beginning of aging). Every function of your body can be inhibited when the mitochondria calcify. Magnesium Mg^{2+} is the fourth most abundant cation in the body and second most cation in the cell (Romani in Vink & Nechifor 2011). Various cellular functions and enzymes (ion channels, metabolic cycles, signalling pathways) are regulated by magnesium. Magnesium is involved in a myriad of biochemical processes including acting as a cofactor in the activation of many intracellular enzymes, is important for protein	A

synthesis and cell proliferation (Rubin, in Vink & Nechifor 2011); and cell membrane stabilization (Ghabriel & Vink in Vink & Nechifor 2011). Dietary magnesium intake is inversely related to levels of C-reactive protein, a marker of inflammation, and levels of E-selectin, a marker of endothelial dysfunction (Song et al. 2007). Rate of protein synthesis is regulated by concentrations of intracellular Mg^{2+} (Rubin, in Vink & Nechifor 2011). (Dean 2014).	
For the medical practitioner: Seelig (1980: Magnesium Deficiency in the Pathogenesis of Disease). Serum magnesium levels of routine blood testing are not a reliable marker of pathological hypomagnesemia (*inter alia* Yablon & Mauskop, in Vink & Nechifor 2011).	
Magnesium deficiency can result in cell membranes over time becoming resistant to the diffusion of oxygen into the cell interior and supplementation is required in order to maintain proper cell oxygenization (Sircus 2015).	
In the face of growing magnesium deficiencies calcium becomes increasingly more toxic to human physiology. Calcium becomes a poison to tissues all over the body when in excess relative to magnesium in deficiency (Sircus 2014c). It is magnesium which controls bone density, not calcium. Strong and prolonged treatment with magnesium in its chloride form. Magnesium chloride is the most versatile, absorbable and effective form of magnesium (can be taken orally and transdermally). Seaweed contains relatively high levels of magnesium, iodine and selenium. Magnesium chloride is useful in preventing and treating unwanted calcifications.	
Magnesium renders calcium more water-soluble; it increases the solubility of calcium in the urine. Sufficient magnesium is required to prevent the build up of calcifications in body tissues (Dean 2014: The Magnesium Miracle). If calcium is not taken with magnesium, it is not highly absorbable. Unabsorbed calcium can lodge anywhere in the body. Calcifications can manifest as heart disease, cancer, arthritis, kidney stones, osteoporosis, dental problems, cataracts, vascular calcifications, senility (when lodging in the brain) and many other health problems.	
Seelig et al. (1975): Suggested that chronic magnesium deficit may contribute to the syndrome of latent tetany, pshychosomatic complaints and weakness. Makes reference to possible metabolic encephalopathy that may be caused by chronic magnesium deficit (op. cit. Seelig et al. 1975). Seelig (1994)	B
Vink & Nechifor (2011): **Magnesium and the Central Nervous System** Cytosolic Mg^{2+} is a function of the energy charge of brain cells and defective mitochondrial respiration results in a derangement of cytosolic Mg^{2+} homeostasis. Magnesium therapy has been used in numerous experimental and clinical settings: migraine, asthma, depression, diabetes, hypertension, atrial fibrillation, sleep disorders, insomnia, chronic fatigue, dementia, osteoporosis, pain, fibromyalgia, eclampsia, constipation, cerebral palsy, lacunar stroke, traumatic brain injury and aneurysmal subarachnoid haemorrhage (op. cit. Ghabriel & Vink, in Vink & Nechifor 2011). According to Billard (in Vink & Nechifor 2011), the long-term increase in magnesium levels promotes the conversion of synapsis to a plastic state, while learning and memory capacities were enhanced in adult animals fed a diet enriched in Mg^{2+} L-threonate. This treatment significantly elevated brain Mg^{2+} and improved learning and memory in aged animals. The findings of Sludsky et al. (2010) suggest that an increase in brain magnesium (with Mg^{2+} L-threonate) enhances both short-term synaptic facilitation and long-term potentiation and improves learning and memory functions. Abumaria et al. (2011) report on the effects of elevated brain magnesium on fear conditioning and fear extinction linked to synaptic plasticity of the prefronatal cortex. Hoane (in Vink & Nechifor 2011) emphasizes the role of magnesium in learning and memory; and provides a review of related literature in respect of cognitive functioning. Particularly Mg^{2+} L-threonate was shown to increase cerebrospinal fluid levels of Mg^{2+} (more so than other magnesium preparations), enhancing cognitive learning abilities in rodents. Yablon & Mauskop (2011) related to the role of magnesium in the pathogenesis of headaches (migraines, tension-type headaches and cluster headaches); and the association of chronic diseases with hypomagnesemia (diabetes, asthma, cardiovascular disease, pre-enclampsia); furthermore including delirium, lethargy, weakness,	

parethesias, tremors, pre-menstrual syndrome, cold extremeties, leg or foot cramps, seizures, ventricular arrhythmias and congestive heart failure. Sendowski et al. (in Vink & Nechifor 2011) explain the role of magnesium in hearing loss, Na et al. (in Vink & Nechifor 2011) in respect of pain (including dysmenorrhea, severe uterine cramps, neuropathic pain), and Cook et al. (in Vink & Nechifor 2011) in relation to central nervous system injury (including the development of post-stroke secondary injury cascades made up of deleterious biochemical and patho-physiological reactions). Saver & Starkman (in Vink & Nechifor 2011) deal with magnesium in clinical stroke, cancer (Leidi et al. in Vink & Nechifor 2011). Oyanagi & Hashimoto (in Vink & Nechifor 2011): magnesium in Parkinson's disease; Chui et al. (in Vink & Nechifor 2011): magnesium and Alzheimer's disease; Papadopol & Nechifor (in Vink & Nechifor 2011): magnesium and neurosis/neuroticism; Nechifor (in Vink & Nechifor 2011): magnesium in psychoses; Eby et al. (in Vink & Nechifor 2011): magnesium and depression; Nechifor (in Vink & Nechifor 2011): magnesium in drug abuse and addiction.	
Magnesium and stress Cuciureanu & Vink (2011; in Vink & Nechifor 2011): Stress and hypomagnesemia potentiate each other's negative effects. Hypomagnesemia has *inter alia* been associated with various stessful conditions, including photosensitive headache, fibromyalgia, chronic fatigue syndrome, audiogenic stress, cold stress and physical stress. A stressor (physically or psychologically) activates activates the hypothalamic-pituitary-adrenal axis (HPA axis) and the autonomic nervous system. Neurotransmitters are involved in the coordination of the endocrine, autonomic behavioural and immune responses to stress. Magnnesium interacts in a number of ways with the activity of neurotransmitters and neurohormones. Psychological stress promotes oxidative stress and decreases anti-oxidant activity. Numerous associated processes are antagonized by magnesium. Cernak et al. (op. cit. Dean 2014) confirmed a negative correlation between magnesium balance and oxidative stress under conditions where chronic psychological stress had resulted in decreases in free and total magnesium concentrations and increases in oxidative stress intensity. Poor magnesium status generally increases sensitivity to stress (see also Henrotte et. al. 1997). Bardgett et al. (2005). Anti-depressant activity of zinc and magnesium (Szewczyk et al. 2008). Magnesium and sleep: experimental magnesium deficiency has also been associated with disrupted sleep patterns, shorter life span and lower fertility (Chollet et al. 2001- DL-MAG). Held et al. 2002: re sleep DL-MS The general adaptation symdrome according to Selye (1978) represents a system according to which the body responds to any demand for change (stressor impact). It represents three stages of adaptation: an initial brief alarm reaction, a prolonged period of resistance and then followed by a stage of exhaustion. Hypomagnesemia is often linked to increased neural excitability, increased anxiety, orofacial tardive dyskinesia, and migraine symptoms; which can apparently be alleviated with a Mg-Vit B6 combination (Garcia-Lopez et al., op. cit. Cuciureanu & Vink in Vink & Nechifor 2011). An inverse relationship has been observed between audiogenic stress and erythrocyte magnesium levels. Similarly, low magnesium levels have been reported with noise sensitivity, noise-induced emotional lability and noise-induced feeling of tenseness (Galland op. cit. Cuciureanu & Vink (in Vink & Nechifor 2011). Exposure to long-term road traffic noise has been found to lead to elevated night-time secretion of noradrenalin and cortisol (Ising & Braun 2000). A correlation has been described between magnesium levels in seum and peritoneal fluid and stress perception in healthy women who were unable to conceive, although no identified organic causes of sterility were evident (Jung et al., op. cit. Cuciureanu & Vink, in Vink & Nechifor 2011; Garalejic et al., op. cit. Cuciureanu & Vink, in Vink & Nechifor 2011). Paolisso & Barbagallo (1997): on the role of intracellular magnesium in hypertension, diabetes and insulin resistance.	*
Magnesium and ADHD: A correlation has been reported between ADHD and magnesium deficiency. Elevated subjective stress levels and stress intolerance tend to be part of the clinical manifestation of adult ADHD (Hirvikoski et al. 2009): Individuals with ADHD reported more self-perceived stress and subjective stress was correlated with the amount of stressors in everyday life. Magnesium deficiency was detected in children with ADHD (Kozielec & Starobrat-Hermelin op. cit. Cuciureanu & Vink in Vink & Nechifor 2011). Magnesium supplementation significantly reduced hyperactivity in children with ADHD (Starobrat-Hermelin & Kozielec 1997). Mousain-Bosc et al. (in Vink & Nechifor 2011) summarize and interpret current knowledge on	

magnesium in relation to ADHD: linked to intracellular magnesium deficiency, affecting mainly neural transmissions which are sensitive to such ionic variations. Successful symptom-relieving treatment with Mg-Vit B6 (6 mg/kg/day Mg and 0.6 mg/kg/day vitamin B 6). Durlach et al. (2000). Pyroluria is commonly associated with *inter alia* intractable mood disorders, depression, alcolholism and ADHD (Gedgaudas 2011). Testing for pyroluria is strongly indicated in cases of ADHD and comorbid disorders.	
Dean (2014: The Magnesium Miracle): Calcium enters the cells of the heart by way of calcium channels that are guarded by magnesium, at a concentration 10 000 times greater than that of calcium in the cells, allowing only a certain amount of calcium to enter to create necessary electrical transmissions. Then immediately ejects the calcium when its work is done. When calcium accumulates in the cell it causes calcification and disrupts cell function (angina, high blood pressure, arrhythmia, asthma, headaches, heart attacks).	B
Durlach et al. (2002): MS MAG-durlach-2002 Magnesium enhances melatonin secretion by the pineal gland through stimulation of serotonin N-acetyl transferase activity, the key enzyme in serotonin synthesis. The sedative effects of magnesium rely on *inter alia* neural mediated effects such as stimulation of inhibitory neuromodulators (GABA, taurine) and antagonism of neuroactive gases. Chronopathological forms of magmesium depletion with decreased production of melatonin: sleep disorders, migraine, chronic fatigue syndrome, fibromyalgia, some forms of asthma and of sudden infant death syndrome.	A
Adverse effects of calcium intake may include high blood calcium levels, kidney stone formation and kidney complications. Elevated calcium levels are also associated with arthritic/joint and vascular degeneration, calcification of soft tissue, hypertension and stroke, mood and depressive disorders, chronic fatigue and general mineral imbalances involving magnesium, zinc, iron and phosphorus. High calcium levels interfere with vitamin D.	
Magnesium controls the fate of calcium in the body. If magnesium is insufficient calcium will be deposited in the soft tissues (kidneys, arteries, joints, brain etc).	A
High doses of calcium carbonate taken alone over a long period will cause low magnesium levels (Cámara-Martos, F. & Amaro-López, M. A. (2002). Researchers currently estimate that the ratio between calcium and magnesium should be 2:1 (Celotti & Bignamini 1999). Magnesium is needed to encourage the correct utilization of calcium in the body to increase bone strength (Jones et al. 2000).	C
While the body uses calcium to buffer excess acidity, excess calcium causes calcifications. Too much calcium running through the body is the real danger of excess acidity. Increased intake of other buffers such as magnesium will safely buffer excess acidity without causing calcifications. The real danger of excess acidity is leeching calcium that it causes. Excess acidity causes soft tissue calcifications. Dr H. Ray Evers: The chemical reaction of magnesium is alkaline (acid binding). It regulates the acid-alkaline balance of the body.	A ph
With a low magnesium intake, calcium goes out of the bones to increase tissue levels, while a high magnesium intake causes calcium to go out of the tissues into the bones. High magnesium leads to bone mineralization.	
Magnesium should be used to buffer acid pH, not the calcium that is being leeched from the bones. Magnesium taken in proper dosages can solve the problem of calcium deficiency (Dr Nan Kathryn Fuchs). AS The higher the acidity the more calcium is needed for acid neutralization which must be complemented with magnesium supplementation.	A ph
Dietary sources of magnesium: Animal-derived Mg sources are superior to plant-derived sources (Dean 2014). MS MAG-magnesium rich foods	Sources
Enhancement of learning and memory by elevating brain magnesium (Slutsky et al. 2010) DL MAGlearningmemory	MENTAL
Acidosis. Catabolic metabolic waste products are highly acidic and acidosis is one of the main contributors that lead to the aging process and various illnesses. One of the first warning signs of an acidic biological terrain is calcium deposits. Acid wastes not effectively excreted will accumulate in body tissues (capillaries, blood vessels) eventually clogging these up. Also, the cells will be deprived of their supply of oxygen	C ph

and nutrients. The greater the acidity, the harder it is for oxygen to be present. Biological terrain becomes more anaerobic. Without adequate oxygenation, unfriendly bacteria, viruses, molds and fungi can prosper. Efficiency of life-giving functions of cells jeopardized (because our biological chemical reactions require oxygen). A pH less than 5.3 indicates an inability to assimilate vitamins and minerals. Furthermore, with capillary blood vessel clogged up, the function of every organ in the body accumulating acidic waste will begin to deteriorate, causing serious illnesses in the long run.	
Therapeutic magnesium supplementation (Sircus 2014): **Magnesium chloride** is dose sensitive. Magnesium chloride (popularly known as magnesium oil) from the Zechstein Sea (250 million year old deposits) **is most effective**. Bath flakes are made from this ancient oil; and Dead Sea salt and Epsom salts for medicinal baths. Magnesium chloride used transdermally is strongly indicated in the treatment of any chronic and some acute diseases. Recommends magnesium chloride (over sulphate). **Magnesium oil massage** (rubbing half to full ounce over body or cover body like one would with a sun screen and go out in the sun). **Full-body baths with magnesium** flakes (1-4 pounds/bath), Dead Sea salts or Epsom salts. Soak body in bath water for 20-30 minutes, at a temperature of about 42.2 °C. Specially sensitive control is required in the case of children regarding dose levels, water temperature and magnesium levels. **Drinking of magnesium chloride** in water or juice. For maximum therapeutic effect combine with one of the transdermal routes. Minerals such as magnesium, **in ionic liquid form** are greatly superior to pill forms (greater absorption; absorption less dependent on stomach hydrochloric acid levels). Five sprays of magnesium oil into a glass of water amounts to about 100 mg of elemental magnesium. Five, ten or even 20 sprays of magnesium chloride in a glass of water represents an effective way of taking magnesium internally. Raising cell levels of magnesium is most effectively undertaken through a combination of oral intake (guided by bowel tolerance; taken just before, during or right after meals; but see Dean 2014 below) and daily transdermal use (applying magnesium oil all over body) or with baths with magnesium flakes, Dead Sea salts or Epsom salts (no oral intake or gargling); mixed with sodium bicarbonate (baking powder). Getting the dosages high enough is of paramount importance (with all protocol items start slow, get used to each substance and then slowly bring the dosages up). **Anyone with kidney failure needs to take extreme caution. As applicable generally, consult professional medical advice and guidance in respect of supplementation protocols.**	
Magnesium bicarbonate (which only exists in seawater; not obtainable in solid form) represents the combination of magnesium chloride and sodium bicarbonate. Sodium bicarbonate (baking powder) increases cell voltage, pH, oxygen levels and CO_2; promotes hydration. Magnesium bicarbonate (as found in seawater): make it for yourself: filter your water and add quality magnesium chloride to taste in the water and some sizable pinches of sodium bicarbonate (Sircus 2014).	
Dean (2014): **Magnesium chloride** is favoured in terms of absorbabilty. Minerals require to be dissolved in gastric acid on order to go into solution, and magnesium chloride has extra chloride molecules to produce hydrochloric acid in the stomach, thereby enhancing its absorption. Also, avoid ingestion of anti-acids before meals. **Picometer magnesium** is a non-laxative liquid form of magnesium which is fully absorbed at the cellular level. **Magnesium taurate** particularly also relates to heart conditions (Magnesium and taurine have synergistic effects in stabilizing cell membranes, calming the nervous system and inhibiting nerve excitation). Magnesium taurate, glycinate and orotate are aminoacid chelates with less laxative effects. (Strictly avoid magnesium glutamate and aspartate). Gastric hydrochloric acid insufficiencies may require digestive support with *inter alia* betaine hydrochloride. As magnesium absorption in the digestive system requires sufficient gastric hydrochloric acid, magnesium in pill form should not be be taken within one hour before and after meals (but preferably one dose in the morning and one dose in the evening). Also, as magnesium is an alkaline mineral it may neutralize stomach acid to a certain extent, thereby impairing digestion.	
Sircus (2014a): Calcification and its treatment with magnesium: Magnesium acts as a natural guide or valve in the brain synapses that regulates influx of calcium into postsynaptic channels from presynaptic neurons in parts of the brain that	B

are involved in mood and behaviour (e.g. hippocampus). With inadequate magnesium (calcium toxicity), this function becomes altered and irritability, anxiety, depression, ADHD, mania, hypomania, bi-polar disorder, hyperexcitability and even psychoses may result (Dean 2014).	

i) Vitamins

Stomach acid for absorption

Food sources of B6-B9-B12 and cofactor sources

Folate/folic acid etc differentiation

Table 2.5.1.3c possible

Neurodegenerative disorders
FOLATE-EPI-mattson

FOLATE-blount

Vitamin B12 (cobalamin) is particularly important for normal nerve activity and brain function. In combination with folate and vitamin B6, homocysteine levels are kept under control.

Folic acid. Wright & Lenard (2001): Folic acid (folate) is a B vitamin which is required to control the amino acid homocysteine towards reduced levels for i.a. healthy functioning of the cardiovascular system and preventing certain birth defects. With advancing age, folate levels tend to decline which is then associated with rising homocysteine levels. Adequate folic acid intake (400-800 micrograms/day) through the diet is often not achieved and its absorption compromised due to stomach acid insufficiency.
Vitamin B12 deficiency (Dr Edward Group; Global Healing Center)
7. **Cognitive impairment**. In the elderly, B_{12} (cobalamin) deficiency cognitive impairment and dementia. This deficiency has also been linked to other neurodegenative disorders such as multiple sclerosis and Parkinson's disease (McCaddon 2013). MS VITB12-mccaddon- 8. **Psychosis**. Depressed mood, hallucinations, seizures and hypertension have been found in subjects who tested positive only for low vitamin B_{12} levels. Administration of vitamin B_{12} has been found to result in recovery within a week (Dogan et al. 2012). MS VITB12-dogan- 9. **Melancholic depression**. Individuals suffering from melancholic depression (caused by physical rather than psychological factors) have consistently displayed an inverse relationship between vitamin B_{12} levels and depression (Seppälä et al. 2013). MS VITB12-seppala 10. **Stroke**.

11. **Alzheimers disease**. A recently published study demonsrated a treatment of folic acid, B_6 and B_{12} as a significant improvement in the reduction of cerebral atrophy (Douaud et al. 2013). DL HYPERHOMOCYSTEINEMA-douaud-vitB-alzheimer
12. **Cardiovascular disease**. Without vitamin B_{12} the body cannot convert homocysteine. This leads to a build-up of homocysteine levels which have been associated with atherosclerosis and increased risk of cardiovascular mortality (Refsum et al. 2006). MS HOMOCYSTEINE-refsum

Vitamin B12 (cobalamin) is particularly important for normal nerve activity and brain function. In combination with folate and vitamin B6, homocysteine levels are kept under control.

MS DEPRESSION-vancampfort-metaboilicsyndrome
MS VITB12-stanger-B6-folicacid
MS VITB12-king
MS HYPERHOMOCYSTEINEMIA-ibrahimagic-parkinson
MS HYPERHOMOCYSTEINEMIA-vandenberg-vitaminB6-plus
MS HYPERHOMOCYSTEINEMIA-modaghegh-folicacid
MS HYPERHOMOCYSTEINEMIA-clarke-folate-B12
DL HYPERHOMOCYSTEINEMIA-douaud-vitB-alzheimer
MS HOMOCYSTEINE-fenech-chromosome-
MS HOMOCYSTEINE-ganzi-factors
MS HOMOCYSTEINE-rasmussen
MS HOMOCYSTEINE-nurk
MS HOMOCYSTEINE-refsum
DIET-HOMOCYSTEINE-arija

Neurodegenerative disorders
FOLATE-EPI-mattson

MS Intrinsic factor wikepedia

Wright & Lenard (2001) Vitamin B_{12} enters the body bound to proteins (mainly animal-derived: meat, eggs, dairy products); for it to be absorbed the vitamin B_{12} molecule must first be separated from the protein with the help of stomach acid and pepsin. Onced free the vitamin B_{12} quickly combines with another type of protein binder originating from the salivary glands, stomach, liver, pancreas and other GI organs. When the re-bound vitamin B_{12} enters the small intestine (near neutral pH) pancreatic proteases break the vitamin free again, which now combines with a substance called intrinsic factor. Intrinsic factor is secreted by parietal cells, the same cells that produce and release HCl. The vitamin B12-intrinsic factor complex then moves through the small intestine to the terminal ileum, where it binds to specific receptors and is absorbed into the blood stream.

2.5.1.4 Feast-famine dynamics at multiple temporal scales

a) Feast-famine: from daily intermittency to transgenerational effects

Our metabolic energy system (as underpinning the LHS-mode PM under feast-famine conditions: 2.2.2e) worked well for our ancestors who lived in an environment of periodic carbohydrate surplus and deficiency (Wallace 2005). However, with unlimited dietary calories, including carbohydrates throughout the year, relevant energy signalling systems remain continuously in the high carbohydrate state. As a result, mitochondrial OXPHOS (oxidative phosphorylation) and associated antioxidant defences are chronically down-regulated (Wallace 2005).

Depending on degree and duration of DR (dietary restriction), it may represent either a state of ***starvation*** (**DR-starvation**) or induce a state of increased metabolic efficiency of energy utilization in association with ***autophagy*** (**DR-autophagy**).
DR (dietary restriction)/CR (calorie restriction) imposes a low-intensity biological stress on the organism Sinclair (2005), eliciting an active defense response, here termed CR stimulus effects. CR stimulus effects induce enhanced metabolic rates (Speakman et al. 2004), underpinning increased rates of catabolic protein turnover and autophagous processes (Sinclair 2005). The enhanced energy use efficiency of CR-cued metabolism underpins performance capacity, but with little trade-off costs in terms of maintenance, as manifesting in widespread autophagy-based health benefits associated with CR-cued metabolism (2.5.1.4b).

Prolonged calorie restriction represents extended starvation which differs from shorter fasting bouts (time-restricted CR: e.g. daily intermittent fasting, day fasts, alternate day fasting) and extended full fasting in its physiological effects. Short fasts incur CR-stimulus effects, thereby establishing states of CR-cued metabolism (2.5.1.4b). Time-restricted feeding/fasting regimes do not require a significant reduction in overall caloric intake in order to produce health benefits; indicating that the state of fasting rather than the reduction in caloric intake is important in producing associated health benefits (Dirks & Leeuwenburgh 2006; 2.5.1.4b).

Extended full fasting involves a switch in metabolic state characterized by the absence of hunger when autophagic self-healing processes then take effect (2.1.2c: Fasting); contrasting the situation during starvation where hunger sensations persist because of sufficient food intake preventing the metabolic shift into the fasting state. Prolonged CR resembles starvation where self-healing based on autophagy is no longer achieved (refer to Füllgrabe et al. 2014; 2.1.2d).

Füllgrabe et al. (2014): The adaptive autophagic stress response has been referred to as being biphasic (Pietrocola et al. 2013, op. cit. Füllgrabe et al. 2014). However, in light of the discovery of autophagy-regulated histone modifications, the presence of a triphasic effect is implicated. After a rapid autophagic response involving the post-translational modification of cytosolic proteins (phase 1), a collection of transcription factors upregulate the expression of genes encoding proteins that sustain and regulate, generally increasing, autophagic flux (phase 2). After prolonged exposure to autophagic stimuli, a global change in histone modifications acts as a negative regulatory feed back loop (phase 3: Pietrocola et al. 2013, op. cit. Füllgrabe et al. 2014). One of the roles of global chromatin silencing durung phase 3 could be the establishment of an autophagy memory'. Histone modifications have the potential to induce stable changes in the chromatin landscape, potentially even affecting subsequent generations (Greer et al. 2011, op. cit. Füllgrabe et al. 2014). Thus, a prolonged starvation response might prepare an organism for a future starvation event.

It is concluded that intermittent states of fasting (CR-stimulus effects: autophagy induction) are responsible for health benefits, rather than calorie restriction *per se* (states of starvation often associated with dietary reduction).

b) Caloric restriction

Sinclair (2005): McCay et al. (1935, op. cit. Sinclair 2005) found that feeding rats with 20 % indigestible cellulose substantially extended mean and maximum lifespan. Variations of such a dietary regimen, currently known as caloric restriction (CR) or dietary restriction (CR), are the most effective way of extending the maximum lifespan of mammals (Masoro 2000, op. cit. Sinclair 2005). Hypotheses intended to explain the life-extending effects of caloric restriction include/relate to I) developmental delay; II) reduced metabolic rate; III) glucocorticoid cascade, IV) decreased fat; V) reduced oxygen species; VI) cell survival hypothesis; VII) protein turnover; VIII) decreased glucose and insulin levels and IX) other endocrinological changes.
With respect to developmental delay (McCay et al. 1935, op. cit. Sinclair 2005), the notion that extended ageing is caused by a genetic program is no longer considered valid (Krystal & Yu 1994, op. cit. Sinclair 2005). Rather, ageing is thought to occur due to an organism lacking sufficient energy to fully prevent and repair cellular damage. However, genes that favour health and fecundity in youth can be maintained

in a population even though they are deleterious in older individuals (e.g. Charlesworth 2000, op. cit. Sinclair 2005). In respect of the reduced metabolic rate hypothesis, it has been shown that CR animals have equal or higher metabolic rates than *ad libitum* fed animals after having experienced an initial drop in metabolic rate during the first six weeks (Masoro 1998, op. cit. Sinclair 2005; Speakman et al. 2004).

Speakman et al. (2004): The 'rate of living-free-radical theory' suggests a negative association between metabolic rate and longevity (Sohal 2002, op. cit. Speakman et al. 2004), whereas the 'mitochondrial uncoupling to survive' hypothesis (which involves a positive association between high metabolism and longevity) suggests that the correlation should be positive. The results of Speakman et al. (2004) support the 'mitochondrial uncoupling to survive' hypothesis; i.e. a positive association between high metabolism and longevity.

Sinclair (2005): Among scientists who consider ROS to be of relevance in the context of CR, some consider that the diet primarily works by decreasing damage hypothesis as ROS production or increasing ROS defences and repair (reviewed by Merry 2004, op. cit. Sinclair 2005). Generally, there remains considerable disagreement about the validity of the free-radical damage hypothesis. In the context of the cell survival hypothesis, it is well accepted that CR modulates the susceptibility of cells to apoptosis. Elevated levels of the SIRT1 protein can lead to decreased apoptosis (Cohen et al. 2004b, op. cit Sinclair 2005). SIRT1 also deacetylates the FOXO3 transcription factor, tipping the scales further toward cell protection and survival (Brunet et al. 2004, op. cit Sinclair 2005). Furthermore, it has been proposed that SIRT1 serves to protect irreplaceable cells (such as neurons and stem cells) from death during times of stress, therewith maintaining physiological function with age (Cohen et al. 2004b, op. cit Sinclair 2005). Protein turnover rates and autophagous processes (auto-digestion) decline with age and this decline is attenuated by CR (Del Roso et al. 2003, op. cit Sinclair 2005; Tavernarakis & Drisoll 2002, op. cit Sinclair 2005).
Recent data support the idea that CR is not simply a passive effect, but an active, highly conserved stress response that had evolved to increase chances of survival of organisms subject to adversity. With this idea as basis, Sinclair (2005) presents a synthesizing hypothesis, the Hormesis Hypothesis of CR, which proposes that CR imposes a low-intensity biological stress on the organism, eliciting an active defense response that also helps the organism by protecting it against the causes of ageing. There is general consensus that the health benefits of CR derive from a defense response of the organism to a perceived threat to its survival. Thus, the effect of CR, as ancient adaptive response, is to provoke an active functional response to stress, actively altering metabolism evolved to promote the survival of organisms during adversity.

Kirkwood et al. (2000): Food-restricted animals show a range of increased stress response mechanisms. It has been suggested to be an outcome of natural selection for life history plasticity. Since maintenance systems can be costly, a significant proportion of basal metabolism can be involved in maintenance and repair. Available studies support the role of somatic maintenance and stress response systems in controlling the rate of ageing. Kirkwood et al. (2000) developed a model for the dynamic optimization of efforts allocation and reproduction in response to fluctuations in food availability. They predict that ageing results from the progressive accumulation of unrepaired cellular damage, eventually leading to disease and death. Lifespan is considered to be influenced by longevity assurance genes controlling the levels of somatic maintenance

and repair. (**AS: the higher the EPIE-load the greater the requirements for somatic repair; accentuating the maintenance/longevity-reproduction trade-off. Also, the higher the environmental stress perception/survival under density stress, the greater the Reproduction vs Survival trade-off**). Long-term calorie restriction results in smaller, leaner animals which are otherwise healthy and active, but with impaired fertility. Somatic maintenance functions are up-regulated (Masoro 1993, op. cit. Kirkwood et al. 2000). An organism with less energy (under CR) up-regulates metabolically/energetically costly physiological processes which are bound to be at the expense of energy available for reproduction. According to Holliday (1989) it is advantageous to increase investment in somatic maintenance at famine-resource levels in order to increase survival rates under conditions suboptimal for reproduction; thereby adaptively allocating resources maximizing fitness under conditions of intermittent food stress (Shanley & Kirkwood 2000, op. cit. Kirkwood et al. (2000).

Kirkwood & Shanley (2005): Features of food-restricted rodents: appear to have a general up-regulation of mechanisms protecting against accumulation of somatic damage: protein turnover, serum corticosteroids (Masoro 1995, op. cit. Kirkwood & Shanley 2005), DNA repair activity (Haley-Zitlin & Richarson 1993, op. cit. Kirkwood & Shanley 2005), cytosolic antioxidants (Yu 1994, op. cit. Kirkwood & Shanley 2005) and the expression of heat shock proteins (Heydari et al. 1996) all remain at youthful levels for longer. Incidence rates of tumors are reduced (Schwartz & Pashko 1994). Calorie restriction virtually eliminated the development of autoimmune diseases in susceptible strains of mice (Weindruch & Sohal 1997, op. cit. Kirkwood & Shanley (2005).
The primary role of the food restriction response is to allocate resources away from reproduction during period of food resource deficits when the likelihood of reproductive success is low, to invest any available resoures into increased somatic maintenance (AS: S investment for successful future reproduction: longevity ≈ reproductive span, reduction of PIE loadings, offspring survival ≈ competitive competence under population density stress. From present to future reproduction ≈ longevity and transgenerational). The potential benefit is that the animals gain an increased chance of survival with a reduced intrinsic rate of senescence, thereby permitting reproductive value to be preserved to after the famine. Laboratory rodents on calorie-restricted diets have extended life spans and retarded ageing. Shanley & Kirkwood (2000) tested the hypothesis that this is an adaptive response involving a shift in resource allocation during periods of food resource shortages away from reproduction and towards increased somatic maintenance. The potential benefit is an increased chance of survival with a reduced intrinsic rate of senescence; permitting reproductive value to be preserved for future times of resource adequacy. Tested with a mathematical life-history model of dynamic resource allocation. Allocation of resources to maximize number of descendants. Found model plausible if maintenance of a reproductive state carries some overhead costs (a minimum investment in reproduction being required in order to initiate a fertile state) and offspring survival is reduced during famine.
Kirkwood & Shanley (2005): On refeeding, female rodents previously kept on restricted diets were able to reproduce at much later ages than fully fed controls (Holehan & Merry, op. cit. Kirkwood & Shanley 2005). Energy allocated to maintenance was used for anti-ageing cellular functions such as DNA repair and free radical scavenging (in the model). The optimum investment in somatic maintenance

and repair varied with food availability level. At intermediate food levels, corresponding with calorie restriction, it was found that there was generally a fitness advantage to be gained from increasing the investment in maintenance (repair). For CR to induce up-regulation of somatic maintenance and repair should pay a reproductive overhead (physiologically primed for fertility) and that juveniles have impaired survival prospects during periods of famine. Even a small restriction in diet results in a beneficial effect on survival (Weindruch & Sohal 1997, op. cit. Kirkwood & Shanley 2005) and the life extension effect is unlikely to solely depend on the existence of a reproductive overhead. Molecular turnover is increased in food-restricted animals and is expected to be a potent mechanism for the rejuvenation of cellular components that may have been damaged by intrinsic processes of ageing.

Pallauf et al. (2013): Incidence of cardiovascular disease CVD is low in certain parts of Asia (e.g. Japan) and in the Meditteranean area (e. g. Italy, Greece). Diets in these areas are typically rich in fruit and vegetables providing considerable amounts of plant bioactives (such as polyphenols, glucosinolates and antioxidant vitamins). Also, oily fish rich in omega-3 fatty acids forms an important part of these Asian and Meditteranean diets. Bioactives occurring in these diets (resveratrol from red wine; hydroxytyrosol, oleic acid and oleuropein from olive oil; and isoflavones in soy, curcumin, catechins in green tea; omega-3 fatty acids in oily fish and seaweed) activate molecular targets (such as Sirt1) similar to those activated during CR (known to increase healthspan). The authors review the role of sirtuin-activating foods in the prevention of chronic disease.
CR-induced body weight loss is associated with beneficial effects (re triglycerides, cholesterol, blood pressure) which prevent or delay the onset of age-related diseases (Speakman & Mitchell 2011). Reductions in body fat are associated with the modulation of leptin and adiponectin, hormones cenral to the regulation of satiety and appetite (Hochberg & Hochberg 2009, op. cit. Pallauf et al. 2013). CR decreases leptin and increases adiponectin levels. Leptin is involved in the regulation of body weight (Friedman & Halaas 1998, op. cit. Pallauf et al. 2013), whereas adiponectin has antiatherogenic, anti-inflammatory and insulin-sensitizing properties (Ziemke & Mantzoros 2010, op. cit. Pallauf et al. 2013).

Insulin sensitivity and autophagic activity decrease with age, but are increased by CR (Cuervo et al. 2005).

Hatori et al. (2012): Mice, under time-restricted feeding (8 hours/day), but consuming equivalent calories than mice feeding on a high-fat diet *ad lib* (food availability throughout day) were protected against obesity, hyperinsulinemia, hepatic steatosis, inflammation and exhibited improved coordination. The temporal spreading of the calorie intake seemed to be of importance since the mice fed the diet *ad lib* perturbed the metabolic pathways entrained by circadian and feeding rhythms; predisposing the organism to obesity and metabolic diseases. The time-restricted feeding regime entrained the circadian clock and metabolic regulators to fixed feeding times and prevented the high-fat/high calorie induced disruption of the normal cellular metabolic program (as genetically determined).

It is concluded that intermittent states of fasting often associated with dietary reduction are responsible for health benefits rather than calorie restriction *per se*.

Dietary restriction has been found to have health benefits (Willcox et al. 2006; Willcox et al. 2007a, b). Studies have also shown that caloric restriction delays the onset and slows the rate of progression of age-related diseases such as diabetes, cardiovascular diseases and neoplasia (Chiarpotto et al., 2006) Dehydroepiandrosterone sulfate (DHEAS) levels (as biomarker for primate aging) decline with age and calorie restriction slows the post-maturational decline in serum DHEAS levels (Lane et al. 1997). According to Mattson (2003) dietary restriction induces a mild cellular stress response in neurons as a result of its effects on energy availability and activity in neural circuits. Neurons respond to this stress by increasing the production of proteins that enhance cellular stress resistance, such as neurotrophic factors, protein chaperones (such as heat-shock proteins) and anti-apoptotic proteins. Peripheral effects of dietary restriction may also benefit the brain: enhanced insulin sensitivity, decreased homocysteine levels, prevention of age-related damage to cerebral blood vessels; may also have beneficial effects on neurons and glia.

Dietary restriction in mice reduced the amount of altered proteins and shortened the half-life of proteins, also of oxidatively modified proteins. Furthermore, dietary restriction, even when initiated later in life, restored the activities of proteasomes implicated in the removal of altered proteins (Takahashi & Goto 2002).

Anson et al. (2003): Sustained long-term caloric restriction has been assumed to be required for associated health benefits (increased insulin sensitivity, stress resistance, reduced morbidity, increased life span). However, on a dietary regime of intermittent fasting in mice, consisting of alternate day fasting and alternate day of compensatory food intake, the overall food intake is not reduced and body weight is maintained. This form of intermittent fasting nevertheless resulted in beneficial health effects (such as glucose/insulin regulation and increased resistance of neurons in the brain to excitotoxic stress) that met or even exceeded those of chronic caloric reduction. Thus, with periods of intermittent fasting, health benefits in mice were found to be at least partially, independent of caloric intake. This confirms that intermittent states of fasting, often associated with dietary reduction, are responsible for health benefits rather than caloric restriction *per se*.

Fernstrom (1986): The importance of of insulin secretion in generating an increase in brain serotonin is confirmed, but such an effect is not likely to occur when insulin levels

are high at night as is the case under *ad lib* feeding (Fernstrom et al. 1975, op. cit. Fernstrom 1986). Once the daily period of food intake has begun, insulin levels rise and tend to stay elevated. Tryptophan is transported across the blood-brain barrier by a specific active transport system which also transports a number of other large neutral amino acids (LNAAs: leucine, isoleucine, tyrosine, phenylalanine and valine) into the brain. Tryptophan competes with these other LNAAs for active transport sites. Therefore, the uptake of tryptophan into the brain does not depend on total concentration on plasma tryptophan alone, but mainly on the plasma ratio of tryptophan to the sum of other LNAAs (tryptophan-LNAA ratio). (Fernstrom & Wurtman 1972, op.cit. Fernstrom 1986). Dietary intakes rich in tryptophan relative to other LNAAs boost tryptophan uptake and thus serotonin production in the brain. Increasing tryptophan in the brain (tryptophan loading) can be achieved by increased carbohydrate intake, especially with the meal following the overnight fasting period (rising insulin levels from low levels), i.e breakfast (Fernstrom 1986).

Dirks & Leeuwenburgh (2006): Studies investigating short- and long-term calorie restriction programs indicated beneficial outcomes on parameters of cardiovascular disease and a variety of pathophysiological parameters (Fontana et al. 2004, op. cit. Dirks & Leeuwenburgh 2006; Weyer et al. 2000, op. cit. Dirks & Leeuwenburgh 2006; Walford et al. 1999, op. cit. Dirks & Leeuwenburgh 2006). The decline in cellular functions occurring with age are attenuated by CR (op. cit. Dirks & Leeuwenburgh 2006).
Little attention has, however, hitherto been given to effects on quality of life and potential pitfalls of long-term calorie restriction in humans. In general, insulin levels and activities of the thyroid, gonadotropic and somatotropic axes decline, while that of the hypothalamus-pituitary-adrenal axis is enhanced (Zhu et al. 2004, op. cit. Dirks & Leeuwenburgh 2006; Sabatino et al. 1991, op. cit. Dirks & Leeuwenburgh 2006). Sympathetic activity is also reduced (Kushiro et al. 1991, op. cit. Dirks & Leeuwenburgh 2006).
A long-term pronounced CR lifestyle has potential negative side effects, including hypotension, loss of libido, menstrual irregularities, infertility, bone thinning, and osteoporosis, cold sensitivity, loss of strength and stamina, slower wound healing, and psychological conditions such as depression, emotional deadening, and irritability. Lowered levels of fat and muscle mass are indicative of states of poor body condition and are associated with suboptimal metabolic functionality, leading to health complications. Depending on age and fitness status, the healthy range for body fat composition for men is 5-25 % and for women is 16-38 %. Body fat below these ranges is considered inadequate and may be associated with elevated health risks. Body fat is necessary and essential for the production of sex hormones, insulation of vital organs, and regulation of body temperature. Pronounced loss of body fat and the concomittent decline in sex steroids can lead to the loss of libido in both sexes and menstrual irregularities, such as amenorrhea and infertility in females (Morgan 1999, op. cit. Dirks & Leeuwenburgh 2006; Morgan et al. 1999, op. cit. Dirks & Leeuwenburgh 2006). Women with a low BMI are a greater risk for pre-term delivery and birth of low birth-weight infants (Allen et al. 1994, op. cit. Dirks & Leeuwenburgh 2006). CR should accordingly not be practiced by women prior to or during pregnancy. Cold sensitivity. Body temperature decreases with CR. Thus appears to be due to a decreased threshold for activation of thermogenesis. Lack of fat stores serving as insulation and preserving heat loss may contribute to cold sensitivity under exposure to colder temperatures (Florez-Duquet & McDonald 1998, op. cit. Dirks & Leeuwenburgh

2006). Caloric restriction results in the loss of muscle mass until a new set-point is reached which is in equilibrium with the enegy intake. Loss of muscle mass during CR equates to less metabolically active tissue and individuals with less muscle mass may have a reduced ability to generate heat via shivering (Florez-Duquet & McDonald 1998, op. cit. Dirks & Leeuwenburgh 2006). The associated cold sensitivity implicates a higher risk for hypothermia, which may lead to stroke, myocardial fibrillation or death. Less adipose tissue equates to less energy reserves in the body; and those engaged in long-term CR are less likely to survive when unexpectently exposed to cold environments, in comparison with subjects with greater body weight and energy reserves. ***However, the daily restriction of calories to a lesser degree (8-25 % rather than 40 %) or a regimen of every-other-day (EOD) feeding already have beneficial effects on specific biochemical and inflammatory biomarkers shown to decrease with 40 % CR. A EOD feeding regime does not require a significant reduction in overall caloric intake in order to produce health benefits. This suggests that the state of fasting rather than the reduction in in caloric intake may be important in slowing the intrinsic rate of ageing*** (refer also to Dirks & Leeuwenburgh 2004, op. cit. Dirks & Leeuwenburgh 2006, and Payne et al. 2003, op. cit. Dirks & Leeuwenburgh 2006).

Masoro (2009): Most gerontologists agree to the following: 1) CR extends life by slowing the rate of ageing; 2) Ageing results from progressive organismic molecular damage due to an imbalance during much of adult life in favour of damaging processes relative to protective and repair processes (rate of ageing being determined by magnitude of of this balance); 3) CR slows ageing by decreasing damaging processes (decreasing the generation of damaging agents) and by augmenting/enhancing protective and repair processes.
Enhanced insulin sensitivity only playing an indirect role in life extension by CR. CR decreases the age-asssociated accumulation of oxidative damage to lipids, protein and DNA (Sohal & Weindruch, op. cit. Masoro 2009). CR effects rather to be explained by a framework of complex interacting systems. Masoro (2009) and Turturro et al., op. cit. Masoro 2009) proposed hormesis as being cenral to such a framework. In the context of ageing, hormesis involves beneficial effects resulting from cellular responses to mild repeated stress. Accordingly, ageing is retarded due repeated exposure to low intensity stress stimulating organismic maintenance and repair processes (Mattson & Cheng 2006).

Concluding this section some central insights are summarized:

1) CR eliciting a stress response

Sinclair (2005) presented a synthesizing hypothesis, the Hormesis Hypothesis of CR, which proposes that CR imposes a low-intensity biological stress on the organism, eliciting an active defense response that also helps the organism by protecting it against the causes of ageing.

2) Enhanced metabolic rate

After having experienced an initial drop in metabolic rate during the first six weeks (Speakman et al. 2004), CR animals have equal or higher metabolic rates than *ad libitum* fed animals. The results of Speakman et al. (2004) support the ‘mitochondrial

uncoupling to survive' hypothesis; i.e. a positive association between high metabolism and longevity. Protein turnover rates and autophagous processes (auto-digestion) decline with age and this decline is attenuated by CR (Sinclair 2005).

3) Energy use efficiency of CR-cued metabolism

The enhanced metabolic rate of CR individuals underpins performance capacity, but with little trade-off costs in terms of maintenance, as manifesting in widespread autophagy-based health benefits associated with CR-cued metabolism (e.g. Kirkwood & Shanley 2005; Cuervo et al. 2005; Masoro 2009).

4) Chronic CR effects

A chronic, long-term pronounced CR lifestyle has substantial negative effects, manifesting in compromised performance vitality (including side effects such as hypotension, loss of libido, menstrual irregularities, infertility, bone thinning, and osteoporosis, cold sensitivity, loss of strength and stamina, slower wound healing, and psychological conditions such as depression, emotional deadening, and irritability: Dirks & Leeuwenburgh 2006). Low body condition, as manifesting in lowered levels of fat and muscle mass, is associated with suboptimal metabolic functionality, with negative health implications (Dirks & Leeuwenburgh 2006). Pronounced loss of body fat and the concomittent decline in sex steroids can lead to the loss of libido in both sexes and menstrual irregularities, such as amenorrhea and infertility in females (Morgan 1999, op. cit. Dirks & Leeuwenburgh 2006; Morgan et al. 1999, op. cit. Dirks & Leeuwenburgh 2006).

5) Time-restricted CR

An Every-other-day (EOD) feeding regime does not require a significant reduction in overall caloric intake in order to produce health benefits. This indicates that the state of fasting rather than the reduction in caloric intake is important in slowing the intrinsic rate of ageing and producing associated health benefits (Dirks & Leeuwenburgh 2006). Animals placed on a restricted diet every other day grow normally but receive similar health benefits (reviewed in Masoro 2000, op. cit. Lamming et al. (2004).

With intermittent fasting beneficial health effects (such as glucose/insulin regulation and increased resistance of neurons in the brain to excitotoxic stress) accrued that met or even exceeded those of chronic caloric reduction (Anson et al. 2013). With periods of intermittent fasting, health benefits are found to be at least partially, independent of caloric intake. This suggests that the state of fasting rather than the reduction in caloric

intake may be important in slowing the intrinsic rate of ageing (Dirks & Leeuwenburgh 2006).

It is concluded that intermittent states of fasting (CR-stimulus effects) often associated with dietary reduction are responsible for health benefits, rather than calorie restriction *per se*.

c) Sirtuin foods

Lamming et al. (2004): Caloric restriction (CR) works in most species, implying a conserved mechanism. It extends lifespan because it is a mild biological stressor activating Sir2, a key components of yeast longevity and the founding member of the sirtuin family of deacetylases. Sirtuins are found in plants, yeast and animals and seem to underly the remarkable health benefits of CR. A class of polyphenolic molecules produced by plants in response to stress apparently activate the sirtuins and extend lifespan by mimicking CR. According to numerous studies it has been documented that CR delays most diseases of ageing, including cancer, atherosclerosis, type 2 diabetes and even neurodegeneration. CR can be started in adult animals and still extend lifespan; and animals placed on a restricted diet every other day grow normally but receive similar health benefits (reviewed in Masoro 2000, op. cit. Lamming et al. (2004). CR is considered a form of hormesis (Masoro 2000, op. cit. Lamming et al. 2004; Anderson et al. 2003a, Lamming et al. 2004; Strauss 2003, op. cit. Lamming et al. 2004), where the term 'hormesis' refers to the process by which mild stress provides health benefits by inducing a defense response in the organism. The hormesis hypothesis of CR is thus based on the notion that low calorie intake is in itself a mild stress, which invokes a general stress response promoting better health and longer life. This theory explains why CR animals are more resistant to a broad array of stresses, and fits in with theories about the allocation of resources to survival and somatic maintenance during times of stress (Kirkwood et al. 2000). Eighteen small molecules that can increase human SIRT1 activity were identified, including resveratrol, butein and piceatannol (Howitz et al. 2003, op. cit. Lamming et al. 2004). ***Plants contain multiple sirtuins and it is thus reasonable to assume that the sirtuin-activating polyphenols are actually stress-signalling molecules that coordinate sirtuin-mediated defences in plants*** (Howitz et al. 2003, op. cit. Lamming et al. 2004). ***Many of the polyphenols that activate sirtuins (such as resveratrol and quercetin) are synthesized during times of stress (infection, starvation, dehydration).*** The notion that this class of polyphenols are signalling molecules contrasts with the mainstream view of them as antioxidants or phytoalexins (Stojanovic et al. 2002, op. cit. Lamming et al. 2004).

Research in ageing has identified important genes and pathways involved in longevity. These include the family of nicotinamide adenine dinucleotide (NAD)-dependent protein deacetylases, known as sirtuins. They represent a unique class of proteins linking protein acetylation to metabolism; thereby having important effects on mammalian physiology and diseases of ageing (Guarente 2011).

Guarente (2013): New data show a systematic redirection by sirtuins of mammalian physiology in response to dietary sirtuins. Data similarly suggest that sirtuins are conserved mediators of longevity. SIRT1-activating compounds (STACs), such as the polyphenol resveratrol found in red wine, were reported to activate the enzyme *in vitro* by lowering its Km for substrate (Howitz et al. 2003, op. cit. Guarente 2013: ***Lowering of the Michaelis constant of SIRT1 for both the acetylated substrate and NAD^+ and increasing cell survival by stimulating SIRT1-dependent deacetylation of p53). The lower Km the higher is the catalytic efficiency***. Sirtuins mediate the effects of CR in mammals. SIRT1 is also induced by CR in humans (Civitarese et al. 2007, op. cit. Guarente 2013). Reciprocally, a high-fat diet leads to the loss of SIRT1 in mice (Chalkiadaki & Guarente 2012, op. cit. Guarente 2013). Obesity has the same effect in humans (Pedersen et al. 2008, op. cit. Guarente 2013). Transgenic overexpression of SIRT1or STACs mitigates disease syndromes much like CR; including diabetes, neurodegenerative diseases, liver steatosis, bone loss, and inflammation (Baur et al. 2006, op. cit. Guarente 2013; Lagouge et al. 2006, op. cit. Guarente 2013; Bordone et al. 2007, op. cit. Guarente 2013; Pfluger et al. 2008, op. cit. Guarente 2013; Herranz et al. 2010, op. cit. Guarente 2013; Guarente 2011, op. cit. Guarente 2013). Compromised sirtuin activity contributes to metabolic syndrome and diabetes (Biason-Lauber et al. 2013, op. cit. Guarente 2013). SIRT1 activators like resveratrol exert effects that overlap those of CR at the level of whole-animal physiology (Lam et al. 2013, op. cit. Guarente 2013). Resveratrol activates ***SIRT1 and the associated improvement in energy utilization and insulin sensitivity closely resembles the benefits of calorie restriction*** (Lam et al. 2013, op. cit. Guarente 2013).
The hallmarks of CR are metabolic reprogramming to oxidative metabolism (in order to gain the most possible energy from fuel sources) and resistence to stress (particularly oxidative stress). Healthy physiological functioning of the brain as driven by various regions of the brain, deteriorates with ageing, and sustaining SIRT1 activity may be of general importance for brain maintenance. For example, SIRT1 protects against neurodegenerative diseases in the cortex and striatum (Kim et al. 2007, op. cit. Guarente 2013; Jiang et al. 2011, op. cit. Guarente 2013) and enhances learning and memory in the hippocampus (Gao et al. 2010, op. cit. Guarente 2013; Michan et al. 2010, op. cit. Guarente 2013). Generally, numerous SIRT1 effects include those in endothelial cells (Potente et al. 2007, op. cit. Guarente 2013; Ota et al. 2007, op. cit. Guarente 2013) and in respect of atherosclerosis. SIRT1 activation by small molecules based on an allosteric site in the protein has been elucidated by Hubbard et al. (2013, op. cit. Guarente 2013).

Cantó & Auwerx (2009): Current data already indicate that caloric restricted Rhesus monkeys were protected from many age-associated pathophysiological changes, such as the development of insulin resistence and type 2 diabetes (Lane et al. 1999, op. cit. Cantó & Auwerx 2009; Kemnitz et al. 1994, op. cit. Cantó & Auwerx 2009), atherosclerosis (Verdery et al. 1997, op. cit. Cantó & Auwerx 2009), oxidative damage (Zainal et al. 2000, op. cit. Cantó & Auwerx 2009) and senescence of the immune system (Messaoudi et al. 2006, op. cit. Cantó & Auwerx 2009). They were also ***protected against age-related reductions in their basal metabolic rate*** (Blanc et al. 2003, op. cit. Cantó & Auwerx 2009) ***and body temperature*** (Lane et al. 1996, op. cit. Cantó & Auwerx 2009).

Cantó & Auwerx (2012): Sirtuin 1 is an evolutionary conserved NAD^+ -dependent deacetylase that is at the innacle of metabolic control (SIRT1 as a modulator of whole-body metabolism). SIRT1 senses changes in intracellular NAD^+ levels, which reflect energy level, and uses this information to adapt the cellular energy output such that it matches cellular energy requirements. Probably evolved as the mediator of the metabolic and transcriptional adaptations to situations of energy stress and nutrient deprivation, ***SIRT1 enhances the ability of organisms to enhance fat consumption and use of mitochondrial respiration as a way to optimize energy harvesting***. Metabolic disease has been strongly linked to impaired energy homeostasis and mitochondrial function. Available studies support the notion that higher SIRT1 activity is protective against metabolic disease without necessarily influencing lifespan.

Baur et al. (2010): The sirtuins, a family of critically important nutrient-sensing proteins promote health span from yeast to mammals, as has been shown by more than 1000 peer-reviewed publications from laboratories around the world. Numerous independent studies show that dietary restriction does not extend lifespan when sirtuins are deleted. Also in humans, there is evidence that sirtuins are involved in mediating the response to dietary restriction and increased health span. For example, SIRT1 levels increase in humans practicing dietary restriction (Civitarese et al. 2007, op. cit. Baur et al. 2010) and there are ***strong associations between alleles that increase SIRT1 expression and increased metabolic rate, as well as protection against type 2 diabetes*** (Lagouge et al. 2006, op. cit. Baur et al. 2010).

Fruit and vegetables/herbs have been central diet components historicall/evolutionary and the role of polyphenols must accordingly be considered crucial for a healthy diet.

Sinclair (2005): An increasing number of studies demonstrate that SIRT1 regulates cell survival during adverse conditions. The proteins/pathways include that mammalian SIRT1 regulates include p53 (Motta et al. 2004, op. cit. Sinclair 2005), Bax-mediated apoptosis (Cohen et al. 2004b, op. cit. Sinclair 2005), neuronal survival (Araki et al. 2004, op. cit. Sinclair 2005), the FOXO family of transcription factors (Brunet et al. 2004, op. cit. Sinclair 2005; Giannakou & Partridge 2004, op. cit. Sinclair 2005) and NF-κB-mediated cell death (Yeung et al. 2004, op. cit. Sinclair 2005). Sirtuin activating compounds (STACs) may be key to extending of lifespan in higher organisms. According to Howitz et al. (2003, op. cit. Sinclair 2005), 18 small molecules from plants were identified that increase human SIRT1 activity *in vivo* and *in vitro*; including resveratrol, butein and piceatannol. The compound resveratrol (a polyphenol found in plant species including grapes, penuts and some Asian medicinal herbs), was found to have the greatest stimulatory effect putatively consistent with it mimicking CR.
Observations have been recoreded that resveratrol is effective against numerous diseases, including esophagial, breast and liver cancers (Bhat & Pezzuto 2002, op. cit. Sinclair 2005; Jang et al. 1997, op. cit. Sinclair 2005), oral herpes (Docherty et al. 1999, op. cit. Sinclair 2005), chronic obstructive pulmonary disease (Culpit et al. 2003, op. cit. Sinclair 2005) and hyperlipidemia (Miura et al. 2003, op. cit. Sinclair 2005). The STACs quercetin and butein showed efficacy against age-related diseases (Knekt et al. 2002, op. cit. Sinclair 2005; Lim et al. 2001, op. cit. Sinclair 2005).

Sinclair (2005) dismisses an anti-oxidant activity of STACs as explanation for the observed effects relating to disease and lifespan. ***Rather, the effects of STACs might be linked to these substances representing plant stress-signaling molecule that coordinate sirtuin-mediated defences in plants*** (Howitz et al. 2003, op. cit. Sinclair 2005). ***Many of the polyphenols that activate the sirtuins, such as resveratrol and quercetin, are known to be synthesized under conditions of stress experienced by plants (stress associated with infection, starvation and dehydration)***. The Xenohormesis Hypothesis states that organisms have evolved to pick up on stress-signaling molecules from other species in their environment because it allows them to shift into survival mode in advance of an environmental decline (Horwitz et al. 2003, op. cit. Sinclair 2005; Lamming et al. 2004). Xenohormesis is not only relevant in the context of sirtuin activation, but STACs are predicted to act on modulating numerous targets working toward increased health and/or longevity (Pervaiz 2003, op. cit. Sinclair 2005).

Haigis & Sinclair (2010): A family of conserved enzymes known as sirtuins affect multiple pathways that increase the lifespan and overall health of organisms. This review summarizes advances in the enzymology of sirtuins, their regulation and their ability to improve mammalian physiology and health span. Given that SIRT1 levels are controlled by environmental stimuli such as daylight, cell stress and CR, it is not surprising that the gene is controlled by numerous transcription factors. ***The authors present a comprehensive review of the role of SIRT1 and mitochondrial sirtuins in regulating adaptation to nutrients (maintenance of energy homeostasis) and healing responses in view of diverse disease states***.

Mediteranean diet: Rich in especially vegetables and fruit as important sources of dietary polyphenols, glucosinolates and antioxidant vitamins, as well as oily fish (omega-3 fatty acids). The health benefits of resveratrol (a red grape constituent) have been widely documented (Baur et al. 2006, op. cit. Pallauf et al. 2013). Data of Pallauf et al. (2013) demonstrate that diets rich in olive oil phenolics (hydroxytyrosol) result in decreased oxidative damage markers and improved expression of cardioprotective proteins. Olive oil phenolics are indicated to induce proteasomal activity and Sirt1 signalling (Menendez et al. 2013, op. cit. Pallauf et al. 2013). Decreased cardiovascular risk associated with olive oil consumption (Buckland et al. 2012). **Asian diet**: Rich in soy (isoflavones) and turmeric, *Curcuma longa*, a source of curcumin (Goel & Aggarwal 2010, op. cit. Pallauf et al. 2013). Seaweed has numerous heath benefits and also, *inter alia*, includes omega-3 fatty acids (Rajapakse & Kim 2011, op. cit. Pallauf et al. 2013).
Controversial results are also in evidence; for example. Red or white wine with a reduced alcolhol content did not decrease LDL peroxidation (De Rijke et al 1996, op. cit. Pallauf et al. 2013) and although moderate red wine consumption could lower LDL peroxidation, the other tested alcoholic beverages had the same effect (Van der Gaag et al. 1999, op. cit. Pallauf et al. 2013).
Conflicting results indicate that more research is required for a better understanding of the effects of dietary components on sirtuin activation and healthy ageing. Hormesis is a term describing the phenomenon where low doses have beneficial effects whereas higher doses toxic or inhibitory effects (Mattson 2008, op. cit. Pallauf et al. 2013). Under intermittent exposure a particular substance as lower dose prepares the cell for the potentially toxic impact of that substance at higher dose levels (Mattson 2008).

Pallauf & Rimbach (2013) note that this hormesis effect may explain some contradictory results in cases of polyphenols acting as autophagy inducers.

Rizza et al. (2014): Data from several studies have shown that individuals eating diets rich in fish and nutrient-dense, minimally processed plant foods have a lower risk of developing cardiometabolic abnormalities and cardiovascular disease than those who consume Western diets rich in empty calories, saturated/trans fatty acids, animal protein and salt.; underpinning the protective role of of fruit and vegetable consumption (Yusuf et al. 2004, op. cit. Rizza et al. 2014). According to a clinical trial on the cardiovascular effects of a Mediterranean diet (supplemented with extra-virgin olove oil or nuts), such a diet significantly reduced the incidence of cardiovascular disorders and stroke (Estruch et al. 2013, op. cit. Rizza et al. 2014). ***The traditional Mediterranean diet is rich in grains, legumes, vegetables, fruits, tree nuts, seeds and olives; with extra-virgin olive oil and fish as primary sources of fat***. It has also been shown that an energy-unrestricted Mediterranean diet rich in alpha-linolenic acid (a main ingredient of walnuts) has beneficial effects in lowering the incidence rates of coronary heart disease events in patients who had already suffered a first myocardial infarction (De Lorgeril et al. 1999, op. cit. Rizza et al. 2014).
Excessive energy and protein intake before puberty, by stimulating the insulin/IGF/mTOR pathway, causes rapid growth rates, and early menarche, which represent a well-established risk factor for breast cancer (Berkey et al. 2000, op. cit. Rizza et al. 2014).
Supplementation with combinations of supplements (i.e. resveratrol, green, black and white tea extracts, pomegrate extract, quercetin, acetyl-l-carnitine, lipoid acid, curcumin, sesamin, cinnamon bark extract, and fish oil), each of which has been shown to have anti-oxidant and anti-inflammatory effects in cell culture or animal studies, do not exert any cardiovascular or metabolic effect in non-obese men and women (Soare et al. 2013, op. cit. Rizza et al. 2014).

Conclusion: A high content of fruit, vegetables and oily fish as contained in Mediterranean and certain Asian diets (the so-called MeditterrAsian diet) was indicated to be the basis of an improved health status (Pallauf et al. 2013). ***These authors point out that plant bioactives, antioxidant vitamins and omega-3 fatty acids probably do not work in isolation, but may act synergistically in preventing chronic diseases***. ***They propose to rather combine healthy food items of the Mediterranean and Asian diets rich in Sirtuin foods in order to achieve the prevention of chronic diseases and healthy ageing***. In this context, Egert & Rimbach (2011) ***caution that complex mixtures of plant secondary metabolites cannot be substituted by single purified compounds as dietary supplements***.

Fontana & Partridge (2015): As part of the response of an organism to catabolic states (associated with of metabolic energy expenditure) is the ***lysosomal degradation pathway autophagy induced via Sirt1 and AMPK***. Both sirtuins and autophagy are induced by CR (Cuervo et al. 2005). ***Healthy-ageing benefits from Sirt1 activation***

by CR or polyphenolic CR mimetics seem to be causally related to autophagy (Pallauf & Rimbach 2013).

Sirt-inducing plant bioactives:

Apart from soy bean products; Fisetin (strawberries, apples, persimmons, grapes); Hydroxytyrosol (olive oil); Kaempherol (cabbage, kale, parsley, beans, cruciferous vegetables); Piceatannol (red wine, grapes); Quercetin (onion, apples, white wine, capers); Resveratrol (red wine, red grapes).

Pallauf & Rimbach (2013): Autophagy functions as a central process in cellular quality control by removing harmful waste or excess proteins, cellular aggregates, microorganisms and organelles. Impaired autophagy favours the pathogenesis of many diseases. Pallauf & Rimbach (2013) ***provide a comprehensive review of the contributing role autophagy plays in the context of CR-induced health benefits and the advantages of polyphenol consumption connected to autophagy induction***.
Autophagy is induced in response to nutrient deprivation. It provides the starving cell with energy from degraded self-components, removes harmful proteins and plays roles in oxidative stress responses, immune responses and endocrine signalling. ***Thus, the health-benefit effects of dietary restriction are at least partly linked to autophagy*** (Mizushima et al. 2008).
Ageing processes include the accumulation of waste molecules, damage by oxidative stress and prolonged insulin-signalling (Terman et al. 2010). Old mitochondria (main source of reactive oxygen species), protein-aggregate build-up and underlying causes, as prolonged insulin-signalling, are removed by autophagy.
Increased autophagy leads to longevity.
The increased deposition of damaged components within the ageing cell is related to an ageing-related decline in autophagy (Cuervo 2008).
Also, autophagy contributes to CR-induced lifespan extension through the inactivation of the insulin-like growth factor receptor (Holzenberger et al. 2003, op. cit. Pallauf & Rimbach 2013). The declining removal of proteins and organelles due to slowing of autophagy, leads to harmful protein aggregates and damaged mitochondria to accumulate, resulting in increased oxygen specis production and stress within the cell, favouring inflammation processes (Cuervo 2008). Impaired insulin sensitivity (insulin resistence) at higher ages and promoted by elevated food intake decreases autophagic activity (Yang et al. 2016, op. cit. Pallauf & Rimbach 2013).

Caloric restriction is considered the most potent autophagy inducer and is accepted as lifespan extending and health-promoting; counteracting processes of ageing (Rubinsztein er al. 2011).

Autophagy is indirectly suppressed by carbohydrate uptake via insulin signalling. Various secondary plant metabolites (notably polyphenols) were shown to regulate

autophagy (Pallauf & Rimbach 2013). Polyphenolic plant metabolics prolonging life via autophagy (Morselli er al. 2010).
Resveratrol (mainly found in red grape skin) was found to promote increased lifespan via Sirt1 activation as mediated by autophagy (Morselli et al. 2010). On the role of cancer prevention through the induction of autophagy by *inter alia* polyphenolics (resveratrol): Hasima & Ozpolat (2014).

Pallauf & Rimbach (2013) list polyphenols which have been shown to be involved in the induction of autophagy (sources op. cit. Pallauf & Rimbach 2013): Curcumin (turmeric *Curcuma longa*), Epigallocatechingallate (green tea *Camellia sinensis*), Genistein (soybeans), Quercetin (onions, apples, berries, capers, grapes), Resveratrol (grape skins/wine, nuts), Silibinin (milk thistle *Silybum marianum*).

Morselli et al. (2010): ***Caloric restriction and resveratrol (a polyphenol) promote longevity through the Sirtuin-1-dependent induction of autophagy***. Caloric restriction and autophagy-inducing agents can prolong lifespan in model organisms. In this study it is shown that transgenic expression of sirtuin-1 induces autophagy in human cells *in vitro*. We conclude that autophagy is universally required for the lifespan-prolonging effects of caloric restriction and pharmacologic Sirtuin-1 activators.

Polyphenol food sources:

Cardona et al. (2013): The biological properties of dietary polyphenols are dependent on their bioavailability, which is largely influenced by their degree of polymerization. Gut microbiota play a key role in modulating the production, bioavailability, and thus the biological activities of phenolic metabolites. In addition, emerging evidence indicates that the activity of dietary polyphenols is involved in the modulation of the colonic microbial population composition and activity. Once ingested, polyphenols are recognized by the body as xenobiotics, and their bioavailability is therefore relatively low in comparison to micro- and macronutrients. Colonic microbiota are responsible for the extensive breakdown of the original phenolic structures into a series of low-molecular-weight phenolic metabolites, which, being absorbable, are deemed responsible for the health effects derived from polyphenol-rich food consumption, rather than the original compounds found in food. The formation of bioactive polyphenol-derived metabolites and the modulation of colonic microbiota may both contribute to host health benefits.
Interventional and epidemiological studies have presented evidence for a wide range of health-promoting activities of dietary polyphenols, including their anti-inflammatory, antioxidant, anticarcinogenic, antiadipogenic, antidiabetic and neuroptrotective potentials; suggesting an association between the consumption of polyphenol-rich foods and a reduced risk of several chronic diseases (Jennings et al. 2012, op. cit. Cardona et al. 2013; Cassidy et al. 2011, op. cit. Cardona et al. 2013; Hooper et al. 2012, op. cit. Cardona et al. 2013; Chiva-Blanch et al. 2012, op. cit.

Cardona et al. 2013; Zamora-Ros et al. 2012, op. cit. Cardona et al. 2013; Hanhineva et al. 2010, op. cit. Cardona et al. 2013).
Individual differences in the composition of the human microbiota may lead to differences in bioavailability and bioefficacy of polyphenols and their metabolites (e.g. Van Dorsten et al. 2010, op. cit. Cardona et al. 2013). Furthermore, polyphenols may be converted by the colonic microbiota to bioactive compounds which affect the intestinal ecology, thereby influencing host health. Certain polyphenols may modify the gut microbial composition; certain bacterial groups may be inhibited, while others thrive in the available niche of the ecosystem. As phenolic compounds alter gut microbiota, they alter the balance between microbiotic genera, e.g. the *Bacteroides*/*Firmicutes* balance (e.g. Lee et al. 2006, op. cit. Cardona et al. 2013; Hervert-Hernandez et al. 2009, op. cit. Cardona et al. 2013). Tzounis et al. (2011, op. cit. Cardona et al. 2013), for example, reported that a flavonol-induced increase in the growth of *Lactobacillus* and *Bifidobacterium* spp. may have been partly responsible for reductions in the plasma C-reactive protein (CRP) concentrations, which are a blood marker of inflammation (refer also to Fogliano et al. 2011, op. cit. Cardona et al. 2013). Queipo-Ortuño et al. (2012, op. cit. Cardona et al. 2013) found that the regular intake of red wine polyphenols generated significant decreases in blood pressure and in the levels of triglicerides, and high-density lipoprotein cholesterol; and partly linked these reductions to polyphenol-induced increases in the growth of *Bacteroides*. Self (2002, op. cit. Cardona et al. 2013) reported a significant decrease in uric acid levels after the consumption of red wine polyphenols, which can be explained by the associated significant increase in *Proteobacteria* which had previously been reported to degrade uric acid. The weight-lowering property of fruits, green tea and vinegar wine in obese people may be partly related to their polyphenol content, which changes the gut microbiota, either through the glycan-degrading capability of Bacteroides (which is higher *Firmicutes*) or through the end products of colonic metabolism of polyphenols (Rastmanesh 2011, op. cit. Cardona et al. 2013).
The bioavailability and effects of polyphenols greatly depend on their transformation by components of the gut microbiota. In the context of the two-way phenolic-microbiota interaction it is clear that dietary polyphenols and their metabolites contribute to the maintenance of gut health by the modulation of gut microbial balance through the stimulation of the growth of beneficial bacteria and the inhibition of pathogen bacteria, exerting prebiotic-like effects.

Martin et al. (2009): The daily consumption of dark chocolate (rich in flavonols, mainly flavan-3-ols) resulted in a significant modification in the metabolism in healthy subjects; with potentially long-term positive health consequences, linked to variation of both host and gut microbial metabolism. Human subjects with higher anxiety traits showed a distinct metabolic profile, indicative of a different energy homeostasis (lactate, citrate, succinate, *trans*-aconitate, urea and proline), hormonal metabolism (adrenalin, DOPA: dihidroxifenila-lanina and 3-methoxy-tyrosine) and gut microbial activity (methylamines, p-cresol sulfate and hippurate). Dark chocolate reduced the urinary excretion of the stress hormone cortisol and catecholamines and partially normalized stress related differences in energy metabolism (glycine, citrate, *trans*-aconitate. proline, ß-alanine) and gut microbial activities (hippurate and *p*-cresol sulfate). The results support the idea that specific foods impact on human metabolism through the modulation of gut microbial activity; as was *inter alia*

observable through the reduction of levels of stress-associated hormones and normalization of the systemic stress metabolic signatures.

Hanhineva et al. (2010): Growing evidence indicates that various dietary polyphenols may influence carbohydrate metabolism at many levels. Dietary items rich in polyphenols have attenuated postprandial glycemic responses and fasting hyperglycemia, and improved acute insulin secretion and insulin sensitivity. Possible mechanisms include inhibition of carbohydrate digestion and glucose absorption in the intestine, stimulation of insulin secretion from the pancreatic ß-cells, modulation of glucose relese from the liver, activation of insulin receptors and glucose uptake in the insulin sensitive tissues and modulation of intracellular signalling pathways and gene expression. The positive effects of polyphenols on glucoe homeostasis observed in relevant studies are supported by epidemiological evidence on polyphenol-rich diets.

Kim et al. (2014): Green tea is rich in polyphenol flavonoids including catechins. Epigallocatechin 3-gallate (EGCG). EGCG directly interacts with proteins and phospholipids in the plasma membrane and regulates signal transduction pathways, transcription factors, DNA methylation, mitochondrial function and autophagy to exert many of its beneficial biological actions. One potential mechanism for beneficial health effects of EGCG may be attributable its antioxidative function (Chen & Zhang 2003, op. cit. Kim et al. 2014). Additional mechanisms of action for EGCG include interactions with plasma membrane proteins, activation of second messengers and signal transduction pathways, modulation of metabolic enzymes and autophagy (Kim et al. 2013, op. cit. Kim et al. 2014; Kim et al. 2009, op. cit. Kim et al. 2014; Kumazoe et al. 2013, op. cit. Kim et al. 2014; Valenti et al. 2013, Zhang e al. 2012, op. cit. Kim et al. 2014). Most polyphenols, including EGCG, resveratrol, quercetin, and curcumin induce autophagy. This may contribute to anti-aging effects of of polyphenols (Pallauf & Rimbach 2013). EGCG was reported to stimulate autophagy and autophagic flux in endothelial cells that helps degradation of lipid droplets (Kim et al. 2013, op. cit. Kim et al. 2014).

Savini et al. (2013): p 10510-10514-10516-10517-conclusion-10518
Weight reduction in obese individuals decreases oxidative damage and inflammation. Lowering energy supply activates proteins of the sirtuin (SIRT) and Forkhead box (sub-group O: FoxO) families (Crujeiras et al. 2008). Sirtuins transcriptionally improve metabolic efficiency, strengthen antioxidant defenses and dampen inflammatory activities (Galli et al. 2011). FoxO proteins modulate transcription of genes in respect of energy homeostasis, cell survival and inflammatory responses (Salminen et al. 2011, op. cit. Savini et al. 2013). The combination of a hypoenergetic diet and regular exercise potentiates the beneficial effects on redox balance (Rector et al. 2007, op. cit. Savini et al. 2013; Montero et al. 2012, op. cit. Savini et al. 2013; Strasser 2012, op. cit. Savini et al. 2013; De Lemos et al. 2012, op. cit. Savini et al. 2013). In recent years numerous studies have provided evidence that polyphenols may be protective against oxidative-triggered pathologies, including CVD, metabolic disorders, cancer and obesity (González-Castejón & Rodriguez-Casado 2011, op. cit. Savini et al. 2013). It is now well-known that polyphenols exert their biological effects through other mechanisms, representing bioactive rather than antioxidant

compounds (Sies et al. 2012, op. cit. Savini et al. 2013). ***Polyphenols may have anti-obesity, anti-inflammatory, anti-diabetic, and anti-cancer properties through multiple mechanisms: acting by modulating inflammation and redox state, by regulating adipocyte differentiation and lipid metabolism, by inhibiting pancreatic lipase activity and intestinal permeability, and by interacting with gut microbiota*** (Leiherer et al. 2013, op. cit. Savini et al. 2013; Baret et al. 2013, op. cit. Savini et al. 2013; De la Garza et al. 2011, op. cit. Savini et al. 2013; Bolca et al. 2013, op. cit. Savini et al. 2013). For example, grape polyphenols reduced high fructose-induced oxidative stress and insulin resistence (Hokayem et al. 2012, op. cit. Savini et al. 2013). A study by Timmers et al. (2011, op. cit. Savini et al. 2013) showed that resveratrol (a stilbene polyphenolic primarily found in grapes and apples) supplementation (150 mg daily) for 30 days lowered oxidative stress and mimicked calorie restriction.
In conclusion, ***polyphenols are thought to exert positive health effects, not only by modulating redox state, but also due to their ant-inflammatory activity and ability to regulate gut permeability and microbiota composition*** (González-Castejón & Rodriguez-Casado 2011, op. cit. Savini et al. 2013; Sies et al. 2012, op. cit. Savini et al. 2013; Leiherer et al. 2013, op. cit. Savini et al. 2013). ***However, such bioactives should be obtained from relevant food sources, whereas supplementation with antioxidant compounds, alone or in combination, is not recommended***.

Manach et al. (2004): The health effects of polyphenols depend on the amount consumed and on their bioavailability. Certain polyphenols (e.g. quercetin) are found in all plant products: fruit, vegetables, cereals, leguminous plants, fruit juices, tea and wine, whereas others are specific to particular foods. In most cases foods contain complex mixtures of polyphenols. Apples, for example contain flavanol monomers, or oligomers, chlorogenic acid and small quantities of other hydroxy cinnamic acids, two glycosides of phloretin, several quercetin glycosides, and anthocyanins. Other than variety, numerous factors affect the polyphenol content of plants; including ripeness at the time of harvest, environmental factors, processing and storage. ***Environmental factors have a major effect on polyphenol content.These factors may be pedoclimatic (soil type, sun exposure, rainfall) or agronomic (culture in green houses or fields, biological culture, hydroponic culture, fruit yield per tree). In general, phenolic acid concentrations decrease during ripening, whereas anthocyanin concentrations increase. Many polyphenols are directly involved in the response of plants to different types of stress*** (**AS: elevated levels of plant polyphenolics under plant growth-curbing conditions: low temperatures, water deficits, low soil nutrient availability levels**). ***The polyphenol content of fruit and vegetables is accordingly higher when produced under conditions of stress***.
Storage may also affect the content of polyphenols that are easily oxidized; concentrations usually declining over time in storage. In contrast, cold storage does not seem to affect the the content of polyphenols. ***Furthermore, methods of culinary preparation also affect the polyphenol content of foods. Peeling fruit and vegetables can eliminate a significant portion of polyphenols because these substances are often present in higher concentrations in the outer parts than the inner parts. Cooking may also have major effects in reducing polyphenol content of food. Boiling, cooking in a microwave oven or even frying leads to major losses. Steam cooking of vegetables, which avoids leaching, is preferable***.

Crozier et al. (2009): Initially, the protective effect of dietary phenolics was thought to be due to their antioxidant properties which resulted in a lowering of the levels of free radicals within the body. ***There is now emerging evidence that the metabolites of dietary phenolics, which appear in the circulatory system in nmol/L to low µmol/L concentrations, exert modulatory effects in cells through selective actions on different components of the intracellular signalling cascades vital for cellular functions such as growth, proliferation and apoptosis***. The concentrations required to affect cell signalling pathways are considerably lower than those required to impact on antioxidant capacity.

Palacios et al. (2010): Studied both loss of function (SIRT1 deficient) and gain of function ($SIRT1^{super}$) in mouse models. The results indicate that SIRT1 is is a positive regulator of telomere length and attenuates telomere shortening associated with ageing. Increased expression of SIRT1 improves telomere length maintenance and significantly increases recombination frequencies at teomeres, centromeres, and chromosome arms. These effects of increased SIRT1expression are potentially beneficial to preserve genome integrity and stability and open new avenues to understand the known effectsof increased SIRT1 expression on health span and protection from some age-associated diseases.

Chang & Guarente (2013): SIRT1 is a NAD^+-dependent protein deacetylase that governs many physiological pathways, including circadian rhythm in peripheral tissues. ***Findings of this study indicate that SIRT1 activates the central pacemaker to maintain robost circadian control in young animals, and a decay in this activity may play an important role in ageing***.

Hasima & Ozpolat (2014): ***Natural polyphenolic compounds present in our diet (such as rottlerin, genistein, quercetin, curcumin, resveratrol) can alter the effects of signalling pathways and induce cell death not only via apoptosis but also via autophagy***. Autophagy, a lysosomal degradation pathway for cellular constituents and organelles, is an essential adaptive process required for cellular homeostasis. It functions as a survival mechanism in response to cellular stressors such as nutrient or growth factor deprivation. Defects in autophagy alter the metabolic state of cells and their capacity for various disease conditions (Mizushima et al. 2008; Klionsky 2005, op. cit. Hasima & Ozpolat 2014; Levine et al. 2011, op. cit. Hasima & Ozpolat 2014). Autophagy can also lead to a non-apoptotic form of programmed cell death (PCD) called autophagy-induced cell death or autophagy-associated cell death (type II PCD). Natural polyphenolic compounds in our diet can trigger type II PCD via various mechanisms; thereby providing a means of cancer cell death. Polyphenols are a structural class of organic chemicals characterized by the presence of large multiples of phenol structural units. These compounds possess anticancer activities in their ability to alter the effects of signalling pathways and induce cell death not only via apoptosis but also autophagy (Tan et al. 2011, op. cit. Hasima & Ozpolat 2014; Alyer et al. op. cit. Hasima & Ozpolat 2014).

Polyphenol-rich foods: blackberry, blueberry, cherry, plum, coffee, aubergine, black currant, black grape, rhubarb, strawberry, red wine, yellow onion, curly kale, parsley, capsicum pepper, orange juice, grapefruit juice, chocolate, beans, apricot, green tea.

Bravo (1998): Food/beverage items of notably high polyphenolic content: Cereals (barley, millet, sorghum); legumes (black gram, chickpeas, cowpeas, common beans, green gram, pigeon peas; vegetables (onion, parsley); fruits (apple, blackcurrant, blueberry, grape, raspberry, strawberry); fruit juices (apple juice, orange juice); beverages (tea, coffee, red wine).

Caloric restriction promotes healthy ageing largely due to autophagy induction, and polyphenolics, by inducing autophagy, can partly mimic the health-promoting effects of caloric restriction (Baur et al. 2006, op. cit. op. cit. Pallauf et al. 2013). Furthermore, polyphenols apparently potentiate the autophagy-inducing effect of one another. Synergisms of autophagy-inducing polyphenolic substances have been revealed (quercetin and others; resveratrol/ellagic acid; op. cit. Pallauf & Rimbach 2013). Health-promoting effects of polyphenol-rich food may thus be evident despite the low bioavailability of any particular polyphenolic. A pro-autophagic diet should therefore be rich in certain vegetables and fruit providing a variety of polyphenols (Pallauf & Rimbach 2013). In this context, Egert & Rimbach (2011) ***caution that complex mixtures of plant secondary metabolites cannot be substituted by single purified compounds in the form of dietary supplements***. (Consumption of artificially produced polyphenol concentrates may incur risks and should be avoided).

The molecular basis of CR is linked to a family of NAD^+ dependent enzymes, now collectively termed sirtuins. Sirtuins catalyse NAD^+-dependent protein deacetylation and are critical regulators of transcription, apoptosis, metabolism (autophagy), and ageing. Synergisms with other autophagy-inducing polyphenolic substances have been revealed (quercetin and others; resveratrol/ellagic acid; op. cit. Pallauf & Rimbach 2013).

Diets with high contents of metabolic rate-stimulating items (nutrient-rich soils/NPK fertilizers: Relatively high dietary protein/carbon ratio) stimulate high metabolic turnover rates promoting fast LHS expression manifesting in high rates of reproduction at the expense of longevity (Table 2.5.1.2e: Nutrition and interactive life history features). Conversely, relatively slow LHS-mode realization (longevity, extended healthy lifespan) is induced by the consumption of dietary items (both plants and animals) subject to growth-curbing conditions (cold-climate, aridity, nutrient-poor

soils). Plants subject to growth-curbing conditions are expected to contain increased levels of polyphenols and multiple sirtuins as these sirtuin-activating polyphenols represent stress-signalling molecules that coordinate sirtuin-mediated defences in plants (Howitz et al. 2003, op. cit. Lamming et al. 2004). Many of the polyphenols that activate sirtuins (such as resveratrol and quercetin) are synthesized during times of stress (infection, starvation, dehydration). Sirtuin-inducing polyphenols (Pallauf et al. 2013): Sirt1 activation appears to mimic CR and these sirt-foods may contribute to healthy ageing.

AS Low PIE loads promoted by autophagic catalysis (sirtuins/growth-curbed food items/phenols) Essence preservation EUE

Both CR-induced sirtuin activity and sirtuin activity induced through the consumption of certain growth-curbed food items, typically rich in sirtuin-inducing polyphenols, are anticipated to have a numerous of health-promoting effects.

Summary

Conditions of perceived energy deprivation such as fasting, caloric restriction and exercise activate various metabolic pathways linked to SIRT1 activity. Mammalian sirtuins have been connected to a wide array of activities encompassing cellular stress resistence, energy metabolism and autophagy.

1) Sirtuin activity as response to CR by optimizing energy metabolism in response to hormetic energy deficiency signals.

As part of the response of an organism to catabolic states (associated with metabolic energy expenditure) is the lysosomal degradation pathway autophagy induced via Sirt1 and AMPK (Fontana & Partridge 2015). Sirtuins and thus autophagy are induced by CR (Cuervo et al. 2005). Healthy-ageing benefits from Sirt1 activation by CR or polyphenolic CR mimetics are causally related to autophagy (Pallauf & Rimbach 2013). Thus, CR or polyphenols (hormetic energy deficiency signals/metabolism under stress: growth-curbed conditions) induce Sirtuin activation, thereby optimizing energy metabolism with the involvement of autophagy.

Pallauf & Rimbach (2013) provided a comprehensive review of the contributing role autophagy plays in the context of CR-induced health benefits and the advantages of

polyphenol consumption connected to autophagy induction. Health-benefit effects of dietary restriction are thus at least partly linked to autophagy (Mizushima et al. 2008).

2) Pathways of sirtuin activity induced by CR or polyphenol consumption.

(I) SIRT1-activating compounds (STACs), such as most polyphenols (e.g. resveratrol found in red wine), are reported to activate the enzyme *in vitro* by lowering its Km for substrate (op. cit. Guarente 2013: ***Lowering of the Michaelis constant of SIRT1 for both the acetylated substrate and NAD$^+$ and increasing cell survival by stimulating SIRT1-dependent deacetylation of p53). The lower Km the higher is the catalytic efficiency***. Sirtuins mediate the effects of CR in mammals. SIRT1 is also induced by CR in humans (Guarente 2013).

(II) Polyphenols are implicated to exert positive health effects, through multiple mechanism, not only by modulating redox state, but also due to their ant-inflammatory activity, by regulating adiposite differentiation and lipid metabolism, and ability to regulate intestinal permeability and gut microbiota composition (op. cit. Savini et al. 2013). The bioavailability and effects of polyphenols greatly depend on their transformation by components of the gut microbiota. In the context of the two-way phenolic-microbiota interaction it is clear that dietary polyphenols and their metabolites contribute to the maintenance of gut health by the modulation of gut microbial balance through the stimulation of the growth of beneficial bacteria and the inhibition of pathogen bacteria, exerting prebiotic-like effects (Cardona et al. 2013).

(III) Findings of Chang & Guarente (2013) indicated that SIRT1 activates the central pacemaker to maintain robost circadian control in young animals, and a decay in this activity may play an important role in ageing. CR (time restricted feeding) moderates/regulates biological clocks as a natural mechanism of metabolic optimization under conditions of limited energy resources (Patel et al. 2016).

3) Maintenance of energy homeostasis.

Haigis & Sinclair (2010) presented a comprehensive review of the role of SIRT1 and mitochondrial sirtuins in regulating adaptation to nutrients (maintenance of energy homeostasis) and healing responses in view of diverse disease states. SIRT1 enhances the ability of organisms for increased fat consumption and use of mitochondrial respiration as a way to optimize energy harvesting (Cantó & Auwerx (2012). Also, following Guarente (2013), data show a systematic redirection by sirtuins of

mammalian physiology in response to dietary sirtuins. Sirtuins mediate the effects of CR in mammals, including humans (Guarente 2013). SIRT1-activating compounds (STACs), such as the polyphenol resveratrol found in red wine, were reported to activate the enzyme *in vitro* by lowering its Km (Michaelis constant) for substrate. The lower the Km, the higher is the catalytic efficiency. Resveratrol activates SIRT1 and the associated ***improvement in energy utilization*** and insulin sensitivity closely resembles the benefits of calorie restriction (Guarente 2013).
The hallmarks of CR are metabolic reprogramming to oxidative metabolism (in order to gain the most possible energy from fuel sources) and resistence to stress (particularly oxidative stress). EUE

4) Egert & Rimbach (2011) caution that complex mixtures of plant secondary metabolites cannot be substituted by single purified compounds in the form of dietary supplements. (Consumption of artificially produced polyphenol concentrates may incur risks and should be avoided).

d) Redox balance

Wu et al. (2009) demonstrated that impairment of autophagy results in the accumulation of damaged and dysfunctional mitochondria and corresponding increase in intracellular ROS levels. Autophagy seems to be required for dietary restriction mediated life span extension (Jia & Levine 2007). Damaged mitochondria tend to produce increased levels of reactive oxygen species (ROS), further increasing mitochondrial damage, leading to more oxidant release and additional mitochondrial damage (Wallace 2005).

Wallace (2005): Calorie Restriction. The role of mitochondrial ROS (reactive oxygen species) production in ageing and degenerative diseases is congruent with the life-extending capacity of caloric restriction (**AS: 2.5.1.4**). Reduction of available calories starves the mitochondrial ETC (mitochondrial electron transport chain) for electrons, thereby reducing ROS and protecting the mitochondria and mtDNAs (mitochondrial DNAs). Ageing alters gene expression in muscle and brain. Genes relating to mitochondrial energy metabolism and antioxidant defences are involved. Calorie restriction normalizes many of these genes (Lee et al. 1999, op.cit. Wallace 2005; Lee et al. 2000, op.cit. Wallace 2005). mtDNA rearrangements mutations have been shown accumulate in proportion to life span (Cortopassi & Arnheim 1990, op. cit. Wallace 2005; Melov et al. 1999, op. cit. Wallace 2005). Reduction in dietary calories reduces

serum glucose, thereby inhibiting insulin secretion by pancreatic β cells. This results in dephosphorylation and activation of the FOXO forkhead transcription factors in the energy-utilizing tissues. Furthermore, caloric restriction reduces cellular NADH/NAD^+ ratios, thereby activating the NAD^+-dependant SIRT1, which further activates the FOXOs by deacetylation (Brunet et al. 2004; Giannakou & Partridge 2004, op.cit. Wallace 2005; Motta et al. 2004, op.cit. Wallace 2005). Various associated processes result in calorie restriction to induce the mitochondria to more completely oxidize dietary reducing equivalents and the antioxidant defense systems to more effectively eliminate ROS; reducing mitochondrial oxidative stress. Caloric restriction also protects the mtPTP (mitochondrial permeability transition pore) from p53-mediated activation and apoptosis (Imai et al. 2000, op.cit. Wallace 2005; Luo et al. 2001, op.cit. Wallace 2005). High carbohydrate diets stimulate insulin secretion which phosphorylates the FOXOs, removing them from the nucleus, thereby downregulating cellular stress response pathways. Futhermore, high NADH/ NAD^+ ratios inhibit SIRT1 functionality (compromising antioxidant and stress response systems). Continued caloric overload counters protective antioxidant and stress response systems. Caloric restriction thus extends life span in three ways: by decreasing mitochondrial generation of ROS, by increasing cellular antioxidant defences, and by inhibiting cell loss through apoptosis. Refer also to section 2.2.2h on oxidative stress and the interlinked role of autophagy (Wu et al. 2009).

Halliwell (2012): The endogenous antioxidant defences are complex, interlocking and closely regulated. The total antioxidant capacity of the body (TAC) however seems unresponsive to high doses of dietary antioxidants and the amount of oxidative damage remains largely unchanged thereby (the antioxidant paradox). Manipulation of endogenous antioxidant levels (e.g. by supplying weak pro-oxidants) seems a more promising approach for the treatment and prevention of diseases in which reactive oxidant species play a role. Often dietary substances considered antioxidant (e.g. polyphenols such as flavonols) have strong *in vitro* antioxidant power, but data that these have antioxidant effects *in vivo* has not been forthcoming (discussed in Møller & Loft 2002, op. cit. Halliwell 2012; Halliwell et al. 2005, op. cit. Halliwell 2012; Halliwell 2007, op. cit. Halliwell 2012; Halliwell 2012). Pro-oxidants may have beneficial effects by exerting a mild stressful challenge triggering a rapid response resulting in activation of endogenous antioxidant defence systems (Mattson & Cheng 2006, op. cit. Halliwell 2012; Schaffer & Halliwell 2011, op. cit. Halliwell 2012). ROS is also involved in the ageing process and appears to have have both positive and negative effects in ageing-related and other metabolic processes (Hekimi et al. 2011). In some clinical studies oxidative damage biomarkers correlated with higher risk of disease (op. cit. Halliwell 2012). Various disease conditions were found to alter oxidative damage levels in humans: obesity, hyperglycemia, body iron levels and diabetes (Halliwell 2011, op. cit. Halliwell 2012; Halliwell 2012, op. cit. Halliwell 2012). Growing evidence suggests that polyunsaturated fatty acids (eicosapentaenoic acid) minimize oxitative damage *in vivo*.
Evidence indicates that ROS play important metabolic and signalling roles. It thus appears that humans and other animals have evolved an integrated network of ROS-generating systems and antioxidant defences that provides for some ROS to perform useful functions while minimising, but not eliminating, their potential to cause oxidative damage to biomolecules.

Although causing tissue damage in chronic inflammatory diseases, ROS act as modulators of inflammation, thereby helping to resolve inflammation (e.g. Sareila et al. 2011, op.cit. Halliwell 2012).

Sohal & Forster (2014): Numerous hypotheses have been proposed in order to explain the biological basis of how CR prolongs the life span of responsive genotypes, including retardation of growth, reduction of body fat, attenuation/postponement of immunologic and hormonal changes, enhanced damage/repair capacity, enhanced autophagy and apoptosis, alterations in IGF/insulin/TOR signalling, hormesis, activation of sirtuins, decrease in body temperature/metabolic rate, and attenuation of reactive oxygen species (ROS) generation/oxidative stress (Masoro 2002, op. cit. Sohal & Forster 2014; Fontana et al. 2010, op. cit. Sohal & Forster 2014; Ramsey et al. 2000, op. cit. Sohal & Forster 2014; Merry 2002, op. cit. Sohal & Forster 2014; McDonald & Ramsey 2010, op. cit. Sohal & Forster 2014). ***Hormesis, a concept that the protective responses evoked by low-intensity stress/damage, or intermittent moderate stress, lead to a state of physiological invigoration*** (Rattan 2000, op. cit. Sohal & Forster 2014; Vaiserman 2011, op. cit. Sohal & Forster 2014) seems to implicate the causal participation of deleterious factors in the aging process. The classic view that oxidants produced under normal physiological conditions are invariably potentially deleterious owing to their attacks on various macromolecules (Pryor 1976, op. cit. Sohal & Forster 2014; Davies 1995, op. cit. Sohal & Forster 2014) has been supplanted by the notion that some oxidants, particularly H_2O_2, play a vital physiological role (Jones 2008, op. cit. Sohal & Forster 2014; Droge 2002, op. cit. Sohal & Forster 2014; Forman et al. 2014, op. cit. Sohal & Forster 2014). At relatively low concentrations they regulate the functions of redox-sensitive proteins via reversible oxidation/reduction of cysteinyl thiols, whereas at high concentrations they my be potentially deleterious owing to overoxidation of such proteins, resulting in the impairment of cellular redox potential and cell signalling mechanisms (Brandes et al. 2009, op. cit. Sohal & Forster 2014; Forman et al. 2010, op. cit. Sohal & Forster 2014; Valko et al. 2007, op. cit. Sohal & Forster 2014; Stone & Yang 2006, op. cit. Sohal & Forster 2014; Veal & Day 2011, op. cit. Sohal & Forster 2014). Multiple redox-sensitive proteins have been identified among ageing pathways (reviewed in Orr et al. 2013, op. cit. Sohal & Forster 2014). It has accordingly been proposed that the classic oxidative stress hypothesis, which emphasized the primacy of radical-induced damage, be amended and retermed as the '***redox stress hypothesis***' to accommodate the the more contemporary understanding of mechanismsby which ROS may be involved in the ageing process (Sohal & Orr 2012, op. cit. Sohal & Forster 2014). ***The redox stress hypothesis of ageing postulates that the rate of mitochondrial H_2O_2 generation progressively increases in the latter part of life, which initiates a cascade of events that result in the disruption of the redox-based mechanisms for the regulation of protein function*** (Sohal & Orr 2012, op. cit. Sohal & Forster 2014; Jones 2008, op. cit. Sohal & Forster 2014). There are indications that CR attenuates cellular redox stress in those genotypes in which it extends longevity; as implicated by the redox stress hypothesis.

Eastwood (1999): ***Epidemiological studies indicate that fruit and vegetables are health-promoting and protective against disease, particularly cardiovascular disease and cancer***. Plant nutrients implicated providing this protection include antioxidants and fibre. Clinical trials with antioxidant supplements give inconsistent results regarding protective effects in terms of various forms of cancer. ***The antioxidants used***

in trials may however be effective only within a more complex system. Antioxidants have differing solubilities which partition across the phases of tissues, cells and macromolecular structures: water-soluble ascorbate, glutathione and urate, lipid-soluble tocopherols and carotenoids and intermediary-soluble flavonoids and hydroxycinnamic acids. ***The health protection provided by fruit and vegetables is accordingly considered attributable to an integrated reductive environment delivered by plant antioxidants of differing solubility in each of the tissue, cellular and macromolecular phases***

(**The intake of antioxidant supplements is to be avoided**).

e) Life history trade-off relationships mediated by caloric restriction

It is generally assumed that dietary restriction (DR) extends lifespan (Nakagawa et al. 2012) and reduces fecundity (Moatt et al. 2016); thereby representing a trade-off (refer also to Table 2.5.1.2e: Nutrition and interactive life history features). Such trade-off relationships are regularly established, but they are not universal, as highlighted by Jasienska (2009).

Depending on degree and duration of DR (dietary restriction), it may represent either a state of ***starvation*** (**DR-starvation**) or induce a state of increased metabolic efficiency of energy utilization in association with ***autophagy*** (**DR-autophagy**). In the broader context of feast-famine alternation, DR (as chronic starvation) reduces the capacity to respond to environmental challenges (lower BMRs, reduced cold tolerance, reduced immunity, slowed wound healing), reducing survival prospects (Dirks & Leeuwenburgh 2006). According to the adaptive resource re-allocation hypothesis selection favours the re-allocation of nutrients from reproduction to somatic maintenance and repair under conditions of nutritional deficits (DR-starvation response: reproduction-maintenance trade-off), thereby increasing the chances of survival during a famine (Adler & Bonduriansky 2014). This interpretation is consistent with the notion of reproductive suppression being adaptive under conditions of energy deficits (Jasienska 2003). As nutrients become plentiful again, the organism reverses the above mode of resource allocation and resumes reproduction. In fully fed animals nutrient-responsive pathways are activated and cellular recycling and repair mechanisms are inhibited, including autophagy and apoptosis. Plasticity of LHS-mode expression provides for P > M LHS-mode realization under feast conditions (with plasticity costs due to P > M trade-off constraints: high reproductive output at the cost of health/longevity: 2.2.2e) and M > P LHS-mode realization under conditions of

famine (plasticity costs due to M > P trade-off constraints: survival at the cost of reproductive output).

Autophagy and apoptosis are two main cellular recycling and repair mechanisms that respond plastically to nutrient availability. Autophagy is a intracellular process whereby portions of the cell are sequestered, broken down and recycled, promoting protection and survival of the cell (e.g. Ravikumar et al. 2010).

According to the **adaptive resource re-allocation hypothesis**, dietary restriction reduces rates of intrinsic aging due to activated autophagy effects, **but at the cost of reproductive output** (Adler & Bonduriansky 2014). Adler & Buriansky (2014) presented an alternative, evolutionary more plausible hypothesis, i. e. that of a highly conserved physiological response to DR where the up-regulation of autophagy and apoptosis represents a **nutrient-recycling, efficient resource use mode** that enables organisms to maximize immediate reproductive output under conditions of resource scarcity (amounting to a relaxation of the production *versus* survival trade-off under resource constraints).

Evolutionary theory predicts that selection will strongly favour reproduction early in life, even at the cost of reduced healthy aging and reduced longevity. According to the alternative framework presented by Adler & Bonduriansky (2014), DR (autophagy) effects, inducing autophagy and increasing apoptosis, are interpreted as part of a suite of facultative physiological responses that enables organisms to maximize immediate reproductive output even under conditions of reduced resource availability, as well as in times of resource surplus. Autophagy is predominantly cytoprotective and beneficial to human health, and reduced autophagy has been associated with accelerated aging (Rubinsztein et al. 2011). However, in the context of an alternative framework (Adler & Buriansky 2014) to the adaptive resource re-allocation hypothesis, emphasis is placed on autophagy as a mechanism by which cytoplasmic molecules can be mobilized to generate energy-rich compounds meeting bioenergetic demands of cells under conditions of declining external and internal resources (autophagy as a dynamic recycling system: Mizushima & Komatsu 2011). Adler & Buriansky (2014) suggest that selection would favour up-regulation of cellular recycling mechanisms under DR (autophagy), allowing animals to **make more efficient use of limited resources**, possibly allowing for some immediate reproduction; as autophagy frees up stored nutrients in cells thereby allowing organisms to function more efficiently.

A baseline level of nutrients must be available before reproduction is possible. According to the interpretation of Adler & Bonduriansky (2014), responses to dietary restriction **lower this baseline, making reproduction more attainable under conditions of relative nutritional constraints**. Under this resource use mode, the organism makes more efficient use of incomimg resources, but with a slower conversion rate that is more than sufficient to accommodate the lower resource intake rate under dietary restriction. Processes such as autophagy and apoptosis could accordingly be considered mechanisms of differential resource allocation, as under dietary restriction stored resources are recycled and put to use for survival or reproduction. This form of differential allocation differs fundamentally from that envisaged under the **adaptive resource re-allocation hypothesis** because it does **not involve sacrificing reproduction for the sake of somatic maintenance**. Reduced P-M trade-off constraints (**nutrient-recycling, efficient resource use mode**: Adler & Buriansky 2014).

Following the interpretation of DR effects involving a nutrient-recycling, efficient resource use mechanism (Adler & Buriansky 2014), LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated. This provides for some concurrence/combination of fast LHS (reproduction) and slow LHS (maintenance of healthy ageing) realization. Plasticity gains at low plasticity costs. This is supported by DR (autophagy) effects being characterized by combined high metabolism and longevity (e.g. Speakman et al. 2004; Kirkwood & Shanley 2005).

Summary

Based on the insights presented above, two types energy-processing metabolic modes are differentiated: I) a balanced energy use efficient EUE-PM supporting metabolic mode (minimized P-M trade-off constraints underpinning a high performance and health/longevity combination) and a II) energy use reactive EUR-P > M traded off metabolic mode (fast LHS extremized, high metabolic turnover HMT). Autophagy as component of the metabolic mode either present (EUE-PM metabolic mode: ‘famine’ induced/response) or absent (EUR-P-M traded off metabolic mode; induced under ‘feast’ conditions).

I) Famine-responsive energy use efficient EUE-PM metabolic mode.

High P capacity based on energy efficient metabolism (autophagy) of food resources. Low plasticity costs. Reduced P-M trade-off constraints. LHS PM. Reduced P/fast LHS (early-life P) vs M/slow LHS (later life P, health, longevity) trade-off constraints/reduced plasticity costs. High P, health and longevity combination. Energy use efficiency mediated by activated autophagy.

II) Feast-responsive energy use reactive EUR-P > M metabolic mode.

Maximum P realization (peak P levels) on the basis of maximum surplus realization (energy inefficient). High plasticity costs. High P/fast LHS-M/slow trade-off constraints (P at the cost of health/longevity). Fast > slow LHS realization. LHS P > M. Plasticity of maximum energy dispositioning (autophagy deactivated). P maximization based on surplus resource use at cost of energy efficiency. Fast LHS P expression (competitive edge-uric acid: 2.2.1c**).**

As induced by CR stimuli, the **famine-responsive energy use efficient EUE-PM metabolic mode**, is characterized by an amelioration of LHS P-fast versus M-slow trade-off constraints; allowing for relatively high P (performance) realization with relatively reduced M (maintenance) trade-off costs; accommodating a P-health combination, as manifesting in traditionally healthy living (THL: 2.5.1.2) populations (performance re reproduction-competitive vitality-health-longevity combination).

Following the interpretation of CR effects involving a nutrient-recycling, efficient resource use mechanism (Adler & Buriansky 2014), LHS trade-off constraints between productivity and maintenance, and fast-slow LHS expression are decreased/mitigated; promoting fast-slow balanced LHS realization. This provides for some concurrence/combination of fast-P LHS (reproduction) and slow-M LHS (maintenance of healthy ageing) realization. This interpretation is supported by results of Speakman et al. (2004) regarding the 'mitochondrial uncoupling to survive' hypothesis according to which a positive association between high metabolism and longevity is implicated in CR animals. This is also consistent with the finding that, on refeeding, female rodents previously kept on restricted diets were able to reproduce at much later ages than fully fed controls (Holehan & Merry, op. cit. Kirkwood & Shanley 2005).

f) Meal timing, frequency and composition

Kahleova et al. (2017): Data from 50 660 subjects ≥ 30 years were analysed. Eating 1 or 2 meals/day was associated with a relative decrease in BMI (-0.05 and -0.03 respectively) compared with eating 3 meals/day. On the other hand, eating > meals 3 (snacking) compared with 3 meals/day was associated with a relative increase in BMI per year of 0.02 (4), 0.02 (5), 0.04 (≥ 6) meals/day respectively. More meals per day were associated with a greater increase in BMI, even within the snacking range. ***Subjects who had a long overnight fast (≥ 18 hours) experienced a relative decrease in BMI per year (-0.02) in contrast to those with a short overnight fast (7-11 hours), whose BMI was relatively increased (0.02)***; both compared with a medium overnight fast of 12-17 hours. ***Breakfast eaters experienced a relative decrease in in their BMI (-0.03) compared with breakfast skippers. Those whose largest meal was breakfast experienced the largest relative decrease in BMI (-0.04) compared with those who ate their largest meal at dinner*** and those who ate lunch as their largest meal experienced a smaller relative decrease in BMI (-0.02). Thus, relative to subjects who ate their lagest meal at dinner, those who consumed breakfast as the largest meal experienced a significant decrease in BMI and those that consumed a big lunch experienced a smaller but still significant decrease in BMI than did those who ate their largest meal at dinner. Eating breakfast and lunch 5-6 hours apart and making the overnight fast last 18-19 hours appears to be a practical strategy for preventing long-term weight gain.
The observed relation between breakfast consumption and a relative decrease in BMI is consistent with previous studies (Purslow et al. 2008, op. cit. Kahleova et al. 2017; Timlin et al. 2007, op. cit. Kahleova et al. 2017). Certain studies have shown that usually skipping breakfast increased the risk of obesity and obesity-related chronic diseases (Ma et al. 2003, op. cit. Kahleova et al. 2017; Odegaard et al. 2013, op. cit. Kahleova et al. 2017).
Hunger has its intrinsic circadian peak in the evening, promoting the tendency to eat the largest meal late in the day (Jakubowicz et al. 2012, op. cit. Kahleova et al. 2017). Eating a large breakfast reduces hunger, notably cravings, and posprandial ghrelin concentrations thus counteract weight gain (Solomon et al. 2008, op. cit. Kahleova et al. 2017). ***Time-restricted feeding seems to improve the circadian oscillations of key metabolic indicators*** such as cAMP, response element-binding protein, mammalian target of rapamycin, and AMP-activated protein kinase (Hatori et al. 2012). ***Regular breakfast consumption seems to increase satiety, reduce total energy intake, reduce blood lipids, and improve insulin sensitivity and glucose tolerance at a subsequent meal*** (Betts et al. 2014; Odegaard et al. 2013, op. cit. Kahleova et al. 2017).

Hatori et al. (2012): The time-restricted feeding regime entrained the circadian clock and metabolic regulators to fixed feeding times and prevented the high-fat/high calorie induced disruption of the normal cellular metabolic program (as genetically determined).

Scheer et al. (2013): ***A pronounced endogenous circadian rhythm in hunger was identified, with a trough in the biological morning (8:00 h) and peak in the evening (20:00 h)***; independent of time since waking up, time since prior meals and of calories consumed. ***Phased endogenous circadian rhythms were present in appetites for sweet, salty, and starchy foods, fruits, meats/poultry, and food overall (high energy foods); but not in the desire to eat vegetables***. The intrinsic circadian evening peak may promote larger meals before the fasting period necessitated by sleep, whereas the ***circadian morning trough would facilitate the extended overnight fast***. The

endogenous circadian rhythm in hunger peaking in the evening may have evolutionary advantage coping with times of food shortages as ***eating the largest meals in the evening aids energy storage***. However, the tendency to eat the largest meal in the evening when high-energy foods are abundantly available would contribute to the rising prevalence of obesity in western countries.

Fontana & Partridge (2015): Severe DR is difficult to practice and sustain and can increase the risk of impaired menstrual and reproductive function, osteoporotic bone fractures, anemia and cardiac arrhythmias (Fairburn & Harrison 2003, op. cit. Fontana & Partridge 2015). ***Limiting daily food intake of an isocaloric diet to a 5-7 hour time window in humans can induce health benefits compared with a standard three to five meals per day*** (Mattson et al. 2014). Accumulating evidence indicates that a restriction of protein or specific amino acids in the diet as promoting healthspan, rather than CR restriction in general (Solon-Biet et al. 2014, op. cit. Fontana & Partridge 2015); Nakagawa et al. 2012).

Microbiota derived factors and healthy ageing: Only ~ 10 % of cells of the human body and less than 1 % of genes are human and the rest come from trillions of microbes in the gastrointestinal tract. ***Accumulating metagenomics data indicate that altered food intake, especially protein and insoluble fibre, have profound effects on gut microbiota structure, function, and secretion of factors that modulate multiple inflammatory and metabolic pathways*** (Muegge et al. 2011, op. cit. Fontana & Partridge 2015; Clemente et al. 2012, op. cit. Fontana & Partridge 2015; David et al. 2014, op. cit. Fontana & Partridge 2015; Thorburn et al. 2014, op. cit. Fontana & Partridge 2015).

Jakubowicz et al. (2013): Meal timing has implications on weight gain, appetite, and glucose and lipid metabolism (Fonken et al. 2010, op. cit. Jakubowicz et al. 2013); Arble et al. 2009, op. cit. Jakubowicz et al. 2013; Wu et al. 2011, op. cit. Jakubowicz et al. 2013; Froy 2010, op. cit. Jakubowicz et al. 2013; Morgan et al. 2012, op. cit. Jakubowicz et al. 2013). Current evidence suggests that the time-of-day of nutrient intake can also influence the metabolic syndrome by affecting circadian rhythms (Fonken et al. 2010, op. cit. Jakubowicz et al. 2013; Arble et al. 2009, op. cit. Jakubowicz et al. 2013; Wu et al.2011, op. cit. Jakubowicz et al. 2013). ***Skipping breakfast and/or overeating in the evening, play an important role in weight gain and obesity*** (De Castro 2007, Leidy et al. 2009, op. cit. Jakubowicz et al. 2013). ***Studies in animals have shown that the daily first meal (equivalent to breakfast) determines the circadian phase of peripheral clocks, whereas the last meal (equivalent to dinner) leads to lipogenesis and adipose tissue accumulation*** (Leidy & Racky 2010, op. cit. Jakubowicz et al. 2013; Wu et al. 2011, op. cit. Jakubowicz et al. 2013).
The two meal plan were either high-calorie breakfast (BF) or high-calorie dinner (D), with a total daily energy of 1400 kcal with identical macronutrient and composition. The energy of the BF meal plan involved a large breakfast (~ 700 kcal, 50 %), medium-sized lunch (~ 500 kcal, 36 %) and a small dinner (~ 200 kcal, 14 %). This was reversed in the D meal plan: a small breakfast and a large dinner. Subjects were asked to eat breakfast at 6:00-9:00, lunch at 12:00-15:00, and dinner at 18:00-21:00.
The results of the study showed that an isocaloric weight loss diet (1400 kcal/day) with exchanged caloric intake between breakfast and dinner differentially influences weight loss, waist circumference, serum ghrelin and lipids, appetite scores, and insulin resistence indices in overweight and obese women with metabolic syndrome. ***The***

greater weight loss and reduction in waist circumference in the BF group is consistent with previous cross-sectional studies that indicated that regular breakfast consumption leads to reduced BMI and body fat (Timlin et al. 2008, op. cit. Jakubowicz et al. 2013; Szajewska & Ruszczynski 2010, op. cit. Jakubowicz et al. 2013). The greater reduction in waist circumference in the BF group is particularly important as elevated waist circumference is a determinant of insulin resistance and cardiovascular disease risk (Rask-Madsen & & Kahn 2012, op. cit. Jakubowicz et al. 2013). According to Almoosawi et al. (2012, op. cit. Jakubowicz et al. 2013), among the components of metabolic syndrome, waist circumference is influenced mostly by the time-of-day of nutrient intake. ***High carbohydrate intake at breakfast is protective against abdominal obesity*** (Almoosawi et al. 2012, op. cit. Jakubowicz et al. 2013). The highest glucose and insulin were observed were observed after a high-calorie dinner consumed by the D goup compared with an isoenergetic meal consumed at breakfast in the BF group.This is consistent with previous studies which have shown that insulin sensitivity and glucose tolerance decreases progressively throughout the day with insulin sensitivity reaching a low-point in the evening (Morgan et al. 2012, op. cit. Jakubowicz et al. 2013; Van Cauter et al. 1992, op. cit. Jakubowicz et al. 2013; Lee et al. 1992, op. cit. Jakubowicz et al. 2013). It was also found that despite the same caloric intake at lunch, serum glucose and insulin responses were significantly lower in the BF group, suggesting protective effects against pospandrial hyperinsulinemia after the second meal (Brynes et al. 2003, op. cit. Jakubowicz et al. 2013). It is speculated that the decrease in the overall insulin concentrations throughout the day in the BF group may be protective against the development of the metabolic syndrome and associated complications.

In summary, regarding two isocaloric weight loss groups, a greater improvement of metabolic markers were exhibited by the group consuming a bigger breakfast and a smaller dinner than vice versa (Jakubowicz et al. 2013).

De Castro (2007): ***The results confirm that intake in the mornng is particularly satiating and can reduce the total amount ingested for the day, amd that intake in the late night lacks satiating value and can result in greater overall daily intake***. The findings demonstrated that the satiating influence of morning intake is primarily due to its ***carbohydrate content*** and that the supplementing influence of evening intake is mainly due to its carbohydrate and fat content. Protein intake did not appear to have as large an effect on intake as carbohydrate or fat intake. According to Cho et al. (2003, op. cit. De Castro 2007), individuals who consumed high-protein breakfasts tended to have higher BMI (Body Mass Index) than those who ate high carbohydrate breakfasts. Concerning the current epidemic of obesity, the modern trend for children and adolescents to eat very little in the morning and shifting the preponderance of their intake till much later in the day (Nicklas et al. 2004, op. cit. De Castro 2007; Siega-Riz et al. 1998, op. cit. De Castro 2007), and for adults to to be less likely to eat breakfast (Haines et al. 1996, op. cit. De Castro 2007), is of relevance here. ***It has been shown that overweight and obesity are associated with skipping breakfast*** (American Heart Association, op. cit. De Castro 2007; Boutelle et al. 2002, op. cit. De Castro 2007; Rampersaud et al. 2005, op. cit. De Castro 2007) ***and eating late in the day*** (Forslund et al. 2002, op. cit. De Castro 2007). With respect to the control of obesity, it is

recommended that a high-carbohydrate breakfast is combined with the intake of low-energy-density foods and a restriction of night-time eating.

Phillips et al. (2016): A study that assessed the satiating effect of protein when provided at different meal occasions further supported the concept of consuming more protein at breakfast (Leidy et al. 2009, op. cit. Phillips et al. 2016). The consumption of a high protein breakfast led to greater fullness, which extended throughout the day and into the evening hours compared with a high-protein lunch or dinner. These data suggest that the timing of protein consumption directly influences satiety, with breakfast eliciting unique effects. When compared with breakfast skipping, the consumption of breakfast (in general) led to reductions in appetite, increases in fullness, reductions in food cravings and voluntary reductions in high-fat and high-sugar evening snacking behaviour (Hoertel et al. 2014, op. cit. Phillips et al. 2016; Leidy et al. 2013, op. cit. Phillips et al. 2016). Consumption of high protein breakfasts resulted in greater modulations in these responses compared with normal protein breakfasts. ***Generally, findings suggest a unique benefit of including ~ 30 g of protein at the morning meal for longer term improvements in weight management. The meal and/or diet recommendations for increased protein consumption are based on studies that include high quality animal-based protein sources (meat, eggs, yoghurt)***.

Mattson et al. (2014): ***Emerging findings suggest that intermittent energy restriction periods of as little as 16 hours can improve health indicators and counteract disease processes***. Mechanisms involve a metabolic shift to fat metabolism and ketone production, and stimulation of adaptive cellular stress responses that prevent and repair molecular damage. Three experimental dietary regimen were considered: I) caloric restriction (CR), in which daily calorie intake is reduced by 20-40 %, and meal frequency is unchanged; II) ***intermittent energy restriction (IER), which involves eliminating (fasting) or greatly reducing (e.g. 500 cal per day) daily food caloric/beverage intake intermittently, for example, 2 days/week***; III) ***time-restricted feeding (TRF), which involves limiting daily intake of food and caloric beverages to a 4- to 6-h time window***. Hunter-gatherer anthropoids, including those living today, often eat intermittently depending on food availability (Cordain et al. 2002a). Many adaptations for an intermittent food supply are conserved amng mammals, including organs for the uptake and storage of rapidly mobilizable glucose (liver glycogen stores) and longer-lasting energy substrates, such as fatty acids in adipose tissue. In conjunction with increasingly sedentary lifestyles, the consumption of high energy meals (especially refined grains and sugar) multiple times each day is considered to have contributed to the emergence of obesity and related diseases as major causes of morbidity and mortality. The mechanism underlying the beneficial effects of are complex. The daily fasting episodes trigger alternative activation of fasting-responsive cAMP response element binding protein (CREB) and AMP kinase, and feeding responsive insulin-dependent mammalian target of rapamycin (m TOR) pathways implicated in metabolic homeostasis. ***These pathways also impinge on the circadian clock and improve robustness of oscillation of clock components and downstream targets*** (Hatori et al. 2012).
Four general mechanisms by which IER protects cells against injury and disease relate to I) adaptive stress responses; II) bioenergetics; III) inflammation and IV) improved repair and removal of damaged molecules and organelles.

I) **Adaptive stress responses**. Beneficial effects of IER involve the general biological phenomenon of hormesis or 'preconditioning', in which the exposure of cells and organisms to mild stress results in adaptive responses that protect against more severe stress. For example, IER increases the production of trophic factors that promote neuronal survival, neurogenesis, and the formation and strengthening of synapses in the brain (Marosi & Mattson 2014, op. cit. Mattson et al. 2014). Numerous studies have shown that IER can protect neurons against oxidative, metabolic and proteotoxic stress in animal models of neurodegenerative disorders, including Alzheimer's and Parkinson's diseases (Mattson 2012, op. cit. Mattson et al. 2014).
II) **Bioenergetics**. In humans IER can increase insulin sensitivity more than daily calorie restriction that achieves similar weight loss (Harvie et al. 2013, op. cit. Mattson et al. 2014). When humans change from eating three full meals a day to **IER** (involving either one moderate size meal every other day or ***only 500-600 calories on two days per week***), they exhibit changes in ***energy metabolism characterized by increased insulin sensitivity, reduced levels of insulin and leptin, mobilization of fatty acids and elevation of ketone levels*** (Johnson et al. 2007, op. cit. Mattson et al. 2014; Harvie et al. 2011, op. cit. Mattson et al. 2014; Varaday et al. 2013, op. cit. Mattson et al. 2014). Ketones are known to have beneficial effects on cells with a high energy demand, such as neurons in the brain (Newman & Verdin 2014, op. cit. Mattson et al. 2014). The shift to ketogenesis may play an important role in suppression of tumor growth by IER/fasting, since tumor cells are largely unable to use ketones as an energy source (Seyfried et al. 2014, op. cit. Mattson et al. 2014).
III) **Inflammation**. Major diseases, including cardiovascular disease, diabetes, neurodegenerative disorders, arthritis, and cancers involve chronic inflammation in the affected tissues, and in many cases systemically (McDade 2012). Overweight and obesity promote inflammation, and ***IER suppresses inflammation in human subjects and animal models of disease***.
IV) **Improved repair and removal of damaged molecules and organelles**. In the context of the mechanism of autophagy, damaged and dysfunctional proteins, membranes and organelles are directed to and degraded in lysosomes (Rubinsztein et al. 2011). When organisms ingest regular meals, their cells receive a relatively regular supply of nutrients and thus remain in a 'growth mode' in which protein synthesis is robust and autophagy is suppressed (Speakman & Mitchell 2011). The nutrient-responsive mTOR pathway negatively regulates autophagy; and ***as fasting inhibits the mTOR pathway it stimulates autophagy in cells of many tissues*** (Kume et al. 2010, op. cit. Mattson et al. 2014; Wohlgemuth et al. 2010, op. cit. Mattson et al. 2014). Autophagy is regulated in a diurnal rhythm in many cell types, and this rhythm can be altered by changing the timing of food intake (meal timing). Accordingly, the frequency of meals and the circadian timing of meals is likely to affect the responses of cellular mechanisms for clearance of damaged proteins and organelles (Ma et al. 2012, op. cit. Mattson et al. 2014).

Ma et al. (2012): ***Circadian regulation of metabolism is mediated through reciprocal signalling between the body clock and metabolic regulatory networks; and autophagy is rhythmically activated in a clock-dependent manner***. In this context it represents a process contributing to nutrient and cellular homeostasis, its cyclic induction possibly providing a link between clock and metabolism. Nutrient and energy metabolism is temporally organized in tissues to synchronize the storage and utilization of energy with light-dark cycles (Asher & Schibler 2011, op. cit. Ma et al. 2012; Green et al. 2008, op. cit. Ma et al. 2012; Rutter et al. 2002, op. cit. Ma et al. 2012). Activities of

many metabolic pathways are restricted not only to to specific tissues, but also to unique periods of the day (Gachon et al. 2006, op. cit. Ma et al. 2012; Pan et al. 2010, op. cit. Ma et al. 2012). The temporal restriction of metabolic functions seemingly provides advantages for organisms as they anticipate and synchronize their feeding and activity cycles to the environment. An example of nutrient sensing in the cell is via NAD-dependent histone deacetylase that deacetylates several clock proteins (Asher et al. op. cit. Ma et al. 2012; Nakahata et al. 2008, op. cit. Ma et al. 2012). Numerous studies reviewed by Ma et al. (2012) underscore a potentially important role of circadian misalignment in the pathogenesis of metabolic disorders in humans. He & Klionski (2009, op. cit. Ma et al. 2012) provided a molecular framework for autophagic degradation and its physiological significance. According to relevant studies, autophagy is critical for cellular homeostasis and nutrient metabolism in the starvation state; and is induced in neonatal and adult tissues in response to starvation (Kuma et al. 2004, op. cit. Ma et al. 2012; Mizushima et al. 2004, op. cit. Ma et al. 2012). Autophagy is induced under conditions of limited nutrient access, restriction of various types of nutrients, such as amino acids, and growth factors, oxygen and energy (Mizushima & Komatsu 2011).
Autophagy in yeast appears to have been restricted to a specific temporal phase that is associated with reductive metabolic activities (Tu et al. 2005, op. cit. Ma et al. 2012). ***It is likely that circadian regulation of associated metabolic cycles is coordinated with autophagy to optimize the supply of nutrients for storage or oxidation***. Rescue of autophagy function in the liver restores hepatic insulin signalling and glucose homeostasis; and also plays a direct role in the hydrolysis of triglycerides stored in lipid droplets (Singh et al. 2009, op. cit. Ma et al. 2012)). ***Autophagy is emerging as an important process for metabolic homeostasis. Periodic activation of autophagy seemingly contributes to proteonome turnover and organelle homeostasis; which collectively define different metabolic phases and the transition among these temporal compartments in tissues***.

Asher & Sassone-Corsi (2015): One of the well-known quotes from Maimonides (a medieval Jewish philosopher and doctor) is: '***Eat like a king in the morning, a prince at noon, and a peasant at dinner***'. Accumulating evidence suggests that meal timing can affect a variey of physiological processes and dramatically affect health; notably obesity and other metabolic disorders. Thus, time of food ingestion is critical for the well-being of an organism, and chrono-nutrition refers to food intake in coordination with the circadian rhythms of the body. Review articles (Asher & Schibler 2011, op. cit. Asher & Sassone-Corsi 2015; Eckel-Mahan & Sassone-Corsi 2013, op. cit. Asher & Sassone-Corsi 2015; Feng & Lazar 2012, op. cit. Asher & Sassone-Corsi 2015). Also, the clock directs the circadian synthesis of NAD^+ and thereby the cyclic activity of NAD^+-consuming enzymes; as is the case of the NAD-dependent deacetylase as SIRT1, an enzyme involved in the control of cellular metabolism, inflammation, and ageing (Guarente 2011). SIRT1 and SIRT6 partition the circadian epigenome, leading to segregated control of cellular metabolism; a finding that could be of relevance in respect of different nutritional regimes (Eckel-Mahan et al. 2013, op. cit. Asher & Sassone-Corsi 2015). Changes in in food composition/feeding time may lead to differential activation of epigenetic and transcriptional control systems through harnessing specialized enzymatic pathways and circadian metabolic sensors. ***Mice under a time-restricted high fat diet consuming equivalent calories as those with ad libitum access were protected against obesity, hyperinsulinemia, hepatic steatosis and inflammation*** (Hatori et al. 2012; Sherman et al. 2012, op. cit. Asher & Sassone-

Corsi 2015). Both studies applied time-restricted high-fat diets, but at completely different times of the day. This suggests that time restriction from food per se, rather than its occurrence at a specific circadian time is of importance. A comprehensive study by Chaix et al. (2014, op. cit. Asher & Sassone-Corsi 2015) ***highlighted the effectiveness of time-restricted feeding against different nutritional challenges, including high-fat, high-fructose, and high-fat combined with high-fructose diets; all of which are known to cause dysmetabolism***.
Fuse et al. (2012) established differential roles of breakfast only (one meal per day) and a bigger breakfast with a small dinner (two meals per day) in mice fed a high-fat diet in respect of induced obesity and lipid metabolism. Mice on two meals manifested reduced body weight gain and improved metabolic indicators compared with those on a single meal or freely fed animals. In humans, early meal times significantly decreased serum lipid levels (Yoshizaki et al. 2013, op. cit. Asher & Sassone-Corsi 2015); and breakfast consumption among adolescents was inversely associated with with weight gain (Timlin et al. 2008, op. cit. Asher & Sassone-Corsi 2015). ***Generally, time-restricted feeding seems to generate sharp feeding-fasting cycles, which consolidate circadian rhythmicity in gene expression and circadian activation of various metabolic pathways***.

Hatori et al. (2012): Mice, under time-restricted feeding (8 hours/day), but consuming equivalent calories than mice feeding on a high-fat diet *ad lib* (food availability throughout day) were protected against obesity, hyperinsulinemia, hepatic steatosis, inflammation and exhibited improved coordination. ***The temporal spreading of the calorie intake seemed to be of importance since the mice fed the diet ad lib perturbed the metabolic pathways entrained by circadian and feeding rhythms; predisposing the organism to obesity and metabolic diseases***. The time-restricted feeding regime entrained the circadian clock and metabolic regulators to fixed feeding times and prevented the high-fat/high calorie induced disruption of the normal cellular metabolic program (as genetically determined).

Johnston (2014): Much evidence now exists linking the circadian timing system to metabolic physiology and nutrition. ***Relationships between processes are often reciprocal, in that the circadian system drives temporal changes in metabolic pathways and changes in metabolic/nutritional status alter core molecular components of circadian rhythms***. Metabolic rhythms include daily changes in glucose homeostasis, insulin sensitivity and postprandial response. Time of day also alters lipid and glucose profiles following individual meals; whereas ***over a longer time scale, meal timing regulates adiposity and body weight***. Diurnal changes in glucose tolerance have been recognized in humans for many years (Van Cauter et al. 1997, op. cit. Johnston 2014). Sensitivity to elevated glucose concentration is greatest in the early morning and then declines over the course of the day (leading to a phenomenon that has been termed 'afternoon diabetes'). ***The daily change appears to be the result of altered glucose glucose and insulin sensitivity, with maximal insulin sensitivity occurring in the early morning and then decreasing throughout the day*** (Van Cauter et al. 1997, op. cit. Johnston 2014). In addition to glucose homeostasis, the regulation of plasma lipids is also subject to daily variation. Basal concentrations of triacylglycerol (TAG: stored as fat droplets, providing good stores of energy) are elevated at night and there are also diurnal changes in postprandial TAG responses. ***Ingestion of a meal at night results in increased plasma TAG that remains elevated***

for longer than the response to the same meal given during the day (Sopowski et al. 2001, op. cit. Johnston 2014). Evidence suggests a role for regular breakfast consumption in the maintenance of healthy body weight (De la Hunty & Gibson 2013, op. cit. Johnston 2014; Casazza et al. 2013, op. cit. Johnston 2014). Energy consumption after 20:00 hours has been associated with higher BMIs independently of age, sex, sleep timing and sleep duration (Baron et al. 2011, op. cit. Johnston 2014).***Women eating more energy at breakfast than dinner lost more weight and also exhibited an improved metabolic profile in insulin sensitivity and TAG concentration*** (Jakubowicz et al. 2013 op. cit. Johnston 2014).

Almoosawi et al. (2016): Several studies reported a positive link between evening energy intake and obesity. ***It is well recognized that food intake, appetite, digestion and metabolism each exhibit circadian patterns*** (Waterhouse et al. 1997, op. cit. Almoosawi et al. 2016). Food intake itself serves as regulator of of the circadian clock, notably so the peripheral circadian clock in tissues such as the liver and the intestine (Damiola et al. 2000, op. cit. Almoosawi et al. 2016; Hara et al. 2001, op. cit. Almoosawi et al. 2016). Also, the central circadian clock, entrained by the dark-light cycle is known to extend its effect on food absorption (Qandeel et al. 2009, op. cit. Almoosawi et al. 2016; Iwashina et al. 2011, op. cit. Almoosawi et al. 2016; Pan & Hussain 2007, op. cit. Almoosawi et al. 2016). ***BMI (Body Mass Index) was positively associated with evening:morning energy intake ratio*** (Aljuraiban et al. 2015, op. cit. Almoosawi et al. 2016). ***Carbohydrate intake at breakfast or mid-morning was particularly protective against abdominal obesity*** (Almoosawi et al. 2013, op. cit. Almoosawi et al. 2016). According to the analyses of Wang et al. (2014, op. cit. Almoosawi et al. 2016) ***higher proportion of energy intake at midday was associated with a healthy BMI***. The odds of having a BMI of ≥25 kg/m2 was almost double in men reporting a higher proportion of energy intake in the evening. Furthermore, overweight/obesity in breakfast skippers was related to a higher energy and carbohydrate intake at dinner. Breakfast skippers had higher BMI with increasing energy and carbohydrate in the evening (Dubois et al. 2009, op. cit. Almoosawi et al. 2016). Greater energy intake at breakfast was associated with a lower BMI in the adolescent group and in the middle-age group, greater energy intake at breakfast and lower energy intakes during the evening were associated with lower BMI (Summerbell et al. 1996, op. cit. Almoosawi et al. 2016). ***The ratio of evening:morning energy intake seems to be important, as evening intake affects BMI differently based on whether individuals were regular or irregular consumers of breakfast*** (Dubois et al. 2009, op. cit. Almoosawi et al. 2016). It should however be noted that organisms are biphasic and animal models indicate that, physiologically, eating two meals a day (a bigger breakfast with a smaller dinner), but not one meal/day (breakfast only) helps control body weight and fat accumulation (Fuse et al. 2012).

Summary

I) Meal frequency and timing in the context of yin-yang dynamics.

The relevance of meal frequency, timing and composition in respect of health outcomes can be elucidated with reference to yin-yang dynamics.

Maciocia (1989): Yin and yang stand for two stages in the process of change and transformation of all things in the universe. Yin and yang as two phases of a cyclic

movement, one constantly changing into the other, such as the day giving way to the night and vice versa. Day corresponds to yang and night to yin, and by extension, activity to yang and rest to yin. The day belongs to yang, but reaching its peak at midday, the yin within it gradually begins to unfold and manifest. Yang corresponds to creation and activity, whereas yin corresponds to materialization. Yin and yang are in a constant state of dynamic balance, which is maintained by continued adjustments of the relevant levels of yin and yang. Besides the normal state of balance of yin and yang, there are four possible states of imbalance: preponderances of yin or yang and weakness of yin or yang. When yin is preponderant; it induces a decrease of yang, i.e. the excess of yin consumes yang. When yang is preponderant, it induces a decrease in yin; i.e. excess yang consumes yin. When yin is weak, yang is in apparent excess (**AS: LT lean-thin body condition type: Table 2.5.1.5c**) and when yang is weak, yin is in apparent excess (**AS: OB: obesogenic body condition type: Table 2.5.1.5c)**.

II) Daily time restriction of feeding.

A daily intermittent fasting induced 24-hour metabolic rhythm (10-18 h daytime eating phase and a nocturnal non-eating period of 16 hours) ensures a high-amplitude yin-yang 24 h cycle (pronounced nocturnal yin and daytime yang expression). A breakfast during the rising yang phase, lunch (yang peak at midday) and dinner during the rising yin phase supports balanced yin-yang metabolic expression. Time-restricted feeding seemingly generate sharp feeding-fasting cycles which consolidate circadian rhythmicity in gene expression and circadian activation of various metabolic pathways (Asher & Sassone-Corsi 2015). Emerging findings suggest that intermittent energy restriction periods of as little as 16 hours can improve health indicators and counteract disease processes (Mattson et al. (2014). Making the overnight fast last 18-19 hours is conducive for the prevention of long-term weight gain (Kahleova et al. 2017). Time-restricted feeding seems to improve the circadian oscillations of key metabolic indicators such as cAMP, response element-binding protein, mammalian target of rapamycin, and AMP-activated protein kinase (Hatori et al. 2012).

Linking circadian rhythmicity, autophagy and daily time-restricted food intake (a, b, c):

a) Circadian rhythmicity. Scheer et al. (2013): ***A pronounced endogenous circadian rhythm in hunger was identified, with a trough in the biological morning (8:00 h) and peak in the evening (20:00 h)***; independent of time since waking up, time since prior meals and of calories consumed. ***Phased endogenous circadian rhythms were present in appetites for sweet, salty, and starchy foods, fruits, meats/poultry,***

and food overall (high energy foods); but not in the desire to eat vegetables. The intrinsic circadian evening peak may promote larger meals for energy storage, whereas the ***circadian morning trough would facilitate the extended overnight fast***. **Johnston (2014)**: Much evidence now exists linking the circadian timing system to metabolic physiology and nutrition. ***Relationships between processes are often reciprocal, in that the circadian system drives temporal changes in metabolic pathways and changes in metabolic/nutritional status alter core molecular components of circadian rhythms***. Metabolic rhythms include daily changes in glucose homeostasis, insulin sensitivity and postprandial response. Time of day also alters lipid and glucose profiles following individual meals; whereas ***over a longer time scale, meal timing regulates adiposity and body weight***. ***The daily change appears to be the result of altered glucose glucose and insulin sensitivity, with maximal insulin sensitivity occurring in the early morning and then decreasing throughout the day*** (Johnston 2014). **Almoosawi et al. (2016)**: Several studies reported a positive link between evening energy intake and obesity. ***It is well recognized that food intake, appetite, digestion and metabolism each exhibit circadian patterns*** (Waterhouse et al. 1997, op. cit. Almoosawi et al. 2016). Also, the central circadian clock, entrained by the dark-light cycle is known to extend its effect on food absorption (Almoosawi et al. 2016). ***BMI (Body Mass Index) was positively associated with evening:morning energy intake ratio. A higher proportion of energy intake at midday was associated with a healthy BMI***. **Jakubowicz et al. 2013**: ***The greater weight loss and reduction in waist circumference in the BF group is consistent with previous cross-sectional studies that indicated that regular breakfast consumption leads to reduced BMI and body fat*** (Jakubowicz et al. 2013; Szajewska & Ruszczynski 2010, op. cit. Jakubowicz et al. 2013). ***High carbohydrate intake at breakfast is protective against abdominal obesity*** (Jakubowicz et al. 2013).

b) Autophagy. Ma et al. (2012): ***Circadian regulation of metabolism is mediated through reciprocal signalling between the body clock and metabolic regulatory networks; and autophagy is rhythmically activated in a clock-dependent manner***. ***It is likely that circadian regulation of associated metabolic cycles is coordinated with autophagy to optimize the supply of nutrients for storage or oxidation***. ***Autophagy is emerging as an important process for metabolic homeostasis. Periodic activation of autophagy seemingly contributes to proteonome turnover and organelle***

homeostasis; which collectively define different metabolic phases and the transition among these temporal compartments in tissues.

c) Daily time-restricted food intake. A comprehensive study by Chaix et al. (2014, op. cit. Asher & Sassone-Corsi 2015) ***highlighted the effectiveness of time-restricted feeding against different nutritional challenges, including high-fat, high-fructose, and high-fat combined with high-fructose diets; all of which are known to cause dysmetabolism***. **Fontana & Partridge (2015)**: Severe DR is difficult to practice and sustain and can increase the risk of impaired menstrual and reproductive function, osteoporotic bone fractures, anemia and cardiac arrhythmias (Fontana & Partridge 2015). ***Limiting daily food intake of an isocaloric diet to a 5-7 hour time window in humans can induce health benefits*** (Mattson et al. 2014). **Fuse et al. (2012)**: ***Generally, time-restricted feeding seems to generate sharp feeding-fasting cycles, which consolidate circadian rhythmicity in gene expression and circadian activation of various metabolic pathways***. **Kahleova et al. (2017)**: ***Subjects who had a long overnight fast (≥ 18 hours) experienced a relative decrease in BMI per year (-0.02) in contrast to those with a short overnight fast (7-11 hours), whose BMI was relatively increased (0.02). Breakfast eaters experienced a relative decrease in in their BMI (-0.03) compared with breakfast skippers. Those whose largest meal was breakfast experienced the largest relative decrease in BMI (-0.04) compared with those who ate their largest meal at dinner***.

Organisms are **biphasic** and eating two meals a day (a bigger breakfast with a smaller dinner), rather than breakfast only, helps control body weight and fat accumulation (Fuse et al. 2012). This is attributed to a balanced yang-yin metabolism underpinned by consuming both a breakfast (rising yang phase) and dinner (rising yin phase).

Breakfast.

'Eat like a king in the morning, a prince at noon, and a peasant at dinner' (Maimonides, a medieval Jewish philosopher and doctor, ex Asher & Sassone-Corsi 2015). According to Almoosawi et al. (2012, op. cit. Jakubowicz et al. 2013), among the components of metabolic syndrome, waist circumference is influenced mostly by the time-of-day of nutrient intake. Relative to subjects who ate their largest meal at dinner, those who consumed breakfast as the largest meal experienced a significant decrease in BMI and those that consumed a big lunch experienced a smaller but still significant

decrease in BMI than did those who ate their largest meal at dinner (Kahleova et al. 2017).

Eating a large breakfast reduces hunger, notably cravings, and posprandial ghrelin concentrations thus counteract weight gain (Solomon et al. 2008, op. cit. Kahleova et al. 2017). Regular breakfast consumption seems to increase satiety, reduce total energy intake, reduce blood lipids, and improve insulin sensitivity and glucose tolerance at a subsequent meal (Betts et al. 2014, op. cit. Kahleova et al. 2017; Odegaard et al. 2013, op. cit. Kahleova et al. 2017).

This is attributed to a balanced yang-yin metabolism underpinned by consuming a breakfast (rising yang phase), a lunch (yang peak phase) and dinner (rising yin phase). Following Maciocia (1989), yang corresponds to creation and activity (intensity of metabolic processing), whereas yin corresponds to materialization (energy storage).

Lunch.

Lunch coincides with the yang peak phase (intensity of metabolic activity/processing). According to the analyses of Wang et al. (2014, op. cit. Almoosawi et al. 2016) higher proportion of energy intake at midday was associated with a healthy BMI.

Dinner.

Dinner coincides with the rising yin phase; supportive of materialization (Maciocia (1989), i.e. energy storage.

Hunger has its intrinsic circadian peak in the evening, promoting the tendency to eat meals later in the day (Jakubowicz et al. 2012, op. cit. Kahleova et al. 2017).

According to Scheer et al. (2013), a pronounced endogenous circadian rhythm in hunger was identified, with a trough in the biological morning (8:00 h) and peak in the evening (20:00 h); independent of time since waking up, time since prior meals and of calories consumed. Phased endogenous circadian rhythms were present in appetites for sweet, salty, and starchy foods, fruits, meats/poultry, and food overall (high energy foods); but not in the desire to eat vegetables. The intrinsic circadian evening peak promotes meals during the rising yin phase, whereas the circadian morning trough facilitates an extended overnight fast period.

This endogenous circadian rhythm in hunger peaking in the evening has an evolutionary advantage in respect of coping with times of food shortages, as eating the largest meals in the evening aids energy storage (as facilitated during the rising yin phase). On the downside, the associated tendency to eat the largest meal in the evening would contribute to the rising prevalence of obesity in western countries, when high-

energy foods are abundantly available (De Castro 2007; Jakubowicz et al. 2013; Almoosawi et al. 2016).

Dinner is of particular importance in the case of normo-adaptive (NA) and lean-thin (LT) body condition types (Table 2.5.1.5c); notably so for the latter, which tend to be associated with a state of yin deficiency. Female reproductive functionality is based on a body condition requiring some level of fat reserves (Table 2.3.2b). Such reserves are most efficiently acquired through food intake during the phase of rising yin, i.e. with dinner. Obesogenic body condition types (yang deficiency; yin excess), on the other hand, should minimize food intake at dinner time.

III) Meal timing and composition.

Breakfast.

De Castro (2007) attributes the satiating influence of food intake in the morning primarily to its carbohydrate content. Iintake at breakfast is protective against abdominal obesity (Almoosawi et al. 2012, op. cit. Jakubowicz et al. 2013). In respect of the satiation effect of protein, the consumption of a high protein breakfast led to greater fullness, extending throughout the day and into the evening hours (Leidy et al. 2009, op. cit. Phillips et al. 2016). When compared with breakfast skipping, the consumption of breakfast (in general) led to reductions in appetite, increases in fullness, reductions in food cravings and voluntary reductions in high-fat and high-sugar evening snacking behaviour (Hoertel et al. 2014, op. cit. Phillips et al. 2016; Leidy et al. 2013, op. cit. Phillips et al. 2016). These findings suggest beneficial effects of including ~ 30 g of protein at the morning meal for longer term improvements in weight management (Phillips et al. (2016). These diet recommendations for increased protein consumption are based on studies that included high quality animal-based protein sources (meat, eggs, yoghurt). Pronounced satiation should be followed by hunger before the next meal (healthy satiation-hunger rhythm), conducive to efficient digestion. It is contended that the sensation of post-satiation hunger is boosted by the protein content of the meal, as it promotes yang activity.

Considering the yin-yang balance of the meal (breakfast) and other considerations (Table 2.5.1.5e), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (mainly starch-rich and fiber-linked carbohydrates) is here recommended.

Lunch.

Considering the yin-yang balance of the meal (lunch) and other considerations (Table 2.5.1.5e), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (including starch-rich, nutrient-dense and fiber-linked carbohydrates) is here recommended. Unlike for breakfast and dinner, nutrient-dense, fresh vegetables/fruit (*inter alia* sirtuin foods) should form important meal components at lunch. Efficient digestion requires peak yang metabolic performance as prevalent during this peak yang phase (and supported by the protein-yang component of the meal); and rest after lunch for efficient digestion in parasympathetic mode (of the Autonomous Nervous System). A post-lunch rest period of 30-60 minutes is thus indicated.

Dinner.

Considering the yin-yang balance of the meal (dinner) and other considerations (Table 2.5.1.5e), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (including starch-rich, nutrient-dense and fiber-linked carbohydrates) is here recommended. Easily digestible high quality protein (dairy > meat-derived) and carbohydrates (starch-rich > vegetables) are relevant.

2.5.1.5 Diets in conformity with evolutionary requirements

a) Nutritional context and the PALEO-diet

Traditional nutrition. The changing availabiliry of meat with fat/green vegetable matter and plant-derived carbohydrates was utilized optimally. During pre-agricultural times carbohydrate resources were spatiotemporally limited. While the consumption of meat and green vegetables underpins a relatively high metabolic rate, a carbohydrate-rich nutrition (grains) is associated with a low weight-specific metabolic turnover (McNab 1986). Mammals with a relatively high metaboilic rate (BMR) have a higher temperature regulation capacity when confronted with low environmental temperatures, and increased post-natal growth and reproduction rates (McNab 1983). Consumed fat / meat served as sources of energy (metabolic turnover), whilst more scarcely available carbohydrates wre stored as fat (fat deposits; notably for times of food scarcity).

Such nutrition was/is characterized by alternating phases of increased metabolic turnover (based on meat, fat and green vegetables) and low metabolic turnover based on carbohydrate-rich food items, underpinning anabolic processes, deposition of fat and other energy-rich storage components (adenosinphosphates: Fahrner 1985); and also muscle and organ regeneration. Seasonally alternating phases with increased metabolic turnover (meat-fat-green vegetables: metabolic performance enhancing) and reduced metabolic turnover (predominantly carbohydrates; anabolic consolidation: muscle- and fat deposition; body condition build-up); as well as involuntary or self-imposed periods of fasting were/are characteristic (2.5.1.2).

With an increasing supply by agriculture of carbohydrate- and meat products and rising living standards, overconsumption of both these dietary components ensued. The inbuilt fasting effect in traditional nutrition was replaced by uninterrupted overconsumption of these dietary components (protein-mast and excessive fat storage). The consequences of protein overconsumption in respect of many disease conditions linked to reduced capillary membrane permeability were comprehensively outlined by Wendt (1985). In a state of a relatively high metabolic turnover (increased energy demand for protein synthesis and breakdown) concurrent sufficiency of calorie resources for the body must be ensured in order to enable the body to fully utilize/process the dietary protein. All proteins not fully utilized or completely processed are deposited onto the basal membranes, causing hypoporopathies (Wendt 1985). This is why an increased fat intake as a source of energy for complete protein processing is important in association with a predominantly meat-fat-green vegetable diet (*vide* Noakes et. al. 2014). For hunter-gatherers subject to periarctic metabolic performance constraints (Table **2.5.1.1a**; subarctic and cool temperate environments), when subject to conditions of marginal caloric intakes, and *lean* meat became the principal source of energy, protein-induced elevated metabolic rates increased caloric requirements and protein catabolism. In order to counteract the associated loss in body condition hunter-gatherers selectively targeted prey animals with high fat contents and were seeking out carbohydrate-rich foods for the accumulation of body fat stores (Speth & Spielmann 1983). Fat as a source of energy, on the one hand, underpins the full processing of and complete utilization of proteins in a metabolic state of increased metabolic turnover (as induced by a relatively high meat/green vegerable intake); and on the other hand, with fat catering for much of the energy demands, it is expected that

the desire for further energy carriers (especially sugar and fat storage supporting carbohydrates) is diminished, and therewith also the intake of larger food quantities (reduced hunger: avoidance of over-consumption of proteins and carbohydrates). Carbohydrate intake induces hunger (addiction), promoting further opportunistic intake for the storage of fat reserves for times of food scarcity.

The Paleo-diet paradigm. According to Eaton et al. (2010), the ancestral diet in comparison to the contemporary Western diet, was characterized by greater dietary bulk, lower caloric concentration (more fiber, fruit and vegetables), carbohydrate intake was primarily from fruit and vegetables (with a low glycemic load and very little refined sugars), with a relatively higher protein intake, a favourable omega-3 polyunsaturated fatty acid content and contained more long-chain essential fatty acids. Furthermore the ancestral diet involved a higher micronutrient intake (also more potassium relative to sodium) with a higher anti-oxidant capacity with an alkaline acid-base effect. The estimated ancestral dietry intake was determined as 35-40 % carbohydrates (percent of daily energy), 25-30 % protein, 30-40 % fat (7.5-12 % saturated fat); wth relatively higher dietary concentrations of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), vitamin C and potassium (less sodium).

DIET-EVOLUTION-eaton

Cordain et al. (2005): The dietary changes towards current Western diets since the introduction of agriculture ≈ 10 000 years ago had occurred too recently on an evolutionary time scale for the human genome to adjust. With the advent of agriculture novel foods were introduced as staples for which the hominin genome had little evolutionary experience. Food processing procedures in the wake of the Industrial Revolution allowed nutrient combinations that had not previously encountered during hominin evolution (resulting in evolutionary discordance manifesting in disease, increased morbidity and reduced reproductive success (Boaz 2002, op. cit. Cordain et. al. 2005; Nesse/Williams 1994, op. cit. Cordain et al. 2005). Food staples (increasing types of foods which had contributed little to preagricultural hominin diets: dairy foods, cereal, refined sugars, refined vegetable oils, alcohol, salt content) and food processing procedures introduced during the Neolithic and Industrial Periods fundamentally altered nutritional characteristics in respect of: 1. Glycemic load (glycemic load = GI x carbohydrate content per serving, quantifying the blood glucose raising potential of a food based on the quantity and quality of dietary carbohydrate (Jenkins et al. 1981,

op. cit. Cordain et al. 2005). Refined grains and sugar usually have much higher glycemic loads than unprocessed fruits and vegetables; sugars and grains with high glycemic load were rarely or never consumed by average citizens as recently as 200 years ago). 2. Fatty acid composition (Western diet is characterized by a low omega-3 to omega-6 polyunsaturated fatty acid content due to an increased intake of omega-6 PUFA in processed vegetable oils and grain fed cattle. 3. Macronutrient composition (according to supporting evidence, protein consumption of Upper Paleolithic Europeans had been substantially higher than current values (*inter alia* Richards et al. 2000, op. cit. Cordain et al. 2005), at the expense of carbohydrate content; with negative health ramifications. High reliance of modern-day hunter-gatherers on animal-based foods, associated with a relatively low carbohydrate content of wild plant foods, resulted in macronutrient consumption ratios in which protein was relatively elevated at the expense of carbohydrates (Cordain et al. 2000). 4. Micronutrient density (refined sugar, grains and milk represent a relatively high proportion of modern diets, but these have relatively low nutrient density ratings, thereby reducing the micronutrient density of the diet by displacing more nutrient dense foods; increasing the risk of mineral and vitamin deficiencies. 5. Acid-base balance (The typical Western diet yields a net acid load, sustaining a chronic, low-grade pathogenic metabolic acidosis that increases with age: Frassetto et al. 1996, op. cit. Cordain et al. 2005). 6. Sodium-potassium ratio (the addition of manufactured salt and displacement of traditional potassium-rich foods by foods introduced during the Neolithic and Industrial periods caused a 400% decline in potassium intake while simultaneously initiating a 400% increase in sodium ingestion (Cordain 2002, op. cit. Cordain et al. 2005); with health ramifications: concentrations of intracellular potassium were negatively correlated with cancer rates, whereas conentrations of intracellular sodium were positively correlated with cancer rates (Jansson 1986, op. cit. Cordain et al. 2005); and 7. Fibre (high fiber contents of traditional diets were displaced with staples of low fibre content during Neolithic and Industrial periods. Anderson et al. (1994) outlined health benefits associated with diets relatively high in fiber content as relating to coronary heart disease, cancer, blood pressure, obesity, diabetes and gastrointestinal disorders.

Frassetto et al. (2009) reported that even short-term consumption of a Paleolithic diet (comprised of lean meats, fruit, vegetables and nuts; but excluding non-paleolithic food types such as cereal grains, dairy products and legumes) improved blood pressure and

glucose tolerance, decreased insulin secretion, increased insulin sensitivity and improved lipid profiles without weight loss in healthy sedentary humans.

Table 2.5.1.5a Health ramifications of dietary deviations from Paleolithic patterns
(Cordain et al. 2005):
1. Glycemic load
Chronic hyperglycemia and hyperinsulinema induced by high glycemic load carbohydrates elicit physiological responses promoting insulin resistance (Reaven 1995; Reaven 2005); metabolic syndrome-linked diseases, but also myopia (Cordain et al. 2002 b), acne, gout and insulin resistance and compensating hyperinsulinemia, polycystic ovary syndrome, epithelial cell cancers; breast, colon, prostate cancer; male vertex balding (Lindeberg et al. 2003). Jenkins et al. (2002): Starchy carbohydrate foods have different effects on postprandial glucose and insulin responses depending on the rate of digestion. Low glycemic index diets are associated with lower urinary C-peptide excretion, a measure of insulin sensitivity. Positive associations between dietary glycemic index and some forms of cancer and chronic disease in general. Augustin et al. (2002): Hyperinsulinemia and insulin resistance (associated factors: high energy intake, obesity, lack of physical activity) are implicated in the etiology of diabetes, coronary heart disease and cancer. Carbohydrates have received much attention as culprit. However, different types of CH produce varying glycemic and insulinemic responses. Low glycemic index foods, characterized by slowly absorbed CH, have been shown to have beneficial effects on glucose control, hyperinsulinemia, insulin resistance, blood lipids and satiety. Dietary fructose may contribute to insulin resistance through its unique ability among all sugars to cause a shift in balance from oxidation to esterification of serum nonesterified free fatty acids (Elliott et al. 2007).
2. Fatty acid composition
Simopoulus (2006): Evidence from relevant studies of the diets of modern day hunter-gatherers and traditional diets indicate that humans evolved on a diet in which the ratio of omega-6/omega-3 essential fatty acids was ≈ 1, whereas in modern Western diets this ratio is around 15-16/1. A high omega-6 to omega-3 ratio promotes the pathogenesis of chronic conditions (cardiovascular disease, diabetes, cancer, obesity, autoimmune diseases, rheumatoid arthritis, asthma, osteoporosis, depression), whereas increased levels of omega-3 polyunsaturated fatty acids exert suppressive effects. The balance of omega-6 with omega-3 fatty acids is important for homeostasis and development. Dietary intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) decrease the risk for cardiovascular disease. Both omega-6 and omega-3 fatty acids influence gene expression. Many chronic diseases begin in utero or early infancy and adequate dietary intake of polyunsaturated fatty acids, even prior to pregnancy is considered important. Omega-3 fatty acids have anti-inflammatory effects (inflammation associated with many chronic diseases), wheras omega-6 fatty acids do not have such effects. Furthermore, a diet supplemented with omega-3 fatty acids with fish oil inhibited adrenal activation induced by mental stress, presumably by regulating sympatho-adrenal reactivity (Delarue et al. 2003).

Skilton et al. (2012): Impaired fetal growth is inversely linked to arterial wall thickening in early childhood associated with an increased risk of cardiovascular diseases in adulthood. Dietary omega-3 fatty acid supplementation in early childhood prevented the association between impaired fetal growth and arterial wall thickening, suggesting that adults which had suffered from impaired fetal growth may have a reduced risk of cardiovascular disease if having had omega-3 supplementation during childhood over the first 5 years of life. Patterson et al. (2012): An increased ratio of omega-6 to omega-3 polyunsaturated fatty acid consumption results in a change of mediators and regulators of inflammation and immune responses towards a pro-inflammatory profile; leading to chronic conditions such as cardiovascular disease, rheumatoid arthritis, obesity and diabetes. In contrast, omega-3 fatty acid derived eicosanoids (EPA: eicosapentaenoic acid and DHA: docosahexaenoic acid) have anti-arrhythmic, antiaggregation, anti-inflammatory, antiapoptotic effects and decrease oxidative stress (Patterson et al. 2012). A balanced omega-3/omega-6 fatty acid dietary composition can only be obtained from animal and marine food resources (Cordain 1999).

3. Macronutrient composition

High protein diets: Notably animal protein is a crucial source of essential and non-essential aminoacids and sufficiency of these are essential for health and performance (Braverman et al. 2003). High protein diets are associated with improved blood lipid profiles with reduced risks of cardiovascular disease, improved glucose and insulin metabolism, notably in the context of diabetes (O'Dea 1984 op. cit. Cordain et al. 2005; O'Dea et al. 1989 op. cit. Cordain et al. 2005); and obesity in general (in obese individuals, hypocaloric high-protein diets improved insulin sensitivity, i.e. reduced insulin resistance, and prevented muscle loss). Hypocaloric high-carbohydrate diets reduced insulin sensitivity and resulted in reductions of fat-free mass (Piatti et. al. 1994). Cardiovascular protective effect of dietary protein (Hu et al. 1999, op. cit. Cordain et al. 2005). Lower blood pressure has been associated with higher intakes of protein (Obarzanek et al. 1996, op. cit. Cordain et al. 2005; Burke et al. 2001, op. cit. Cordain et al. 2005). Stroke mortality is inversely related to protein and fat intake (Burke et al. 2001, op. cit. Cordain et al. 2005; Klag and Whelton 1993, op. cit. Cordain et al. 2005).

Protein has more than three times the thermic effect than of either fat or carbohydrate and a greater satiety value The thermic effect of food contributes to the satiating power of foods (Crovetti et al. 1998, op. cit. Cordain et al. 2005); increased dietary protein may thereby represent an effective weight loss strategy for obesogenic body condition types (Cordain et al. 2005). Animal protein intake is a superior source of magnesium compared with plant-derived magnesium (Dean 2014).

4. **Micronutrient density**

Adequate intake of folate and vitamin B_6 prevents the accumulation of homocysteine in the bloodstream. Elevated blood concentrations of homocysteine represent an independent risk factor for the development of cardiovascular disease, stroke and deep vein thrombosis (Wald et al. 2002, op. cit. Cordain et al. 2005; Meleady & Graham 1999, op. cit. Cordain et al. 2005). Elevated homocysteine levels were associated with hippocampal neuron degeneration in mice maintained on a folate deficient diet. Dietary supplementation with 400µg of folic acid can decrease homocysteine levels by 2 to 5 µmol/L (Mattson 2003). Wild plant foods known to be consumed by hunter-gatherers generally maintain higher micronutrient concentrations than their domestic counterpart, as does the muscle meat of wild animals. The Neolithic introduction of dairy foods and cereal grains as staples caused

the average micronutrient content of the diet to decline; a situation worsened by cereal milling developed in the Industrial era. The decline in dietary mineral and vitamin density has far-reaching health implications (promoting the development of vitamin deficiency, infectious and chronic diseases: Cordain 1999). Cordain et al. (2005): lower nutrient density and Mg/Ca ratios of contempory whole grain and milk: 0.27; fruit, vegetables, seafood, lean meat: 0.64. Price (1939): traditional diet Mg/Ca ratio 2.75; see also other nutrient densities in traditional vs Western diets.

5. **Acid-base balance**

Health benefits of net base-yielding diet: including prevention and treatment of osteroporosis (Sebastian et al. 1994), age-related muscle wasting (Bushinsky 1996, op. cit. Cordain et al. 2005), hypertension and slow progression of age- and disease-related chronic renal insufficiency (op. cit. Cordain et al. 2005). Sebastian et al. (2002): Retroprojected net endogenous acid production of preagricultural diets was negative, i.e. 87% of diets were net base-producing, with contempory diets generally positively net endogenous acid producing. The historical shift from negative to positive net acid production was attributed to the displacement of high bicarbonate yielding plant foods (roots, tubers, green leafy vegetables, vegetable fruit, fruit) by cereal grains and high energy dense, nutrient poor foods in the contempory diets. Health benefits of a lifelong dietary net base load/systemic metabolic alkanizing effects: prevention and treating osteoporosis (Burshinsky, op. cit. Sebastian et al. 2002), age-related muscle wasting (Frassetto et al. 1997, Sebastian et al. 2002), calcium nephrolithiasis (Leman et al., op. cit. Sebastian et al. 2002), sodium chloride-sensitive hypertension (Morris et al., op. cit. Sebastian et al. 2002), improving exercise performance (McNaughton et al., op. cit. Sebastian et al. 2002), treating infertility (Maas et al., op.cit. Sebastian et al. 2002), and slowing the progression of age-related and disease-related chronic renal insufficiency (Frassetto et al. 1996, Sebastian et al. 2002).

6. **Fiber**

Herschlag (2015) lists the following benefits of adequate fiber levels in the diet: a) maintains health of the digestive tract, b) persistant starch (insoluble fiber) increases insulin sensitivity when eaten together with caloric carbohydrates, c) reduces appetite (slowing down rate of digestion), d) reduces fat absorption and e) lowers intestinal pH (increasing the absorption of dietary minerals); specifically confirmed for magnesium absorption in humans (Coudray et al. 2003).

Espeseto & Giugliano (2006): Higher fiber content of whole-grain food items was found to be associated with a reduced likelihood elevated C-reactive protein (CRP: a marker of inflammation) regardless of age and BMI (King et al. 2003, op. cit. Espeseto & Giugliano 2006). High intakes of cereal fiber were furthermore associated with higher plasma concentrations of adiponectin (an insulin-sensitizing adipocytokine).

Anderson et al. (1994): High fiber intakes are associated with lower serum cholesterol concentrations, lower risk of coronary heart disease, reduced blood pressure, enhanced weight control, better glycemic control, reduced risk of certain forms of cancer, and improved gastrointestinal function. Dried beans, oat products and certain fruits and vegetables are good sources of soluble fiber. Most plant foods and whole grains are good sources of insoluble fiber.

Greger (1999): Fiber and compounds associated with fiber in cereal products (e.g. phytates) have been found to reduce the apparent absorption of minerals (such as calcium, magnesium, zinc and manganese). In contrast, however, the addition of soluble forms of fiber (such as pectins, gums, resistant starches, lactulose,

oligofructose, inulin) has been found to add viscosity to the gut contents, promote fermentation, and the production of volatile fatty acids in the cecum, have a trophic effect on the ceca and increase serum enteroglucagon concentrations; and thus often have been found to improve absorption of minerals.

Eaton and Konner (1985): Our ancestral line maintained the versatility of the omnivore diet that typifies most primates. The range of diets available to preagricultural humans represents the nutrition for which human beings are in essence genetically programmed (Yudkin op. cit. Eaton & Konner 1985). Developments such as the Industrial Revolution, agribusiness, and modern food-processing techniques have occurred too recently to have any evolutionary effect. Most modern disease conditions having emerged in Western societies and patterns of nutritional disease generally appear to be a function of the stage of civilization (Mayer 1967). Associated modern disease conditions are virtually absent in contempory surviving hunter-gathering populations whose way of life and eating habits closely resemble those of preagricultural humans (Trowell op. cit. Eaton & Konner 1985).
Fruits comprised the main component of hominid nutrition in the Miocene (24 to *ca* 5 million years back; Stini, op. cit. Eaton & Konner 1985). Between about 1.8-1.6 million years BC (*Homo erectus*) increasing amounts of meat were consumed. The food intake of *Homo erectus* and early hominids still involved over 50 % of plant origin (Isaac, op. cit. Eaton & Konner 1985). Cro-Magnon and other modern humans increasingly took to the hunting of large wild game animals and meat began to exceed 50 % in the diet (Foley, op. cit. Eaton & Konner 1985). In a relatively short preagricultural time period (reduced availability of large game animals, human population increase, climatic changes) the proportion of foods of plant origin increased again and resulted in a versatile omnivore nutrition (similar to to that of modern hunter-gatherer groups). Agriculture then changed human nutrition decisively (MacNeish, op. cit. Eaton & Konner 1985). The meat component of diets was drastically reduced, with over 90 % being of plant origin (protein calorie deficit).

Subject to the Paleo-diet paradigm, as outlined above, Cordain (2011) developed the PALEO-diet which he recommended to form the basis for modern human nutrition (Table 2.5.1.5b).

Table 2.5.1.5b PALEO-DIET (Cordain 2011)
Over a time period of more than two million years our ancestors consumed a diet rich in natural meats and fats; providing for about 50 % of the calorie requirements. This Stone Age nutrition involved lots of meat (lean meats: from wild animals seafood), fresh fruit, vegetables and health-promoting fats. Wild game meat (withy organs) was predominant in Paleolithic nutrition (relative high protein intake),

whereas carbohydrates contributed relative less to the diet. Carbohydrates consumed were in the form of starch-poor, but fiber-rich fruits and vegetables. Fats consisted primarily as poly-unsaturated fatty acids (omega-3 fats).

Modern Paleo-nutrition following Cordain (2011):

- Lean meat*, organ meats, fish and seafood
- Fruits and starch-poor vegetables
- Health-supporting fats

Largely to be avoided are grain products, beans (Leguminosae), dairy products and processed/refined nutritional items of plant or animal origin.

*Lean meat (*ca* 80 % protein and 20 % fat; wild game). Fat-rich meat from domesticated animals, raised under artificial and intensive husbandry, contains preservatives (nitrites) and residues of salt. Feeding with fructose-rich maize syrup and wheat results in unfavourably high concentrations of omega-6 fatty acids in comparison with health-promoting omega-3 fatty acids.

Fruit and starch-poor vegetables: Wild fruit and vegetables of the Paleo-nutrition were rich in antioxidants, phytochemicals and fiber, but had low glycemic indices in comparison with modern starch-rich grain cereals.

Health-promoting fats: unsaturated fats such as olive oil, linseed oil, walnut oil and avocado oil; but no canola oil. Omega-3 fatty acids. Poly-unsaturated fatty acids in fish oils.

Lean meat has twice the metabolic rate increasing-effect as fats and carbohydrates. Is also associated with a more pronounced satiation reflex (reduced appetite, increased metabolic turnover rates, accelerated burning of calories.

European *Homo sapiens* before 30 000 years, with a good availability of meat, were about 15 cm taller, on average, than their descendants after the emergence of regular agriculture (Angel op. cit. Eaton & Konner 1985). Since the Industrial Revolution the proportion of meat (protein) in western diets has increased and body size has again increased to that of the first modern humans (before *ca* 30 000 years).

Whether with a meat proportion of as high as 80 % or as low as 20 %, Paleolitic nutrition was substantially different to that of modern Western societies. Four food groups can be differentiated: meat and fish; vegetables and fruit; milk and other dairy products, and grain cereals/breads. Adults in preagricultural times satisfied their nutritional requirements mainly from the first two groups (meat, fish, vegetables, fruits), whereas modern diets are dominated by items from groups 3 and 4 (milk, dairy products, cereals/breads). Furthermore, an uninterrupted oversupply of nutritional items exists (affluent malnutrition), in contrast to pre-industrial times when seasonal food supply bottlenecks and years of food scarcity generally occurred (with body mass losses: fasting effects). In comparison with modern Western nutrition, Paleolithic nutrition, irrespective of the meat proportion, consisted of a variety of plant components with higher vitamin content, and essential fatty acids with a higher ratio of polyunsaturated to saturated fats. Generally, domesticated food plants contain more starch relative to proteins inn comparison with wild plant forms (Harris op. cit. Eaton & Konner 1985). Wild animal meat contains five times more polyunsaturated fats than that of domesticated sanimals (Crawford 1968, op. cit. Eaton & Konner 1985). Substantial amounts of eicosapentaenoic acids occur in the fat of wild animals, with very little of these in the fat of domesticated cattle (Crawford 1969, op. cit. Eaton & Konner 1985). The meat of wild animals contains less calories and more protein per unit of weight (Crawford 1968, op. cit. Eaton & Konner 1985).

b) Metabolic body condition types

A body mass index (BMI = mass/height^2, kg/m^2) of 20-23.9 was associated with the lowest mortality risk. All-cause mortality of men increased with BMIs < 20 and ≥ 30 (Shaper et al. 1997, op. cit. Samaras & Elrick (1999). Men weighing 20 % below average for men of the same age and height were the healthiest (Lee et al. 1993, op. cit. Samaras & Elrick (1999). A BMI of between 19-22 was found ideal for good health and long life (Elrick et al. 1978, op. cit. Samaras & Elrick 1999). Both excess lean body mass and excess fat mass are indicative of chronic disease (Samaras et al. 2002).

Table 2.5.1.5c Metabolic body condition types (Stoffwechselkonditionstypen)	
Reduced functional efficiency on the basis of pathoinformation-engram loadings accentuates metabolic trade-off constraints between the capacity for high metabolic rate performance and anabolic metabolic capacity. Due to an associated reduced performance breadth, segregation into **high metabolic turnover types at the cost of anabolic capacity** (LT: lean-thin body condition types) and **low metabolic turnover types with anabolic capacity, but lacking capacity for high metabolic rate performance** (OB: obesogenic body condition types). With sufficient vitality and thus adaptable performance breadth, **normo-adaptive metabolic turnover types** (NA: normo-adaptive body condition types) are manifest.	
According to Chinese Medicine (Maciocia 1989), the constitution (fundamental physical and mental make-up of an individual) involves three factors: i.e. Essence, Qi and Mind. Essence is the foundation of the other two. If the inherited Essence is strong, this will constitute a basis for a healthy life, both physically and mentally. As interpreted here, inherited Essence represents a state of the absence of any significant patho-information-engram loading of the biocybernetic system of the body. Essence (not a substance), but a state of metabolic plasticity, with little or no plasticity costs. Represented by the PM-LHS-mode, based on minimal PIE load engrainment in the biocybernetic system (minimized P/fast versus M/slow LHS trade-off constraints).	
Defined body condition types: LT Lean-thin – NA normo-adaptive – OB obesogenic	
Body condition is based on two components, the capacity for high metabolic rate settings underpinning growth and reproduction and the capacity for anabolic condition build-up manifesting in the storage of reserve components, primarily fat (energy storage); notably important for female reproductive performance. Plasticity of **normo-adaptive metabolic turnover types** caters for both of these two components (low functionality trade-off constraints); whereas the capacities for anabolic processes are restricted in LT-types and capacities for high metabolic turnover rate performance constrained in OB-types.	

Maciocia (1989): When yin is weak, yang is in apparent excess (LT lean-thin body condition type) and when yang is weak, yin is in apparent excess (OB: obesogenic body condition type). When yin is preponderant; it induces a decrease of yang, i.e. the excess of yin consumes yang (OB: obesogenic body condition type). When yang is preponderant, it induces a decrease in yin; i.e. excess yang consumes yin (LT lean-thin body condition type).	
Maintenance of high metabolic rate settings is supported by dietary meat and fat, whereas anabolic condition build-up is based on dietary carbohydrates as substrate for fat storage. Pathologically distorted types: LT (prominence of over-active high metabolic turnover processes interfere with anabolic condition build-up: relatively increased requirements of dietary carbohydrates) and OB (predominance of anabolic processes are not compatible with high metabolic turnover rates): low-carbohydrate/high protein-fat diets required. ***Animal-protein/fat and vegetable carbohydrates (cooked) combined in the same meal are mutually enhancing in building and sustaining body condition***.	
Without stored energy as body fat, ketones as energy source for brain functional processes during fasting periods, including daily periods of sleep, results in (nocturnal) energy deficits for brain function and development ().	
Healthy males appear relatively lean (not lean-thin) due to genderspecific relatively high metabolic turnover rate settings, healthy females exhibit relatively rounded body shapes (partly due to an anabolic body condition, with some fat storage) and healthy babies appear chubby (subcutaneous fat storage to meet ketone requirements for brain development: Cunane & Crawford 2003). Mothers build up fat storage depots during pregnancy in order to provide mothers milk rich in fat content during lactation.	
Female reproductive condition: Multiple variables are involved in female reproductive capacity (Ellison 2008; Table 2.3.2b). Ovarian function responds sensitively to energetic deficits in relation to 1) fat stores, 2) energy balance and 3) energy flux (rate of energy turnover). Sufficiency of metabolic energy availability in respect of all three components is required and metabolic states of caloric deficiencies, anabolic-catabolic imbalances and obesity (impeded metabolic turnover rates) are likely to manifest through menstrual disruption (LT and OB body condition types thus particularly prone to associated dysfunctionalities). Thus, both ***high metabolic rate*** and ***anabolic*** metabolic processes in a state of dynamic balance are required for male and female body condition, but specifically so for female reproductive condition. Due to compromised functional efficiency (vitality) associated with accumulated patho-information-engram (PIE) loadings in populations subjected to transgenerational influences of Western civilization, adrenal insufficiency/fatigue has emerged as a prevailing subclinical condition (Table on protein digestion; Wilson 2014). This condition (resembling a state of chronic yang deficiency) places limitations on high metabolic rate functionality, an important component of reproductive condition. Wilson (2014) specifically emphasized that the treatment of this condition is unlikely to be successful on a vegetarian diet, but requires animal protein/fat and carbohydrates included together in meals. This follows from animal protein supporting high metabolic rates (yang energy). Refer to Table Integrated Paleo-diet, Table Efficient Protein Processing/Digestion **(2.3.1.3a)** and Table	

Daily Intermittent Fasting on the central role of sustaining a dynamic anabolic-catabolic metabolic balance (especially for female LT and OB body condition types which are otherwise prone to menstrual dysfunction). Jasienska et al. (2006); Jasienska et al. (2004); Jasienska & Ellison (1998); Ziomkiewicz et al. (2008) ALSO GENDER COMPLEMETARITY	

c) Nutritional significance of dietary components

Macronutrient composition.

Animal-derived protein. The protein to non-protein energy intake ratio affects lifespan, total energy intake, metabolism, immunity and the risk of developing obesity and related metabolic disorders (Simpson & Raubenheimer 2009). In the context of the context of the Peri-Arctic diet-lifestyle an animal protein/fat and vegetable carbohydrate dietary combination is indicated. If the objective of a meal is to attain the anabolic effect of increased insulin to enhance recovery and muscle building, combining carbohydrates and proteins is indicated (Table 2.5.1.5e: PeriArctic-diet lifestyle). Higher protein ingestion leads to an increased level of satiety (Latner and Schwartz 1999); both a high protein lunch and a balanced lunch results in lower food intake at an evening meal than an equicaloric high carbohydrate lunch. These findings support other research demonstrating that protein reduced later food intake and self-reported hunger more so than carbohydrates (Latner and Schwartz 1999). Rabinovitz et al. (2013) demonstrated that a big breakfast rich in protein and fat, rather than a smaller carbohydrate-based breakfast, reduced hunger, improved satiety and measures of glycemic control. This should not be interpreted to favour an early breakfast, but supports the notion that the first meal (late breakfast) results in lower food intake at a subsequent meal (Latner and Schwartz 1999), under a daily intermittent fasting schedule (Table **2.5.1.5d**), if the macronutrient composition involves the combination of protein, fat and carbohydrates. Meat-carbohydrate combination supports body condition build-up: slows rate of digestion and improves digestion efficiency; an associated increased insulin response supports fat storage. In addition, Blom et al. (2006) also recorded slower rates of gastric emptying with relatively high protein contents of the meal (breakfast). These findings are consistent with those of Halton & Hu (2004) that relatively higher protein intakes promote satiety and reduced subsequent energy intake. Subject to these factors the total daily protein intake should be moderate (diminishing the risk of protein storage in basal membranes and associated diseases *re*

Wendt 1985) and protein digestion efficiency should be maximised (Table **2.5.1.3a**). This is also consistent with only moderate intakes of animal protein by THL populations (Section **2.5.1.2**). The role of animal-derived protein is furthermore placed in context by Milton (1999).

Milton (1999): Healthy humans are not known to derive any particular benefit from eating excessive amounts of protein (Speth & Spielman 1983; Speth 1989, op. cit. Milton 1999); indeed some evidence suggests that excessive protein consumption is unhealthy for humans (Lambert 1998, op. cit. Milton 1999; Karasov & Diamond 1985, op. cit. Milton 1999). Excessive protein consumption "idles" the body engine faster while producuing no demonstrably favourable metabolic effects (Nelson 1975, op. cit. Milton 1999). The metabolic costs of protein conversion to energy exceed those of converting carbohydrates and fat (Nelson 1975, op. cit. Milton 1999; Speth 1989, op. cit. Milton 1999). Howevrer, Milton (1999) states that the interpretation that the incorporation of animal matter into the diet played an absolutely essential role in human evolution. Animal protein not only provides all of amino acids humans require in the proper complements and proportions for human protein synthesis, but also is more efficiently digested than plant protein. We furthermore need to bear in mind that omnivores (and carnivores) do not eat only muscle tissue or only muscle and fat, but instead eat brains, viscera, bone marrow, the liver and other organs. Importantly, humans able to satisfy their total protein and much of their essential mineral and vitamin requirements with animal matter rather than plants would free space in their gut for energy-rich plant foods such as fruit, nuts, starchy roots, other plant parts or honey. Using animal matter primarily to satisfy requirements for essential nutrients and plant foods primarily for energy is a dietary strategy that is compatible with hominoid gut anatomy and digestive kinetics, as well as evidence from the human fossil and archeological record (Milton & Demment 1988, op. cit. Milton 1999).

A high quality diet involves more fat and meat (higher concentrations of nutrients and energy) and less plant material. Genes controlling fetal fat deposition needed to be expressed because fat deposits are needed as insurance for the developing brain (Cunnane & Crawford 2003). This required long-term stability in the maternal nutrient and energy supply during pregnancy and lactation.

Animal-based protein and fat: meat (including organ meat, fat) and milk products (fat-rich yoghurt, cheese, etc.). Much of the nutritional benefits in THL population of consuming meat was associated with them consuming all parts of the animal, notably also relying on its fat content. Bone broth. Ancestral and THL populations typically use(d) all parts of an animal: meat, organs, fat and gelatin made from tendon and cartilage material (Table 2.5.1.5f). Fat content of available meat is low (except of domesticated pig meat which should be avoided). Importance of animal-derived protein (Braverman et al. 2003: amino acids).

MACRONUTRIENT BALANCE MS SATIETY-holt; MS DIET-little; MS ENEGY DENSITY-rolls DL DIET-dairy protein MS DIET-acheson-protein

Fats. Fat provides for efficient energy intake with relatively low volumes. The capacity of the stomach-intestinal tract is limited and a high energy demand can only be satisfied through fat intake (*inter alia* op. cit. Wendt 1985).
Ben-Dor et al. (2011) addressed the question posed by Wrangham et al. (1999) 'If dietary consumption of animal protein and raw plant material is physiologically limited, how could *H. erectus* provide for his caloric requirements?' The need to consume animal fat is the result of the physiological ceiling on the consumption of protein and plant foods in omnivores (Wrangham et al. 1999). Consumption of animal fat is thus obligatory (Ben-Dor et al. 2011). Whereas a larger percentage of protein escapes digestion (Halton & Hu 2004), fat digestion is nearly complete, i.e. fat is a very efficient energy source. Ben-Dor et al. (2011) conclude that it is therefore not surprising that the most recent human genetic adaptations are to high starch (source of fat reserves) consumption, a component generally in short supply in the diet of our lineage during the Pleistocene.

Carbohydrates (energy-dense/nutrient-dense). The consumption of energy-dense carbohydrates is essential in order to build up fat reserves for optimal body condition. Body fat has numerous functions and its presence in thin-lean and normo-adaptive body condition types (Table **2.5.1.5c**) is associated with adequate body condition; it is, *inter alia* necessary for the production of sex hormones, as insulation of vital organs and temperature regulation (Dirks & Leeuwenburgh 2006). Adequate body fat reserves are crucial for reproductive condition (Table 2.3.2b). Loss of body fat and the associated decline of sex steroids can lead to loss of libido in both sexes, menstrual irregularities and infertility in females (Dirks & Leeuwenburgh 2006). The demand for fat-derived energy (based on carbohydrate intake) is not only driven by physical activity, but generally high metabolic rate-supported processes such as intensity of brain work and the need for ketone energy derived from fat stores (costly brain functional processes, notably also during the night). REF Protein and fat intake provide for immediate energy for high turnover metabolic processes, whereas carbohydrates provide the substrate for building of body condition, involving some fat storage. The latter is of special

importance for female reproductive success, which is dependant on a level of fat storage above a certain threshold, especially also on the metabolic capacity to build up sufficient fat reserves during pregnancy (). For both males and females fat storage provides a source of ketones during intermittent fasting periods, notably during sleep; as well as for thermoregulation during cold periods of the year.

Body condition/storage and net base producing diets. CH content for body condition and dietary net base load in combination with animal-derived protein proportion (30%). Sebastian et al. (2002): It is the combined effect of substituting cereal grains and nutrient poor dietary components (refined foods) with non-grain plant foods that can account for the transition from a net acid to a net base-producing modern diet. Sebastian et al. (2002) emphasize that, for the contempory diet, the net base-producing effect of replacing both cereal grains and nutrient-poor foods with non-grain plant food items (nutrient-dense carbohydrates) could be achieved without changing the proportional content of the acid-producing animal foods in the diet (meat, cheese, milk, yogurt, eggs). That means a net base producing diet can be achieved, yet including a considerable component of animal-derived protein. Especially for skinny/lean body condition types (Table): Net base-producing diet: Kraut & Madias (2016) ACIDOSIS Kidneys. Kraut (2011) MS: ACIDOSIS-kidneys ACIDOSIS ACIDsebastian Plaskett (2003)

MS GUT-russell-high protein on the importance of CH for a healthy intestinal microflora

Fiber. DL H20-regulation of body weight; DL H65-text re fiber: the reduction in mean peak rise in blood glucose concentration for each substance correlated positively with delay in mouth-to-caecum transit time. Vicous types of dietary fiber are therefore most likely to be therapeutically useful in modifying postprandial hyperglycemia (Jenkins et al. 1978). McCay et al. (1935, op. cit. Sinclair 2005) found that feeding rats with 20 % indigestible cellulose substantially extended mean and maximum lifespan.

H65dietary fiber
FIBRE-king

d) Maintenance of body condition in a feast-famine context.

Sympathetic-parasympathetic mode of functionality (TL; male versus female body condition requirements); sympathetic performance (under stress, competition, career,) versus body condition build-up requiring to be in parasympathetic mode (stress-free, effective digestion, storage of nutrient resources, notably fat storage for female reproductive success). Mg for parasympathetic state, anti-stress, sleep
Stress (Mg, rest, good quality sleep, Ca-Mg balance and nutrient storage)
Macro-nutrient diet composition (P-CH combination)
Proper (protein) digestion: Table on efficient protein digestion, bone broth, absence of over-eating per meal (fat component)
Adrenal fatigue-catalysm
Incorporate above YELLOW

Loy et al. (2017) DIET-NIGHT FAST-loy- 2017
Not to be confused with alternate day fasting.
Kahleova et al. (2017) IDF-BREAKFAST-kahleova-2017

INTEGRATE INTO TABLE BELOW Halberg et al. (2005): Study subjects maintained their body weight and percentage fat throughout the intermittent fasting intervention period by eating abundantly every other day. Intermittant fasting increased insulin sensitivity on the whole body level and that of adipose tissue. These findings support the view that regular cycles of feast and famine as inducer of thrifty gene expression (Chakravarthy et al. 2004) are important for improved metabolic function. Referring to alternate day fasting, Anson et al. (2003) implicate alternating periods of anabolism and catabolism as playing a mechanistic role in triggering increases in cellular stress resistance and the repair of biomolecules and cells resulting from a cellular stress response induced by the fasted state. During phases of limited carbohydrate supply, ß-hydroxybutyrate levels increase in various tissues, including the brain. Mice on the intermittent fasting regime (but sustained calorie intake), rather than those on a daily lowered calorie intake, had larger adipose reserves and a greater ketonic response (ketones are products of fat breakdown for energy). Ketogenesis and ß-hydroxybutyrate have been identified as cytoprotective/neuroprotective in rodent models; supporting the notion that intermittent fasting can enhance health (Anson et al. 2003).
DL BRAIN-mattson

Table 2.5.1.5d Daily Intermittent Fasting (Daily rhythm *re* Traditional Healthy Living populations (2.5.1.2), Maimonides op. cit. Herschlag 2015)
Expansion of the overnight fasting period, by beginning it earlier and ending it later, represents daily intermittent fasting, yielding decisive health benefits. It is healthy to have breakfast three up to six hours after waking (taken to take place at 6:00 h) and not to ingest anything but water three to four hours before bedtime, say at around 21-22:00 h (*inter alia* Maimonides ex Hershlag 2015). First meal (late breakfast): 10:00, 11:00 or 12:00 h and second meal (early dinner): at 16:00, 17:00 or 18:00 h. Leaving fasting periods of between 13 and 15 hours and 11 to 9 hours for food processing. **The here recommended daily intermittent fasting schedule (Table 2.5.1.5e): First meal at 10:00 h, lunch at 13-14 h and a light evening meal at 17:00 h; providing for a daily period between the last (evening meal) and the first/late breakfast the next day of 17 hours.** Hershlag (2015) emphasises the importance of gradually adapting from a schedule of early breakfasts and late dinners to that of daily intermittent fasting. Physical activity before meals, followed by rest after meals, as also practised by traditional healthy living populations (Section 2.5.1.2).
THL populations (Section **2.5.1.1**) experience various forms of intermittent fasting, either voluntarily or involuntarily. The daily rhythm of some resemble daily intermittent fasting. Wendt 1985
Intermittant fasting versus extended fasting
The morning snack should be limited in size and should not contain any carbohydrates (consist of one egg and half a cup of bone broth) since such, particularly in combination with proteins induce an insulin response which should be avoided during the circadian phase of rising cortisol levels. Protein/carbohydrate mixed meals (regarding the two main meals, especially the first one) are however important for the maintenance of body condition under a regimen of daily intermittent fasting and the associated reduced daily calorie intake (in alignment with body condition types). The mixed meal (protein and carbohydrates) is understood by the body as a time of plenty, a time to store fuel in its most economical form, namely fat. The extra insulin derived from the mixed meal blocks the breakdown of fat and causes the deposition of more (Phillipson 1997).
If to be successful, daily intermittent fasting must establish alternate states of relatively extended autophagous functionality and peak metabolic performance within the same diurnal cycle of 24 hours. A dynamic anabolic-catabolic balance must prevail, but with pronounced amplitudes of functionality at low (extended nocturnal phase) and high metabolic rates (shorter daylight phase). In order to achieve both anabolic-catabolic balance and phase pulsatility of metabolic performance, a metabolism in yang-yin balance must be supported. **This requires that both meals include animal-based protein for yang energy (raised metabolic rate) and carbohydrates/fat as energy sources for effective protein digestion and modulating the anabolism-catabolism balance**. The first meal should be the more important one; notably including a protein-carbohydrate combination for optimal body condition build-up. This approach should also support a sufficiently high

metabolic turnover required for pulsatility of metabolic responses, such as the adequate emergence of hunger before meals (especially the first, bigger of the two meals); an indication that efficient digestion can be expected.

1. **Avoidance of concurrently high levels of cortisol and insulin**
   Cortisol (raising blood sugar levels; inducing catabolic processes; releasing stored fats) and insulin (lowering blood sugar levels; directs fat metabolism towards fat storage from carbohydrates, an anabolic process) are functionally antagonistic. Circadian cortisol levels are at their highest at 8:00-9:00 h (lowest levels at about midnight; Chan & Debono 2010) and when an early breakfast is then eaten, the insulin secreted in order to lower raised sugar levels from the breakfast is then partly ineffective as a result of the countereffects of cortisol (insulin resistance). High amounts of insulin will then be released to lower blood sugar levels (Hershlag 2015). In agreement with this we find that the insulin response is higher in the morning (higher cortisol levels) than in the afternoon (Jakubowicz et al., op. cit. Hershlag 2015). When blood sugar levels decrease to low levels after a meal, hormones such as adrenaline, glucagon and cortisol will be released in order to again raise blood sugar levels. Continued daily early breakfasts result in chronically high levels of adrenaline, glucagon and cortisol, counteracting high levels of insulin and becoming toxic to the body. This results in various health risks (e.g. hyperinsulinemia, **metabolic syndrome**: Walker 2006), including an increase in the number of fat cells (Hauner et al. 1987).
   It appears that insulin resistence may be associated with a state of secondary cortisol resistance: overall relatively high cortisol levels, but low cortisol sensitivity and reduced amplitude of circadian cortisol rhythmicity. This is expected to favour predominance of functionality of the nervous system in sympathetic mode, which is not conducive to efficient digestion and nocturnal autophagy which require functioning in the parasympathetic state (for *inter alia* efficient protein digestion which is of crucial importance *vide* Wendt 1985).

   In summary, this state of insulin/cortisol resistance impedes anabolic and catabolic metabolic processes and compromizes self-healing mechanisms of the body; also rendering self-healing support measures (such as therapeutic supplementation) partially or completely ineffective.

   Healthy physiological and self-healing processes are typically pulsatile with pronounced amplitude and daily intermittent fasting promotes leeway for this to occur.

2. **Enabling efficient burning of fat**
   According to the natural hormonal daily cycle of fat-burning, appropriate fat-burning hormones induce ketone production at night during sleep when energy directly available from food in the intestinal tract is lacking. Associated daily fat-burning metabolic processes are extended when following a daily intermittent fasting schedule. Ketosis is a metabolic state when the body uses fat as fuel in preference to glucose (directly derived from carbohydrates and sugar). The body makes ketones from fat when dietary

glucose is low (Cunnane and Crawford 2003). Ketosis through long daily fasting episodes and associated autophagy promotes positive health benefits. Autophagy seems to mediate some neuroprotective benefits of ketogenic diets (McCarty et al. 2015).

3. **Cleansing the body of toxins and avoiding harmful effects of bad digestion**
   When the digestive tract is resting, detoxifying processes take place and become more effective as the lengh of the fasting/resting period increases. The main benefits of detoxification are achieved during the last three to four hours of the daily overnight fast of 14-16 hours (Hershlag 2015). Sleep inhibits digestion and residual food from a late evening meal is not digested effectively; resulting in toxic reactions and gases (Hershlag 2015; Rauch 1986).
4. **Increased deep sleep and HGH secretion**
   Digestion disturbes sleep and associated revitalising processes dependent on deep sleep, such as *inter alia* maximum human growth hormone (HGH) secretion, are inhibited. Other functions (Table on sleep). Avoiding inhibition of HGH by avoiding insulin secretion at night. Late-night meals, which include carbohydrates, result in insulin secretion which inhibits HGH secretion.
5. **Counteracts the development of hyperinsulinemia**
   Mice fed a high-fat *time-restricted diet*, as opposed those fed a high-fat *ad lib* diet (disruption of the normal feeding cycle), were protected against obesity, hyperinsulinemia, hepatic steatosis and inflammation (Hatori et al. 2012).

6. **Assisting in limiting caloric intake**
   Chronic calorie reduction is associated with a feeling of hunger, whereas reduced appetite becomes habituated with daily intermittent fasting (Hershlag 2015).

   Refer to Section 2.5.1.4

Caloric restriction is considered the most potent autophagy inducer and is accepted as lifespan extending and health-promoting; counteracting processes of ageing (Rubinsztein er al. 2011).

Dietary restriction has been found to have health benefits (Willcox et al. 2006; Willcox et al. 2007a,b). Studies have also shown that caloric restriction delays the onset and slows the rate of progression of age-related diseases such as diabetes, cardiovascular diseases and neoplasia (Chiarpotto et al., 2006) Dehydroepiandrosterone sulfate (DHEAS) levels (as biomarker for primate aging) decline with age and calorie restriction slows the post-maturational decline in serum DHEAS levels (Lane et al. 1997). According to Mattson (2003) dietary restriction induces a mild cellular stress response in neurons as a result of its effects on energy availability and activity in neural circuits. Neurons respond to this stress by increasing the production of proteins that enhance cellular stress resistance, such as neurotrophic factors, protein chaperones (such as heat-shock proteins) and anti-apoptotic proteins. Peripheral effects of dietary restriction may also benefit the brain: enhanced

insulin sensitivity, decreased homocysteine levels, prevention of age-related damage to cerebral blood vessels; may also have beneficial effects on neurons and glia.

Hatori et al. (2012): Mice, under time-restricted feeding (8 hours/day), but consuming equivalent calories than mice feeding on a high-fat diet *ad lib* (food availability throughout day) were protected against obesity, hyperinsulinemia, hepatic steatosis, inflammation and exhibited improved coordination. The temporal spreading of the calorie intake seemed to be of importance since the mice fed the diet *ad lib* perturbed the metabolic pathways entrained by circadian and feeding rhythms; predisposing the organism to obesity and metabolic diseases. The time-restricted feeding regime entrained the circadian clock and metabolic regulators to fixed feeding times and prevented the high-fat/high calorie induced disruption of the normal cellular metabolic program (as genetically determined). **It is concluded that intermittent states of fasting often associated with dietary reduction are responsible for health benefits rather than calorie restriction *per se*.**

7. Facilitation of autophagy

Caloric restriction is considered the most potent autophagy inducer and is accepted as lifespan extending and health-promoting; counteracting processes of ageing (Rubinsztein er al. 2011).

Autophagy is a crucial mechanism for the clearance of damaged cells (notably oxidatively damaged cells) and otherwise damaged or worn-out macromolecules and organelles (Terman 2006). Refer also to **Section 2.1.2: Fasting**. Anti-aging strategies would accordingly also involve the stimulation of cellular degradation systems, including different forms of autophagy, proteasomes and cytosolic/mitochondrial proteases (Terman 2006). (Bergamini et al., 2007): Similar beneficial anti-aging effects in terms of median and maximum life span of caloric restriction were observed for animals on 40 % reduced or on every-other-day *ad libitum* feeding. In both cases animals were forced to experience effectively long time periods in a state of fasting and activated autophagy. Mizushima et al. (2008): Autophagy counteracts disease states through cellular self-digestion and autophagic dysfunction is associated with cancer, neurodegeneration, microbial infection and ageing. Masiero et al. (2009: Autophagy is required to maintain muscle mass): The persistence of dysfunctional organelles in muscle tissue activates catabolic pathways, leading to muscle deterioration. Maintaining an autophagous flux is necessary to rejuvenate organelles by preventing the accumulation of dysfunctional mitochondria and preventing excessive protein breakdown.

Cuervo et al. (2005): Dysfunction of the autophagic system with age is interactively linked to a decrease in turnover of cellular components and intracellular accumulation of altered macromolecules and organelles. The consequences of dysfunction of the autophagic system with age (as associated with damage to proteins, especially oxidative damage, impairment of cell and tissue functioning; accumulation of extralysosomal waste: damaged mitochondria and cytosolic protein aggregates, and of intralysomal waste) are at least partially counteracted by phases of calorie restriction

(fasting induced autophagy). The findings of Alirezaei et al. (2010) suggest that upregulation of autophagy by food restriction may be neuroprotective. However, chronic starvation can inhibit autophagy and be damaging rather than protective in respect of neurons (op. cit. Alirezaei et al., 2010). Autophagy is furthermore also expected to remove pathological protein deposits in basal membranes (*vide* Wendt 1985).
With daily intermittent fasting a high amplitude anabolism-catabolism rhythm for full expression of alternating building of body condition and autophagy, on a daily basis, is pursued; as also practised by most THL populations (Section 2.5.1.2). Current/daily procursive impacts are more efficiently neutralized on a daily basis; preventing/minimizing a build-up of the patho-information-engramm load and facilitating precursive healing.

Based on long-standing medical practice and personal experience, Wendt (1985) recommended a lifestyle basically resembling that of intermittent fasting: two meals per day (no breakfast), the first meal at noon after a strong feeling of hunger is being experienced and a lighter evening meal. Resting of between one half to one hour after the first meal is obligatory. A strong hunger impulse especially before the first meal is of great importance since only then can the digestive processes effectively cater for both anabolic and catabolic metabolic functionality.

Bracht (2018) summarized the healing functions of daily intermittent fasting:

- Activation of cell repair molecules called sirtuins. 27
- Down-regulation of over-activated growth-activators. This is longevity promotive as the body initiates a self-healing program. 21
- Counteraction against chronic inflammatory processes; healing of underlying causes and thereby inhibiting destructive biochemical processes. 31
- Old protein deposits are recycled and made available to the body in the form of amino acids for use as new building material. 23
- Irreparably damaged cells are induced towards cell death by ketones produced during the fasting metabolism. 24-27 Ketone bodies are fatty acid molecules produced through the breakdown of fat reserves. Energy production with ketone bodies requires relatively less oxygen than that from glucose, resulting in less ROS production. After about twelve hours of fasting, fat breakdown is initiated (notably of abdominal fat) and fat is converted into ketones. Ketones typically act as energy source in times of hunger or starvation. They ensure energy availability to the heart, brain and other vital organs. Ketones activate nerve

cells, thinking capacities and the formation of new brain cells. In conjunction, neurotransmitters, notably serotonin, are produced. Good functionality of the serotonergic system supports psychological well-being (p 79)

Ketones

CR-KETONES
Kirkwood & Shanley (2005) CR-evolution-kirkwood

DL KETONES-rho
DL KETONES-masino **revisit**
DL KETONES-thio-NB-metabolism
DL KETONES-bergquist
DL KETONES-miranda
DL KETONES-prins

Serotonergic system p 79

e) From Paleolithic to Neolithic-PeriArctic nutrition

Milton (2000): PRINTED REF p 345 2513 a?

Many of the chronic metabolic diseases currently prevalent in the industrialized world are attributed to be result of a way of life that is mismatched to human evolutionary history; and it was suggested that the Paleolithic diet should serve as a reference standard for modern human nutrition (2.5.1.4a). According to the underlying mismatch hypothesis, the notion of a single type of ancestral diet was introduced; based on an assumed mismatch between our evolved physiology and modern environments which had arisen at the boundary between the Paleolithic and Neolithic eras with the introduction of agriculture. However, as noted by Turner and Thomson (2013), variation in ancestral diets has been implicated for some time to be more than just a function of hunting-gathering versus agriculture; but also a function of geography, food availability, seasonality and climatic conditions.

Turner and Thomson (2013): In their seminal paper Eaton & Konner (1985), first posited that many of the chronic metabolic diseases now prevalent in the industrialzed

world result from a way of life that is mismatched to human evolutionary history.They suggested that the “Paleolithic diet”, an ancestral diet characterized by higher protein, less total fat, more essential fatty acids, lower sodium, and higher fiber, should serve as a reference standard for modern human nutrition. More recent mismatch studies have modelled differential nutritional outcomes of modern versus non-agricultural populations related to specific macro- (Cordain etal. 2001, op. cit. Turner and Thomson 2013: fatty acids; Eaton 1990, op. cit. Turner and Thomson 2013: fibre; Eaton 1992, op. cit. Turner and Thomson 2013: lipids) and micronutrients (Eaton 1991, op. cit. Turner and Thomson 2013: calcium) and factors such as net dietary acidity (Sebastian et al. 2003, op. cit. Turner and Thomson 2013), diet breadth (Bogin 1998, op. cit. Turner and Thomson 2013; Turner et al. 2008, op. cit. Turner and Thomson 2013), seasonality, physical activity (Chakravarthy et al. 2003, op. cit. Turner and Thomson 2013; Cordain et al. 1998, op. cit. Turner and Thomson 2013) and the production of toxic byproducts by cell mitochondria (Wallace 2005). Under the mismatch paradigm, explanations for the dramatic increase in obesity and diabetes are attributed to populations adopting Westernized diets and lifestyles (Lieberman 2003, op. cit. Turner and Thomson 2013); as emerging research demonstrated that restricting refined carbohydrates and dairy products and emphazing vegetables and lean proteins leads to reductions in fat mass, serum cholesterol and circulating glucose levels (Frassetto et al. 2009; Lindeberg et al., op. cit. Turner and Thomson 2013). However, the evolutionary discordance model centers on the assumption that “our current gene pool is hardly changed from that of Stone Age humans” (Eaton & Cordain 1997, op. cit. Turner and Thomson 2013; Sebastian et al. 2002) and that “genetically, man remains adapted for the foods consumed during the Paleolithic” (Eaton 2006, op. cit. Turner and Thomson 2013), which has led to a “dissociation between our genes and our lives” (Eaton et al. 2002, op. cit. Turner and Thomson 2013). This perspective fuels perceptions that: I) the diet of the evolutionary past (EEA: environments of evolutionary adaptation) was more or less universal, II) the microevolutionary changes of the past twelve millennia were not sufficiently significantor adaptive to outweigh traits originating in the Paleolithic, and III) human dietary behaviour is determined primarily through instinctual and/or genetic mechanisms. All three of these assumptions are problematic. Proponents of the mismatch hypothesis rely on the idea of a single type of ancestral diet and place the mismatch between our evolved physiology and modern environments at the boundary between the Paleolithic and Neolithic eras with the introduction of agriculture. However, variation in ancestral diets has been thought for some time to be more than just a function of hunting-gathering versus agriculture; but also a function of geography, food availability, seasonality and climatic conditions (Casimir 1991, op. cit. Turner and Thomson 2013; Leonard et al. 2010, op. cit. Turner and Thomson 2013; Ungar 2007, op. cit. Turner and Thomson 2013; Ungar 2006, op. cit. Turner and Thomson 2013; Ungar 2011, op. cit. Turner and Thomson 2013). Growing evidence further indicates that agricultural diets are not as easily associated with “diseases of civilization” as first thought. For example, the mismatch hypothesis assumes that prior to cultivation, hunter-gatherers obtained very few of their carbohydrates from cereal grains (Eaton & Konner 1985, op. cit. Turner and Thomson 2013; Konner & Eaton 2010, op. cit. Turner and Thomson 2013); and, because carbohydrates from fruits and vegetables are somehow better than hose from grains, were less likely to suffer from cardiometabolic diseases such as obesity, T2DM and cardiovascular disease (Elton 2008, op. cit. Turner and Thomson 2013). Modern hunter-gatherers and horticulturalists, however, have a wide range of carbohydrate intakes (Milton 2000; Ströhle & Hahn 2011); and even those relying on single cultivars high in carbohydrates

remain free from many of the “diseases of civilization”. Recent studies reveal that humans have continued to evolve well into the Neolithic period, perhaps even at accelerated ratesrelative to those of the Paleolithic (Hawks et al. 2007, op. cit. Turner and Thomson 2013). The most important of these evolutionary changes are directly tied to changes to diet and subsistence (Rolls et al. 1981, op. cit. Turner and Thomson 2013); including variation in the number of genes that for amylase production depending on starch consumption (Perry et al. 2007, op. cit. Turner and Thomson 2013) and the parallel evolution of lactase persistence in ancestral pastoral populations (Holden & Mace 1997, op. cit. Turner and Thomson 2013; Tishkoff et al. 2007, op. cit. Turner and Thomson 2013; Itan et al.2010, op. cit. Turner and Thomson 2013).

Four food groups can be differentiated: meat/fish, vegetables/fruit, cereal grains/breads and milk/milk products. According to Cordain (2011; Table 2.5.1.5b), nutritional requirements of adults during pre-agricultural times were primarily satisfied from the first two groups; whereas in modern diets, components from the latter two food groups predominate. This was considered to result in negative health outcomes (2.5.1.4a); but refer to a corrective perspective by Turner and Thomson (2013).

Regional health-sustaining diets of THL populations of the peri-arctic realm: Burusho tribes (including Hunza; Table 2.5.1.2a: Kafiristan in Afghanistan/Pakistan), of Abkhasia and Georgia (upper Greater Caucasus: Table 2.5.1.2b), the traditional Bulgarian diet/lifestyle (Table 2.5.1.2b), the traditional Mediterranean diet/lifestyle (Ikaria, Greece; Sardinia, Italy: Table 2.5.1.2b; Ratjen et al. 2017) and the Nordic diet (Bere & Brug 2008; Olsen et al. 2011) all involve whole grain and dairy products as health-supporting components; in addition to foods in the meat/fish and vegetable/fruit groups. The diets thus substantially involve ingredients from all four main food groups (meat/fish; vegetables/fruit; grains/bread and milk/milk products). The same also applies to subtropical-high altitudinal tropical THL populations (Table 2.5.1.2c: Okinawa Island, Japan; Nicoya, Costa Rica: Vilcabamba, Ecuadorian Andes).

Ratjen et al. (2017): Two post-diagnostic diets of long-term colorectal cancer survivors were investigated as to their effcts on all-cause mortality. The two diets involved, a modified Mediterranean diet (beneficial components: vegetables, fruit, nuts, legumes, cereals and fish; also the ratio of unsaturated to saturated lipids) and a healthy Nordic diet (originally developed by Olsen et al. 2011: based on cabbage, root vegetables, whole grain/rye bread, oats, apples and pears, fish and shell fish). Adherence indices regarding the dietary components were developed; and for both diet types; and an inverse association was found between adherence and all-cause mortality.
Across the Mediterranean a wide variety of diets is present, but the health-enhancing Mediterranean diet includes olive oil, fruits, vegetables, grains (mostly unrefined),

fish, dairy in moderate amounts, low quantities of meat and meat products, and a regular but moderate intake of alcohol (Trichopoulou et al. 2003, op. cit. Bere & Brug 2008).

Bere & Brug (2008): Most of the top determinants of the burden of disease are diet related (Ezzati et al. 2002, op. cit. Bere & Brug 2008). Nutrients do not function in an isolated manner, but interact with other nutrients and food components. Based on two recent reviews, for example, reported no clear effect of supplementation with antioxidants (Bjelakovic et al. 2007, op. cit. Bere & Brug 2008) or n-3 fatty acids (Hooper et al. 2006, op. cit. Bere & Brug 2008) on mortality; and it is considered probable that it is whole foods (e.g. fruits, vegetables, fish) and dietary patterns, rather than specific nutrients, that are inversely related with disease risks. Generally, in most countries four or five food groups are recognized that contribute to a balanced healthful diet: i) bread, rice, cereals and other foods rich in starch; ii) fruits and vegetables; iii) dairy products; iv) meat, fish and alternatives; and v) oils and fats. Regional diets provide climate-, soil- and culturally appropriate ingredients for health-enhancing eating in present-day societies.
Bere & Brug (2008) presented a regional health-enhancing Nordic diet tailored to regional circumstances; including the following ingredients: i) native berries; ii) cabbage; iii) native fish and other seafoods; iv) wild (and pasture-fed) land-based animals; v) rape seed oil; and vi) oat/barley/rye.
Ingredient 1: Native berries. In a Norwegian study assessing concentrations in 124 plant foods, berries were identified as the plant foods with some of the highest levels of total antioxidants (Halvorsen et al. 2002, op. cit. Bere & Brug 2008). A recent study showed that three wild berries (blueberries, clodberries, cowberries) also contain significant amounts of omega-3 fatty acids (in the same amounts as found in fish), when measured per unit of energy; and more than fifteen times greater than levels found in the three most commonlty eaten fruits (Bere 2007, op. cit. Bere & Brug 2008).
Ingredient 2: Cabbage. Cabbage, kale, broccoli, cauliflower, and Brussels sprouts are all varieties of the same species (wild cabbage, *Brassica oleracea*) and have been included in Nordic diets for a long time. They thrive in cold climates. Together with other close relatives, such as rutabaga, turnip, radish, rape and mustard, cabbage belongs to the group of cruciferous vegetables. Cruciferous vegetables are known for their probable cancer-preventing effects (Murillo & Mehta 2001, op. cit. Bere & Brug 2008). Cabbage is a very good sorce of vitamin K (Bolton-Smith et al.2002, op. cit. Bere & Brug 2008) and contains ample amounts of omega-3 fatty acids (Ayaz et al. 2006, op. cit. Bere & Brug 2008).Some types (kale, red cabbage, Brussels sprouts) contain more antioxidants than most other vegetables (Halvorsen et al. 2002, op. cit. Bere & Brug 2008). Several of the cruciferous vegetables are also considered among the dark, green leafy vegetables which are known as excellent sources fibre, folate and a wide range of carotenoids.
Ingredient 3: Native fish and other seafood. Sea food, especially fatty fish is regarded as healthy food, largely because of its content of essential fatty acids (especially long-chain omega-3 fatty acids such as EPA and DHA) and as dietary source of vitamin D, selenium, iodine, as well as protein and vitamin B_{12}.
Ingredient 4: Wild and pasture-fed land-based animals. Several soecies are hunted for their meat: moose, deer species, hare, birds like goose, duck and grouse. The fatty acid composition in wild animals is better in that it has more polyunsaturated fatty

acids (PUFA) and relatively less saturated fatty acids(SFA); and pasture-fed meat has a fat content and fatty acid profile in between wild and feedlot-fed meat (Cordain et al. 2002, op. cit. Bere & Brug 2008).
Ingredient 5: Rapeseed oil. Rape (*Brassica napus*) is a cruciferous vegetable. In rapeseed oil, as in olive oil, the majority of the fatty acids are monounsaturated. Also, rapeseed oil contains more PUFA and especially more omega-3 fatty acids than olive oil, and it has a more favourable n-3/n-6 ratio. Rapeseed oil accordingly possesses a better fatty acid profile than most edible oils and fats.
Ingredient 6: Oat/barley/rye. Oat, barley and rye all grow better in a cold climate than wheat (Norwegian Agricultural Authority 2007, op. cit. Bere & Brug 2008). Oat, barley and rye are more often eaten as whole grains and therefore tend to have a lower glycemic index (Foster-Powell et al. 2002, op. cit. Bere & Brug 2008). Compared with wheat, oat/barley/rye contain more antioxidants, more ß-glucans and less gluten.

Refer to sections 2.5.1.3e in respect of grains (Slavin 2004; authors) and 2.5.1.3f regarding dairy products (authors).

Olsen et al. (2011): The negative health impact of several of the food items characterizing the modern Nordic/Western diet are well proven and a general/traditional Nordic dietary pattern (Slimani et al. 2002, op. cit. Olsen et al. 2011) is therfore generally not considered to be positivrely related to health outcomes. The Nordic climate restricts crop diversityand pant food such as berries, cabbages, apples, pears, root vegetables, oats and rye thive, and long coastlines provide rich sources of fish (Bere & Brug 2009, op. cit. Olsen et al. 2011). These traditional foods have all been ascribed bebneficial health effects (Boyer & Liu 2004, op. cit. Olsen et al. 2011: apple phytochemicals; Mozaffarian & Rimm 2006, op. cit. Olsen et al. 2011: fish; Higdon et al. 2007, op. cit. Olsen et al. 2011: cruciferan vegetables; Yashodhara et al. 2009, op. cit. Olsen et al. 2011: omega-3 fatty acids; Flint et al. 2009, op. cit. Olsen et al. 2011: whole grains; Darby et al. 2001, op. cit. Olsen et al. 2011). A healthy Nordic food index, consisting of items with expected health-promoting effects (fish, cabbage, rye bread, oatmeal, apples and pears, root vegetables was extracted and associated with mortality by Cox proportional hazard models in middle-aged (50-64 years) Danes. Significantly lower mortality rate ratios were associated with higher healthy Nordic index scores in both men and women. When the index componnts were evaluated separately, whole grain rye bread intake was the factor most consistently associated with lower mortality in men, cabbages for both men and women and root vegetables in women.
Fish is a main source of omega-3 fatty acids that have been related to lower incidence of heart disease (Hu &Willett 2002, op. cit. Olsen et al. 2011). Intake of whole grain cereals (both rye and oats) are broadly promotedfor preventive effects in respect of heart diseaseand type 2 diabetes, but also cancer (Flint et al. 2009, op. cit. Olsen et al. 2011; Murtaugh et al 2003, op. cit. Olsen et al. 2011; Haas et al. 2009, op. cit. Olsen et al. 2011). As fruits, apples and pears are part of this proven healthy food group; and cabbages are part of an equally important food group of vegetables (Koushik et al. 2007, op. cit. Olsen et al. 2011; Mente et al. 2009, op. cit. Olsen et al. 2011). Root vegetables, especially carrots, have been discussed for their ß-carotene content (Darby et al. 2001, op. cit. Olsen et al. 2011). Two of the foods, whole grain rye bread and cabbages, can be considered among the healthiest food items within their respective

food groups. Whole grain rye potentially holds even more positive effects than other whole grain cereals, as has been shown with regard to inhibition of the late postprandial decrease in blood glucose and tumor inhibition in prostate cancer (Bylund et al. 2003, op. cit. Olsen et al. 2011; Kallio et al. 2008, op. cit. Olsen et al. 2011; Wikstrom et al. 2005, op. cit. Olsen et al. 2011). With regard to cabbages, their content of isoyhiocyanides and inducing effects on the phase II-detoxifying systems have been of great interest (Higdon et al. 2007, op. cit. Olsen et al. 2011). Traditional Nordic berries, such as cloud beries, blue berries and cowberries are known to contain substantial amounts (n-3) fatty acids (Bere 2007).

In terms of macronutient composition, three fundamentally different diets can be distinguished: low carbohydrate-high protein (the classical PALEO-diet: Table 2.5.1.5b: Cordain 2011; the Banting-diet: Noakes et al. 2014), low protein-high carbohydrate (Intervallfasten: Bracht 2018) and high protein-high carbohydrate combination (PeriArctic Diet-Lifestyle: Table 2.5.1.5e below).

A health-sustaining lifestyle, however, involves various components: an appropriate diet, embedded in a fasting schedule, sufficient exercise and rest periods.

The **PeriArctic Diet-Lifestyle** here developed represents a form of diet involving selected principles and components of the original PALEO-diet (2.5.1.5a: Cordain 2011: Table 2.5.1.5b) and adaptive Neolithic peri-arctic zone diets (this section: 2.5.1.5e), differentiation according to body condition types (Table 2.5.1.5c) and integration with a daily intermittent fasting schedule (Table 2.5.1.5d; 2.5.1.5d; 2.5.1.4) and other forms of fasting (2.1.2). This should not be confused with many (daily) interval fasting protocols available in the public domain which are mainly emphasising body weight loss and are associated with low carbohydrate diets (and thereby inappropriate for uninterrupted adherence). In contrast, the PeriArctic-diet-Lifestyle is geared to sustain amplitudinal daily phases of body condition maintenance/build-up (the daily eating phase) and self-healing (the daily fasting phase). As also protein deposition stores are accumulated during the building of body condition, such may need to be emptied/lowered periodically through bouts of protein fasting *vide* Wendt (1985; 2.1.2c) included in the annual dietary schedule. Such a dietary lifestyle resembles that of traditionally healthy living (THL) populations (2.5.1.2) for people inhabiting and adapted to the periarctic realm (Tables 2.5.1.1a, 2.5.1.2a and 2.5.1.2b). Effective recursive healing however requires additional forms of fasting to be included into the lifestyle (2.1.2; 2.1.3.3).

Table 2.5.1.5e PeriArctic Diet-Lifestyle

Life style components **for the establishment and maintenance of an energy use efficient EUE-PM metabolic mode** (2.2.2f; 2.5.1.4e/f)
Annual schedule:

- Meal timing and composition
    1) Three meal schedule within a daily restricted feeding period (c. 7 hours)
    2) Maintenance of daily anabolic/catabolic metabolic rhythm (meal composition: 2.5.1.4f)
    3) One or two days per week on food restriction (only lunch 500 kcal)
- As indicated, protein fasting events (3 months per annum: in separate months or adjoining two or three months *re* Wendt 1985). For the removal of heteroprotein deposits on basal membranes, protein fasting is insufficient (Wendt 1985), and forms of fasting involving autophagy is required (extended fasting).
- Extended fasting events (once c. 4 weeks per annum: Schrothkur-fasting or extended fasting: 2.1.2)

This schedule makes provision for CR stimuli effects in order to establish an **Efficient Energy Use metabolism** (2.5.1.4e); supporting health and vitality. Daily intermittent fasting (Table 2.5.1.5d), caloric restriction effects (2.5.1.4b), sirtuin food effects (2.5.1.4c) are involved. Daily time-restricted food intake potentiates circadian metabolic rhythmicity and autophagy (2.5.1.4f).

Fasting *versus* starvation effects (2.5.1.4a). Prolonged calorie restriction (CR) represents extended starvation which differs from shorter fasting bouts (time-restricted CR: e.g. daily intermittent fasting, day fasts, alternate day fasting) and extended full fasting in its physiological effects; and should be avoided. Short fasts incur CR-stimulus effects, thereby establishing states of CR-cued metabolism (2.5.1.4b). Time-restricted feeding/fasting regimes do not require a significant reduction in overall caloric intake in order to produce health benefits; indicating that the state of fasting as metabolic cue rather than the reduction in caloric intake is important in producing associated health benefits (Dirks & Leeuwenburgh 2006; 2.5.1.4b). Extended full fasting involves a switch in metabolic state characterized by the absence of hunger when autophagic self-healing processes then take effect (2.1.2c: Fasting); contrasting the situation during starvation where hunger sensations persist because of sufficient food intake preventing the metabolic shift into the fasting state. Prolonged CR resembles starvation where self-healing based on autophagy is no longer achieved (refer to Füllgrabe et al. 2014; 2.1.2d).

Maintence of healthy body condition: Maintenance of daily anabolic/catabolic rhythm. Catabolism. Chemical processes which result in the breakdown of more complex organic molecules. Harnassing of life-sustaining energy. Anabolism. Chemical processes in which simpler substances are combined to form more complex molecules. Anabolic reactions build new molecules/biochemical structures and/or store energy: storage of metabolic products, fat and non-fat. Caloric restriction facilitates catabolic states and self-healing through autophagy). Starvation: predominance of catabolic over anabolic metabolic stages resulting in diminishing body condition (to be avoided).

Daily schedule:
1) Breakfast: 10:00 h (Protein-carbohydrate combination, whole-grain carbohydrate component)
2) Lunch: 13 or 14 h (including sirtuin foods) 3) After-meal rest (30 min plus)
4) Lighter evening meal: 17:00h) 5) Sufficient daily exercise

I) Meal frequency, timing and composition (2.5.1.4f).

Meal frequency: A schedule of three meals within the eating period (10:00-17:00h) in order to capitalise on specific nutritional roles of meals at specific phases of the circadian metabolic rhythm (breakfast, lunch, dinner: 2.5.1.4f).
Meal timing: Breakfast facilitates a balanced, efficient metabolism (2.5.1.4f) and the evening meal supports energy (fat) storage and is thus of importance for body condition build-up, especially in females, notably of the TL (thin-lean body condition type: 2.5.1.5b); wheras evening meals should be reduced in obesogenic body condtion types. A balanced yang-yin energy-efficient metabolism is underpinned by consuming a breakfast (rising yang phase), a lunch (yang peak phase) and dinner (rising yin phase). Following Maciocia (1989), yang corresponds to creation and activity (intensity of metabolic processing), whereas yin corresponds to materialization (energy storage).
Meal composition: Considering the yin-yang balance of the meal and other considerations (this Table), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (including starch-rich, nutrient-dense and fiber-linked carbohydrates) is here recommended.
Breakfast. Considering the yin-yang balance of the meal (breakfast) and other considerations. (this Table), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (***mainly starch-rich and fiber-linked carbohydrates***: whole grains) is here recommended.
Lunch. Considering the yin-yang balance of the meal (lunch) and other considerations (this Table), a macronutrient composition of 30 % protein (meat and/or milk-derived), 15 % fat and 55 % carbohydrate content (including starch-rich, nutrient-dense and fiber-linked carbohydrates) is here recommended. ***Unlike for breakfast and dinner, nutrient-dense, fresh vegetables/fruit*** (*inter alia* ***sirtuin foods***) ***should form important meal components at lunch***. Efficient digestion requires peak yang metabolic performance as prevalent during this peak yang phase (and supported by the protein-yang component of the meal); and rest after lunch for efficient digestion in parasympathetic mode (of the Autonomous Nervous System). A post-lunch rest period of 30-60 minutes is thus indicated.
Dinner. Easily digestible high quality protein (dairy > meat-derived) and carbohydrates (starch-rich > vegetables) are relevant.

II) Protein-carbohydrate mixed meals.
Higher protein ingestion leads to an increased level of satiety (Latner and Schwartz 1999); both a high protein lunch and a balanced lunch results in lower food intake at an evening meal than an equicaloric high carbohydrate lunch. Halton & Hu (2004): Convincing evidence that a higher protein intake increases thermogenesis and ***satiety*** compared to diets of a lower protein content. High protein meals lead to a reduced subsequent energy intake, thereby facilitating reduced total calorie intake.

These findings support other research demonstrating that protein reduced later food intake and self-reported hunger more so than carbohydrates (Latner and Schwartz 1999). Protein/carbohydrate mixed meals are important for the maintenance of body condition under a regimen of daily intermittent fasting and the associated reduced daily calorie intake (in alignment with body condition types).

The mixed meal (protein and carbohydrates) is understood by the body as a time of plenty, a time to store fuel in its most economical form, namely fat. The extra insulin derived from the mixed meal blocks the breakdown of fat and causes the deposition of more (Phillipson 1997). Starchy carbohydrates are important for metabolic functionality supporting fat storage for appropriate body condition (especially

important for female reproductive condition; particularly so in the case of thin-lean TL-body condition types (Table 2.5.1.5c); and insuffiency of protein digestion associated with pathological high metabolic turnover acceleration).

III) Protein storage
Protein is also stored (Wendt 1985) and the associated purine metabolism supports enhanced metabolic turnover metabolism with uric acid as performance catalyst (2.2.1c). However, excess protein stores must be emptied periodically with protein fasting periods (2.1.2) in order to prevent disease states associated protein storage overload (Wendt 1985; 2.5.1.3b) and counter-regulatory blocking of further body condition build-up/maintenance. For those with an inherently compromised protein processing/digestion capacity, Wendt (1985) recommends eating meat (not referring to dairy products) only once a day and having one meat-free day per week (refer also to protein fasting: 2.1.2c) or alternatively insert protein fasting periods into the annual schedule (2.1.2).

4) Incorporating rest/sleep component is important for body condition build-up (parasympathetic efficiency of the autonomous nervous system: Table 2.3.2a); especially TL-females with a costly high metabolic turnover disbalance in TL body condition types (Table 2.5.1.5c).

Exercise. Physical activity on a daily basis is a core element of a healthy lifestyle, as manifested in traditionally healthy living (THL) populations (2.5.1.2).

IV) Macronutrient balance.

a) Macronutrient balance (on the basis of energy contribution): 30% protein 1g = 4 calories), 30 % fat: 1g = 9 calories), 40 % carbohydrates: 1g = 4 calories). In crudely quantitative terms this is taken to amount to a recommended macronutrient composition of **30 % protein**, **15 % fat** and **55 % carbohydrates**.

b) Protein
Sources: Meat (animal-derived, bone broth, cold water fish) and dairy products (fermented: yoghurt, sour milk, kefir, cheese).
Eating mode: restful eating with long, thorough chewing. To allow for the satiation reflex to occur at an appropriate stage of intake before the stomach is completely filled/overfilled. Improves digestion (Table). Adherence to the principles of efficient protein digestion (Table 2.5.1.3a: Efficient Metabolic Protein Processing/Digestion); with special emphasis on sufficiency of gastric acid levels (2.5.1.3a; Wright & Lenard 2001).

c) Carbohydrates (starch-rich, nutrient-dense and fiber-linked carbohydrates)
Starch-rich: whole-grains, root vegetables, cooked vegetables
Nutrient-dense fresh vegetables and fruit
Locally grown fresh green vegetables (press juice)

Cruciferous vegetables: cabbage, broccoli, cauliflower, brussels sprouts, radish, rape seed, kohlrabi, water cress, black and white mustard, brassica, perennial wall rocket, land cress.

Sirtuin foods (2.5.1.4c): Food/beverage items of notably high polyphenolic content: Cereals (barley, millet, sorghum, rye); legumes (black gram, chickpeas, cowpeas, common beans, green gram, pigeon peas; vegetables (onion, parsley, cabbage, kale,

cruciferous vegetables, rhubarb, yellow onion, curly kale, capsicum pepper, aubergine, capers); fruits (apple, blackcurrant, blueberry, blackberry, red grape, raspberry, strawberry, cherry, plum, persimmons, apricot); fruit juices (apple juice, orange juice, grape fruit juice); beverages (tea, green tea, coffee, red wine, white wine). Also, olive oil and chocolate.

d) Fats

Poly-unnsatured fatty acids (PUFA). Simopoulus (2006): Evidence from relevant studies of the diets of modern day hunter-gatherers and traditional diets indicate that humans evolved on a diet in which the ratio of omega-6/omega-3 essential fatty acids was ≈ 1, whereas in modern Western diets this ratio is around 15-16/1. A high omega-6 to omega-3 ratio promotes the pathogenesis of chronic conditions (cardiovascular disease, diabetes, cancer, obesity, autoimmune diseases, rheumatoid arthritis, asthma, osteoporosis, depression), whereas increased levels of omega-3 polyunsaturated fatty acids exert suppressive effects. The balance of omega-6 with omega-3 fatty acids is important for homeostasis and development. Dietary intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) decrease the risk for cardiovascular disease. Both omega-6 and omega-3 fatty acids influence gene expression. Many chronic diseases begin in utero or early infancy and adequate dietary intake of polyunsaturated fatty acids, even prior to pregnancy is considered important. Omega-3 fatty acids have anti-inflammatory effects (inflammation associated with many chronic diseases), wheras omega-6 fatty acids do not have such effects. Furthermore, a diet supplemented with omega-3 fatty acids with fish oil inhibited adrenal activation induced by mental stress, presumably by subduing sympatho-adrenal reactivity (). Main source: fish oil (Delarue et al. 2003). A balanced omega-3/omega-6 fatty acid dietary composition can only be obtained from ***animal and marine food resources*** (Cordain 1999).

Fat stores are the source of ketones. Bracht (2018): Ketone bodies are fatty acid molecules produced through the breakdown of fat reserves. After about twelve hours of fasting, fat breakdown is initiated (notably of abdominal fat) and fat is converted into ketones. Ketones typically act as energy source in times of hunger or starvation. They ensure energy availability to the heart, brain and other vital organs. Ketones activate nerve cells, thinking capacities and the formation of new brain cells. In conjunction, neurotransmitters, notably serotonin, are produced.

AS: Fett als Stoffwechselenergiequelle (Proteinverdauung); sodass Kohlehydrate als Fettreserven angelagert werden können (besonders wichtig für den weiblichen Stoffwechsel; Reproduktion).

V) Body condition types and diet

AS: Sufficient good quality carbohydrate content is required for anabolic condition build-up in both males and females, but especially for females where reproductive condition is dependant on and manifested in some fat storage. Generally, more of importance in skinny types/high metabolic rate than obesogenic types; but also for normo-adaptive body condition types.

Under an intermittent fasting schedule: higher CH intake, ensuring slow CH absorption, glutamine-BCAA (branched chain amino-acids: leucine, isoleucine, valine) supplementation

V) Fermentation

VI) Amino acids, vitamins and minerals

Further core considerations

1) **Nutrient dilution.** Modern, commercial agriculture pursues high productivity; which on the one hand, results in fast-growth cued nutritional food items partly due to fertilization, with induction of high metabolic turnover in consumers (Table 2.5.1.2e), thereby distorting LHS expression; and on the other hand, results in nutrient dilution (Vogtmann 1985: 2.5.1.2 IV) and compensatory bulk feeding. Low nutrient concentrations result in deficiencies of certain ntrients and compensatory bulk feeding (increased food intake in order to obtain suffiency of critical/limiting nutrients; cravings). It is thus advisable to source food items produced under growth rate curbing conditions (usually cold, arid or nutrient-stressed environments; as typically applicable in THL populations: 2.5.1.2); as far as practically possible.

2) **Minimize imported nutritional items** (especially from outside of the peri-artic realm). Fresh and locally grown (2.5.1.2 III Table 2.5.1.2d) The importance of fresh vegetables and fruit in the diet is generally accepted (Milton 2000) and locally grown in home-linked gardens provides for the ready availability of such food items in alignment with seasonal rhythmicity. Local rearing of domestic live stock is also practised. Biogenic information contained in such produce reflects *subtle organizing energy fields* (Table 2.5.1.2d: Life Force Model of Nutrition: Biogenic content of food *vide* Robinson 2012) arising from interactions of the food organisms with the local environment. An alignment of the genetic-epigenetic and biogenic information systems is accordingly sustained. Under genomic and environmental spatiotemporally sustained conditions, **transgenerational genetic-epigenetic alignment** with the environment (2.5.1.2 II: bio-cybernetic alignment; including biogenic information: Table 2.5.1.2d) is sustained, with survival advantages in specific geographic regions, as manifested in health and longevity of THL populations (Tables 2.5.1.2 abc).

3) **Sirtuin foods**

Sirtuin activity, as response to CR or sirtuin activating substances (STACs: plant polyphenols) optimises energy metabolism (energy homeostasis) in response to hormetic energy deficiency signals (2.5.1.4c**).**

Healthy-ageing benefits from Sirt1 activation by CR or polyphenolic CR mimetics are causally related to autophagy (Pallauf & Rimbach 2013). Thus, CR or polyphenols (hormetic energy deficiency signals/metabolism under stress: growth-curbed conditions) induce Sirtuin activation, thereby optimizing energy metabolism with the involvement of autophagy. SIRT1-activating compounds (STACs), such as polyphenols, are reported to activate the enzyme *in vitro* by lowering its Km (Michaelis constant). The lower the Km, the higher is the catalytic efficiency. Activated SIRT1 and the associated ***improvement in energy utilization*** and insulin sensitivity closely resembles the benefits of calorie restriction (Guarente 2013).

Environmental stress factors have a major effect on polyphenol content as many polyphenols are directly involved in the response of plants to different types of stress. Such stress factors may be pedoclimatic (AS: elevated levels of plant polyphenolics under plant growth-curbing conditions: low temperatures, water deficits, low soil nutrient availability levels) or agronomic (with lowered levels under favourable growth conditions: culture in greenhouses, biological culture, hydroponic culture, fruit yield per tree). The polyphenol content of fruit and vegetables is generally higher when produced in plants under conditions of stress (Manach et al. 2004).

Storage may also affect the content of polyphenols that are easily oxidized; concentrations usually declining over time in storage. In contrast, cold storage does not

seem to affect the the content of polyphenols. Furthermore, methods of culinary preparation also affect the polyphenol content of foods. Peeling fruit and vegetables can eliminate a significant portion of polyphenols because these substances are often present in higher concentrations in the outer parts than the inner parts. Cooking may also have major effects in reducing polyphenol content of food. Boiling, cooking in a microwave oven or even frying leads to major losses. Steam cooking of vegetables, which avoids leaching, is preferable (Manach et al. 2004).

4) Dairy products fermentation 2.5.1.3f

5) Grain products soaking of whole grains 2.5.1.3e

6) Acid-base balance (apple cider vinegar) 2.5.1.3c

7) **Bone broth** (Table 2.5.1.5f)
Animal-based protein and fat: meat (including organ meat, fat and cold-water fish) and milk products (mainly fermented forms: fat-rich yogurt, cheese, etc.). Much of the nutritional benefits in traditionally healthy living THL populations of consuming meat was associated with them consuming all parts of the animal, notably also relying on its fat content. Ancestral and THL populations typically use(d) all parts of an animal: meat, organs, fat and gelatin made from tendon and cartilage material These substances are captured in the **bone broth**. Fat content of available meat is low (except of domesticated pig meat which should be avoided). Importance of animal-derived protein (Braverman et al. 2003: amino acids).

Bones for the broth should originate from animals (preferably beef, not chicken) subject to growth-curbed conditions (preferably raised under cold and arid conditions: unfertilized grass-fed; and without growth-accelerating chemicals applied to the animals). Wild-living animals (game as available) and animals subject to harsher living conditions are preferable as sources of bones for broth-making (2.5.1.2 IV).

Ideally drink half to one cup of bone broth a day. Bone broth also important as source of magnesium (Dean 2014): In 3.8 liter of water, 1 kg (or more) of organic bones (beef, chicken), 1 onion, 2 carrots, 2 stalks of celery, 2 table spoons of apple cider vinegar (mandatory: to allow nutrient extraction from the bone). Optional: 1 tablespoon of sea salt, herbs or spices to taste. Two coves of garlic and parsley added in the final 30 minutes. Bring to boil and then reduce heat to a low setting (simmering). Allow broth to simmer for at least 12 hours, but simmering for 24 for hours makes more nutrients available (up to 48 hours in the case of beef broth). Collagen is contained in the top layer of the broth; do not get rid of this layer. Let cool and remove residual bone and vegetable material with a fine metal strainer. Store in fridge for up to 5 days or freeze for later use. Do not re-heat with microwaving. Microwaving converts I-proline to d-proline. Neurotoxic, nephrotoxic and hepatotoxic effects are linked to d-proline (Lubec et al. 1989).

Required for detoxification processes. Higher levels required during pregnancy. Helps digestion by enhancing gastric acid secretion. Only proteins (amino acids) stimulate gastric acid secretion, but not all amino acids do so (Richardson et al. 1976). Glycine is one that does (Wald & Adibi 1982). Too little hydrochloric acid impairs protein digestion and vitamin C absorption, allows vitamin Bs to be destroyed and prevents

minerals to reach the blood (Davis 1972). Gelatine improves digestion and absorption of minerals due to its ability to normalize both hydrochloric acid deficiencies and excesses and is considered a peptogenic substance favouring the flow of gastric juices. Food combining rules (*Fit for Life* Diamond & Diamond, op. cit. Daniel 2003) discourage eating proteins together with starches. However, Pottenger (op. cit. Daniel 2003) found that if gelatin is included as part of the meal, digestive action is distributed throughout the mass of the food and digestion of all components proceeds effectively. Gelatin is consistently rich in proline, hydroxyproline and glycine. It increases the utilization of proteins in wheat, oats and barley, the digestion of beans is improved and helps the digestion of meat protein (Gotthoffer op. cit. Daniel 2003); increasing the utilization efficiency of protein in general. Gelatin can improve the digestion of milk and milk products, notably also the digestion and absorption of milk fat. Early researchers indicated that gelatin (glycine) assists the liver in its detoxification role (Ottenberg op. cit. Daniel 2003).

8) **Magnesium** (Table **2.5.1.3b**)
Magnesium insufficiency is of particular relevance in societies subject to many social, dietary and environmental stressors, resulting in sympathetic nervous system over-dominance (Gedgaudas 2011). Prevalent epigenetic high patho-information-engram loadings are associated with metabolic functional insufficiencies and low fight-flight reaction thresholds (2.1.2; 2.1.3); predisposing towards dominance of the sympathetic mode of functionality of the autonomous nervous sysyem. We were however designed for predominance of functional efficiency in the parasympathetic state (*inter alia* Gedgaudas 2011). **Magnesium** is of critical importance for the healthy functioning of both the sympathetic and **parasympathetic nervous systems**, **especially the latter** (Gedgaudas 2011; Dean 2014). Animal and plant sources (including *inter alia* green leafy vegetables such as spinach, yoghurt/kefir, almonds).
With modern-day sources of nutritional items and the prevalence of functional inefficiencies due to generally high patho-information-engram loadings, certainly Caucasians are expected to generally suffer from hypomagnesemia. In **order to ensure a healthy Mg/Ca ratio, routine supplementation with magnesium chloride is indicated, particularly so when dairy products, providing ample calcium, are consumed (**Table 2.5.1.3b**). Magnesium glycinate in the evening supports parasympathetic functionality and therewith sleep quality.**

This type of nutrition should include a good proportion of green vegetables in order to support an appropriate acid-base balance (Jentschura & Lohkämper 2014: supported by basic vegetable juices and herbal teas). Meat of unhealthy and stressed animals, especially that from domesticated pigs (Reckeweg 1986: Sutoxine).

Role of dietary CH: Body condition/storage and net base producing. Carbohydrate content for body condition maintenance and dietary net base load in combination with animal-derived protein proportion (30%). Sebastian et al. (2002): It is the combined effect of substituting cereal grains and nutrient poor dietary components (refined foods) with non-grain plant foods that can account for the transition from a net acid to a net base-producing modern diet. Sebastian et al. (2002) emphasize that, for the contempory diet, the net base-producing effect of replacing both cereal grains and nutrient-poor foods with non-grain plant food items could be achieved without changing the proportional content of the acid-producing animal foods in the diet (meat, cheese, milk,

yogurt, eggs). That means a net base producing diet can be achieved yet including a considerable component of animal-derived protein. Especially for skinny/lean body condition types (Table): Net base-producing diet: Kraut & Madias (2016) ACIDOSIS Kidneys. Kraut (2011) ACIDsebastian MS GUT-russell-high protein on the importance of CH for a healthy intestinal microflora	
DIET-plaskett Plaskett (2003)	
DIET Martin et al. () Wakefield et al. (2011)	
Carbohydrates: Ströhle & Hahn (2011) FXFATCH Plaskett (2003) DIET-plaskett	
Role of starch-rich CH re body condition (fat); role of nutrient-dense CH re acid-base balance (mineralisation required during acid-based metabolic processes). Fresh vegetable juices.	
Liquid consumption Hard water; time factor Wrangham COOKING	

Table 2.5.1.5f Bone Broths: Vitally Important Dietary Ingredient
Bone broth. Ideally drink half to one cup of bone broth a day. Bone broth also important as source of magnesium (Dean 2014): In 3.8 liter of water, 1 kg (or more) of organic bones (beef, chicken), 1 onion, 2 carrots, 2 stalks of celery, 2 table spoons of apple cider vinegar (mandatory: to allow nutrient extraction from the bone). Optional: 1 tablespoon of sea salt, herbs or spices to taste. Two coves of garlic and parsley; to be added in the final 30 minutes. Bring to boil and then reduce heat to a low setting (simmering). Allow broth to simmer for at least 12 hours, but simmering for 24 for hours makes more nutrients available (up to 48 hours in the case of beef broth). Collagen is contained in the top layer of the broth; do not get rid of this layer. Let cool and remove residual bone and vegetable material with a fine metal strainer. Store in fridge for up to 5 days or freeze for later use.
Daniel (2003): Proline, glycine and gelatin
Many researchers suggest that both proline and glycine should be considered conditionally essential (together with arginine, cysteine, glutamine, serine, taurine, tyrosine: Irwin & Hegsted op. cit. Daniel 2003); meaning that under most conditions proline and glycine must be obtained from food in order to ensure an adequate supply.
Proline Sourced from adequate protein intake. Proline needs to be metabolised into the active form of hydroxyproline; this requires sufficiency of both vitamin C and iron. Without the enzyme prolyl hydroxylase in active form (maintained by vitamin C), proline and lysine in procollagen cannot be hydroxylated. **The combination of proline and vitamin C is involved in various vital functions** (e.g. Linus Pauling and Matthias Rath, op. cit. Daniel 2003).
Glycine Involved in the production of other amino acids, and in the synthesis of haemoglobin, creatine, porphyrin, bile salts, glutathione and the nucleotides DNA and RNA. Also in glucogenesis (low levels may result in hypoglycemic-type symptoms). **Required for detoxification processes**. Higher levels required during pregnancy. **Helps digestion by enhancing gastric acid secretion**. Plays a vital role in wound healing. Although the body can make glycine, researchers found that the endogenous synthesis of glycine in adult men on low-protein diets failed to satisfy normal metabolic demands.
Only proteins (amino acids) stimulate gastric acid secretion, but not all amino acids do so (Richardson et al. 1976). **Glycine is one that does** (Wald & Adibi 1982). Too little hydrochloric acid impairs protein digestion and vitamin C absorption, allows vitamin Bs to be destroyed and prevents minerals from reaching the blood (Davis 1972). The inability to properly digest protein may contribute to asthma, diabetes, food allergies, osteoporosis, iron deficiency anemia, pernicious anemia, candida,

rheumatoid arthritis, intestinal infections, psoriasis, vitiligo, hives, excema, dermatitis, herpetiformis and acne (Davis 1972).

Children and pregnant women require good amounts of glycine in the diet. Glycine deficiency could limit growth in infants and the demands of the growing fetus are very high in both absolute terms and in relation to other amino acids. By optimizing the intake of glycine, the outcome of pre-term infants could be improved (Jackson 1989). Glycine is the limiting amino acid for rapid growth (Pesaud et al. 1989). Glycine status is considered an important marker of normal pregnancy. Endogenous production of glycine may be insufficient to satify increasing needs towards later pregnancy (Tikanogia, op. cit. Daniel 2003). In an infant feeding study it was shown that the sum of free amino acids in plasma increased after feeding, but the ratio of glycine to valine fell. This relative glycine deficiency was speedier normalized by breast feeding than formula feeding (Gotthoffer op. cit. Daniel 2003). These studies support the notion that glycine deficiency during the early months of life could limit growth and as children grow up the need for glycine does not decline. Brawley et al. (2005): glycine in pregnancy and lactation

Gelatin The traditional way to ensure adequate proline and glycine in the diet. **Gelatin is consitently rich in proline, hydroxyproline and glycine**. **It increases the utilization of proteins in wheat, oats and barley, the digestion of beans is improved and helps the digestion of meat protein** (Gotthoffer op. cit. Daniel 2003); **increasing the utilization efficiency of protein in general**. **Gelatin can improve the digestion of milk and milk products, notably also the digestion and absorption of milk fat**. Infants fed on gelatin-enriched formulas showed reduced allergic symptoms, colic, vomiting, diarrhea, constipation and respiratory ailments than those on cow milk (Gotthoffer op. cit. Daniel 2003). **Gelatine improves digestion due to its ability to normalize both hydrochloric acid deficiencies and excesses and is considered a peptogenic substance favouring the flow of gastric juices**. Food combining rules (*Fit for Life* Diamond & Diamond, op. cit. Daniel 2003) discourage eating proteins together with starches. However, Pottenger (op. cit. Daniel 2003) found that if gelatin is included as part of the meal, **digestive action is distributed throughout the mass of the food and digestion of all components proceeds effectively**.

At the turn of the century **gelatin was found useful to heal digestive disorders, the intestinal mucosa and all allergies**. Gelatin will protect gastric mucosal integrity (Samonina et al., op. cit. Daniel 2003). Docters of the past knew of the value of gelatin in treating celiac disease (Gotthoffer op. cit. Daniel 2003).

Early researchers indicated that gelatin (glycine) assists the liver in its **detoxification role** (Ottenberg op. cit. Daniel 2003). Collagen hydrolysate found useful in the treatmemt of **osteoporosis and osteoarthritis** (Moskowitz 2000).

Reliance should not be placed on commercially manufactured gelatin products to have the expected beneficial results. The highest quality gelatin product is homemade made, with skin, cartilage and bone from organic meat (Pottenger op. cit. Daniel 2003). **Bone broths should never be cooked or reheated in the microwave**. Microwaving converts I-proline to d-proline. Neurotoxic, nephrotoxic and hepatotoxic effects are linked to d-proline (Lubec et al. 1989). The I-configuration of proline and proper molecular size are considered essential in order to achieve beneficial effects in memory and the prevention of depression (Cherkin & Van Harreveld, op. cit. Daniel 2003). **Amino acids in gelatin and amino acids in general can only be adequately utilized when the diet contains sufficient fat-soluble activators (vitamins A and D) found exclusively in animal fats**. Use cream in broth-based soups, souces and stews and ensure adequate dietary intake of vitamins A and D by including *inter alia* butter, egg yolks and cod liver oil (Daniel 2003).

Glycine as neurotransmitter. Glycine is a major inhibitory neurotransmitter in the mammalian central nervous system (Betz et al. 2006). Aragón & López-Corcuera (2003): Glycine has various functions in the central nervous system; mainly as an inhibitory neurotransmitter. **In some areas of the CNS it is apparently co-released with GABA, the main inhibitory amino acid neurotransmitter**. Of central importance in the context of anxiety disorders syndrome (Scott 2011). Potentially of value in the treatment of *inter alia* neurodegenerative disorders.

The Healing Power of bone broth (Fawne Hansen: The Adrenal Fatigue Solution by Hansen & Wood) Bone broth also considered helpful in the case of adrenal fatigue. **Collagen** also occurs in bone, marrow, tendons and cartilage. Protects and soothes the lining of the digestive tract. Known to help irritable bowel syndrome symptoms, Crohn's disease, acid reflux and ulcerative colitis. **Gelatin** is produced through the breakdown of collagen. It has proven useful in food allergies (including intolerances relating to gluten and dairy). It supports probiotic growth and balance. Provides the body with bone building minerals. Since gelatin promotes the health of the gut lining, it is helpful in cases of leaky gut syndrome and certain autoimmune disorders. Reduces the appearance of cellulite and wrinkles. **Amino acids** Conditional amino acids are those amino acids which are not produced in

sufficient amounts required under certain circumstances (poor diet, illness); and generally need to be replenished through consumption. Some important of these are contained in bone broth: arginine, proline, glycine and glutamine. These amino acids are involved in numerous processes required for health: *inter alia* the release of growth hormones, regeneration of damaged liver cells, improving sleep and memory, regeneration of cartilage (joints), improving metabolism and building muscle.

f) Supplementation

Das derzeitige Nahrungsangebot ist überwiegend denaturiert und nährstoffunvollständig (moderne Landwirtschaft; generally applicable crop productivity/plant growth enhancement results in lowered nutrient concentrations, i.e. nutrient dilution), die körperliche Funktionseffizienz herabgesetzt (vorliegende Patho-Information-Engrammbelastung) und abnehmend mit dem Alter. Da Nährstoffsubstanzen synergistisch zu voller Wirkung kommen ist die Unterversorgung gewisser Substanzen (z B. Enzyme, Minerale wie Magnesium, Magensäure) stark funktionsstörend und gezielte Supplementierung durchaus angebracht im Rahmen einer Rekursionsheilung (Funktionskatalyse). Fish oil (Delarue et al. 2003) DL DIET-fish oil-delarue

MS POLYPHENOLS-mennen

HOWES

Intermittancy principle important

VITAMIN-BUCH: artificial supplementary substances, such as *inter alia* vitamins are unphysiologically concentrated and with sustained exposure of the body to such substances the body may consider these as toxic/detrimental and progressively block their absorption, resulting in secondary deficiency of such substances.

2.5.1.6 Life style factors relating to health and longevity

In a study carried out in the United States of America, Gavrilov & Gavrilova (2013) identified the following factors as positively associated with longevity: **parental longevity**, **young maternal age**, **farming occupation** and **timing of birth in the second half of the calendar year** (Northern hemisphere: autumn: September-November). Multivariate analyses revealed parental longevity as the strongest predictor

of longevity in both men and women; consistent with the results of Gavrilov & Gavrilova (2012); indicative of a pronounced genetic effect. Between-family analyses confirmed that parental longevity is a strong independent predictor of survival to age 100 (Gavrilov & Gavrilova 2013). Farming occupation increased the likelihood of a long life in males,

but not for wives of farmers, as shown by the between-family study (Gavrilov & Gavrilova 2013; Gavrilov & Gavrilova 2012). Survival to advanced ages was linked to childhood farm residence (Gavrilov & Gavrilova 2007 CHECK); particularly with farm ownership status and was also influenced by geographic region within the United States of America. Odds for households to be in the centenarian group, Males: Mountain West and Pacific West > North Central ≈ Southeast and Southwest ≈ New England and Middle Atlantic. Females: Mountain West and Pacific West > North Central ≈ Southeast and Southwest > New England and Middle Atlantic (Gavrilov & Gavrilova 2007). MS LONGEVITY-gavrilov-2013Stronger genetic influence on male longevity. The regions conducive to longevity are characterized by aridity and pronounced cold seasonality. This is consistent with environments typically occupied by tradidionally healthy living populations (2.5.1.2d), where slow growth realization of plants serving as food supports life history features favouring, *inter alia*, longevity (Table 2.5.1.2e). Of relevant interest in this context are the findings of Lesthaeghe & Neidert (2009) revealing that US counties less advanced in terms of the second demographic transition dimension coincide with those with higher odds for households to be in the centenarian group (see above). Combination of R and S SEASON-lam-1994

However, Northeast and Midwest were found to be the best regions for survival to age 85+ (Hill et al. 2000, op. cit. Gavrilov & Gavrilova 2007), contrasting the results for centenarians where residence in the Northeast region was not favourable for reaching such advanced ages. Literacy was positively associated with chances of survival to age 85+, wheras no such relationship with survival to age 100 was found (Gavrilov & Gavrilova 2007). (Centenarians in the New England Centenarian Study had higher levels of education than the general population: Perls et al. 2002, op. cit. Gavrilov & Gavrilova 2015). Analysing US centenarians born during 1880-1895 (Gavrilov & Gavrilova 2015) found that gender-specific predictors of male longevity were occupation as farmer at age 40, Northeastern region in the United States and birth during the last months of the year. Furthermore, they found that wives of male centenarians, who shared life-style and living conditions, had significantly better

survival in comparison with wives of the brothers of the centenarians, attesting to the importance of a shared familial environment and lifestyle in human longevity. Northeastern and Midwest regions were relatively advanced in the demographic transition (Lesthaeghe & Neidert 2009), which also typically applies to the wealthier and more educated, possibly implying a higher incidence of literacy in these regions which is apparently positively associated higher education levels in centenarians (Perls et al. 2002, op. cit. Gavrilov & Gavrilova 2015).

Parental age. Young maternal age was most important as predictor of exceptional survival (Gavrilov & Gavrilova 2013). The within-family analyses by Gavrilov & Gavrilova (2013) demonstrated that being born to a younger mother increases the chances of becoming a centenarian (see also Gavrilov & Gavrilova 2012). The within-family approach allows for the elimination of between-family variation (genetic variation and childhood living conditions). Individuals born to older parents have an increased chance to be affected from a load of deleterious mutations. MS LONGEVITY-PARENTAL AGE-gavrilov Delayed motherhood (with negative influences of the intra-uterine and post-natal environments) is associated with higher morbidity and mortality risk later in life (Kemkes-Grottenthaler 2004). Late fatherhood is associated with higher risks of inheritable-mutation disorders (Sartorelli et al., op. cit. Kemkes-Grottenthaler 2004). Evidence from animal research supports the contention that maternal age, to a lesser extent also paternal age, may have shaped the evolution of ageing (Priest et al. 2002). Older mothers produce offspring with lower survival if their reproduction is delayed to late age, whereas continuous reproduction throughout life is associated with higher life expectancy (Priest et al. 2002). DL MATERNAL AGE-priest Paternal age at birth was negatively associated with offspring longevity; more pronounced and statistically significant for female offspring (Kemkes-Grottenthaler 2004). Daughter's lifespan more affected; as consistent with the findings of Gavrilov & Gavrilova (2000; 2001). Lends support to the mutation theory of ageing since paternal age seems to be the main factor determining human spontaneous mutation rates. LONGEVITY-gavrilov-2007 LONGEVITY-gavrilov-2001-reliable-theory; LONGEVITY-gavrilov-gender The lifespan of offspring (in both male and female offspring) decreases with maternal age at birth (Kemkes-Grottenthaler 2004). Sons born to mothers at optimal childbearing age, but life expectancy was lowest

in teenage mothers; whereas female offspring survivability was actually found to be higher in young mothers. Some empirical evidence indicates that the quality of female eggs in humans sharply declines with age (Comings & MacMurray 2006). Another hypothesis is based on the telomere theory of female reproductive senescence according to which eggs ovulating in older females have shorter telomeres due to a later exit from the oogonial production line, with incomplete restoration by telomerase (Keefe et al. 2005). Also, Gloria-Bottini et al. (2005) reported on negative mother-foetus relationships (negative effects on foetal developments and predisposition to diseases) related to maternal age. Results based on within-family analyses are consistent with the reliability theory of ageing and in particular the high initial damage load hypothesis (Gavrilov & Gavrilova 2004). CHECK Early-life/ fetal programing (LIT). Additional arguments suggesting the importance of early life conditions in later life health outcomes come from the reliability theory of ageing and longevity according to which biological species, including humans, are starting their lives with high initial damage loads and are accordingly sensitive to early life conditions affecting the level of initial damage (Gavrilov & Gavrilova 2004). The concept of high initial damage load *inter alia* predicts later life health outcomes for early-life indicators such as parental age at conception and month of birth. Substantial evidence supporting the concept of fetal origins of degenerative diseases in adulthood (MS FETAL PROGRAMMING-hypertension-alexander; DL GESTATION-mcmillen; DL DEVELOPMENTAL PROGRAMMING-joseph-kramer-1996; DL DEVELOPMENTAL PROGRAMMING-victora; DL DEVELOPMENTAL PROGRAMMING-smith; Godfrey et al. 1996; Godfrey 1998; Godfrey & Barker 2000) and early-life programming of ageing and longevity has been emerging (Gluckman et al. 2007; DL DEVELOPMENTAL PROGRAMMING-langley-evans-NB; DT-enthringer; DT-entringe-2015) DL AGEING-lindner Gavrilova et al. (2003) Early life predictors

Gavrilov & Gavrilova (2012) Maternal age and physical characteristics

DL DELAYED PARENTHOOD-tarin

DL MATERNAL AGE-bottini

MATERNAL AGE-bingley

Seasonal timing of birth. Birth in autumn (second half of year; October/November) favours longevity; as shown in both within-family (Gavrilov & Gavrilova 2011) and between family analyses (Gavrilov & Gavrilova 2013). Month of birth seems to be a useful proxy characteristic for environmental effects impacting during *in utero* and early infancy development and having a long-lasting effect still observed in siblings having survived to age 70; similar to long-lasting effects of maternal age (Gavrilov & Gavrilova 2013). Longevity (northern hemisphere) higher for those born in the fourth quarter (autumn) and first quarter (winter) and lower for those born in spring/summer (Gavrilov & Gavrilova 2007).

Refer to section 2.2.2g

Results are in agreement with other studies (Doblhammer & Vaupel 2001; Vaiserman et al. 2002) Vaiserman
LONGEVITY ref to 2.2f
REFER TO ILLNESS IN THIS CONTEXT and LHS-modes (2.2.2g)

AS refer to seasonality alignment of diet (both nutritional and biogenic information Table) for health in this context (locally grown and seasonally consumed in THL populations) TABLE-FIGURE re longevity and diet

Socioeconomic status. Section 2.2.2k
Lantz et al. (1998).

2.6 Lifestyle imperatives for transgenerational systemsecological healing

a) Pregnancy and childhood

Medical Disclaimer
All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

Developmental programming

DIET-lucas-neonates

DL DELAYED PARENTHOOD-tarin

MS MATERNA AGE-wang

DL MATERNAL AGE-bottini

MATERNAL AGE-bingley

MATERNAL STRESS-emack

MATERNAL STRESS-essex

MATERNAL STRESS-barry

Pregnancy.

Gloria-Bottini et al. (2005) DELAYED CHILDBEARING-gloriabottini

Idealerweise sollten Frauen schon vor ihrer gewünschten Schwangerschaft eine Entsäuerungs- und Entgiftungskur machen (Dreisprung der Entschlackung; ein langgehegter Kinderwunsch geht zuweilen erst nach einer solcherartigen Kur in Erfüllung (Jentschura & Lohkämper 2014, Tabelle). Generell, Fortschritte in der Rekursionsheilung sollten schon vor der Schwangerschaft erziehlt werden um epigenetisch-vererbbare Pathogeninformationsbelastungen zu minimisieren. *Candida* (Acetaldehyd absondernd) bei Schwangeren verursacht (secondary causation) eine gestörte Ausbildung des fötalen Immunsystems (Rochlitz 1989).

PREGNANCY-van den bergh-2005 NBNB

Wasser (1994)

Skinner et al. (2010):

Table 2.6a Fetal exposure to procursive impacts and adult-onset disease
Skinner et al. (2010): Although numerous environmental factors influence and promote adult-onset disease (such as nutrition and stress), this review focuses on endocrine disruptors, as this group of environmental compounds is one of the largest people are exposed to in society. Endocrine disruptors are environmental chemicals that affect the function of the endocrine system by mimicking or blocking the actions of hormones, altering hormone signalling or disrupting hormone production (Crisp et al. 1998, op. cit. Skinner et al. 2010). Several disease states are promoted by endocrine disruptors. Many endocrine disruptors with reproductiive hormone actions (e.g. estrogen or androgen) influence reproduction and fertility; includimg bisphenol-A (BPA), dichlorodiphenyltrichloroethane (the insecticide DDT) and vinclozolin. Activation of the male and female reproductive systems at an inappropriate time during

development by endocrine disruptor chemicals can alter normal physiology (Danzo 1998, op. cit. Skinner et al. 2010). For example, prenatal exposure to diethylstilbestrol (DES) produces several developmental abnormalitiesin the male mouse reproductive tract and increases tumor incidence (Bullock et al. 1988, op. cit. Skinner et al. 2010). Embrionic exposure to the pesticide methoxychlor during the period of sex determination affects the cellular composition of the embryonic testis, and germ cell number and survival (Cupp et al. 2003, op. cit. Skinner et al. 2010). Embrionic testicular cord formation is also affected when embrios are exposed in vitro to vinclozolin. Transient *in utero* exposure to vinclozolin increases apoptotic germ cell numbers in the testis of pubertal and adult animals, which correlates with reduced sperm motility and number in the adult (Uzumcu et al. 2004, op. cit. Skinner et al. 2010). *In utero* exposure to the plastic-derived compounds phthalates also disrupts differentiation of androgen-dependent tissues in male rat offspring (Gray et al. 1999, op. cit. Skinner et al. 2010). A more recent example of an endocrine disruptor is the plastic component BPA which acts as an estrogenic compound causing numerous pathologies including prostate cancer in low doses (Ho et al.2006, op. cit. Skinner et al. 2010). Other examples include the plant-derived estrogenic compounds (phytoestrogens) such as genistein which influence several reproductive organs (impaired fertility, reproductive effects, breast cancer protection: Moutsatsou 2007, op. cit. Skinner et al. 2010; Tomar & Shiao 2008, op. cit. Skinner et al. 2010); aflatoxin-contaminated food which has been correlated with the incidence of liver cancer (International Agency for Research on Cancer 1976, op. cit. Skinner et al. 2010); tobacco, which contains cadmium, an estrogenic endocrine disruptor (Henson & Chedrese 2004, op. cit. Skinner et al. 2010), and its use can cause reproductive problems in addition to carcinogen-induced lung cancer. Accordingly, a large number of environmental compounds have endocrine disruptor activity; and the early life exposure to endocrine disruption can promote adult-onset diseases.

Epigenetic influences have neen observed with environmental compounds, nutritional factors (Bertram et al. 2008, op. cit. Skinner et al. 2010; Heijmans et al. 2008, op. cit. Skinner et al. 2010) such as methyl donors (e.g. folate: Cooney et al. 2002, op. cit. Skinner et al. 2010; Cropley et al. 2006, op. cit. Skinner et al. 2010), inorganic contaminants such as arsenic (Singh & Du Mond 2007, op. cit. Skinner et al. 2010; Waalkes et al. 2004, op. cit. Skinner et al. 2010), airborne polycyclic aromatic hydrocarbons (Perera et al. 2009, op. cit. Skinner et al. 2010), drugs such as cocaine (Novikova et al. 2008, op. cit. Skinner et al. 2010), endocrine disruptors such as BPA (Dolinoy et al. 2007, op. cit. Skinner et al. 2010; Yaoi et al. 2008, op. cit. Skinner et al. 2010), phytoestrogens (Dolinoy et al. 2006, op. cit. Skinner et al. 2010; Guerrero et al. 2008, op. cit. Skinner et al. 2010), and chemicals used as fungicides (Anway et al. 2005, op. cit. Skinner et al. 2010) or pesticides (Andersen et al. 2008, op. cit. Skinner et al. 2010). Some studies have also demonstrated behavioural effects on DNA methylation, including maternal effects on nursing behaviour (Champagne et al. 2006, op. cit. Skinner et al. 2010) or depression (Oberlander et al. 2008, op. cit. Skinner et al. 2010). Exposures to environmentally relevant doses of BPA during the neonatal developmental period in rats produced DNA methylation changes associated with carcinogenic processes (Ho et al. 2006, op. cit. Skinner et al. 2010). Maternal exposure to BPA has been shown to alter methylation in the fetal mouse forebrain (Yaoi et al. 2008, op. cit. Skinner et al. 2010) and to roduce changes in behaviour responses in the offspring (Palanza et al. 2008, op. cit. Skinner et al. 2010). These findings correlate with other studies showing epigenetic changes resulting from endocrine disruptor exposure, which affected aspects of neuronendocrine systems (Gore 2008, op. cit. Skinner et al. 2010) and behavioural neurorendocrinology (Crews 2008, op. cit. Skinner et al. 2010; Crews et al. 2007, op. cit. Skinner et al. 2010; Skinner et al. 2008, op. cit. Skinner et al. 2010).

When embryonic rats were exposed through maternal administration to vinclozolin, an anti-androgenic environmental endocrine disruptor, during gonadal sex determination, adult onset disease occurred in the first generation and persisted for four subsequent generations (Anway et al. 2005, op. cit. Skinner et al. 2010). This phenomenon was found to be caused by male germline changes in DNA methylation. The pathology of adult onset disease from vinclozolin exposure during embryonic life included testicular, prostrate and renal abnormalities, and increased the incidence of tumors (33/84/85). A modification of the sperm epigenome appears to have occurred following vinclozolin exposure at the time of gonadal sex determination, which enabled transgenerational transmission to subsequent generations to promote adult-onset disease (Jirtle & Skinner 2007). A follow-up study by a company that produces vinclozolin found that oral administration of doses used in the study by Anway et al. (2005, op. cit. Skinner et al. 2010) did not have transgenerational effects nor major effects in the F1 generation (Schneider et al. 2008, op. cit. Skinner et al. 2010). Discrepancies in results may be explicable by variability in dosage, exposure timing and duration. Several other recent studies confirm the ability of environmental agents to promote transgenerational phenotypes (Salian et al. 2009, op. cit. Skinner et al. 2010), and a recent independent study confirmed epigenetic

transgenerational actions of vinclozolin (Stouder & Paoloni-Giacobino 2009, op. cit. Skinner et al. 2010).

Stress (excessive adrenocortical and adrenocorticotropic hormones) leading to hormonal imbalances in the maternal body and prenatal offspring has a variety of negative effects manifesting in neonates, *inter alia*, underdevelopment of the brain and higher levels of overt aggressiveness (Geist 1978). Abnormal maternal care leads to abnormal offspring. Presence of the maternal female protects the neonate against stress (Moore 1968, op. cit. Geist 1978). Furthermore, females that were poorly mothered, mothered their offspring poorly in turn, producing low quality adults (Moore 1968, op. cit. Geist 1978). While mild stress promotes adjustment in individuals, severe stress leads to underdevelopment of the cortex, a relatively low IQ and overt aggression and flight behaviour in developing individuals (op. cit. Geist 1978).

Children and pregnant women require good amounts of glycine in the diet. Glycine deficiency could limit growth in infants and the demands of the growing fetus are very high in both absolute terms and in relation to other amino acids. By optimizing the intake of glycine, the outcome of pre-term infants could be improved (Jackson 1989). Glycine is the limiting amino acid for rapid growth (Pesaud et al. 1989). Glycine status is considered an important marker of normal pregnancy. Endogenous production of glycine may be insufficient to satify increasing needs towards later pregnancy (Tikanogia, op. cit. Daniel 2003). In an infant feeding study it was shown that the sum of free amino acids in plasma increased after feeding, but the ratio of glycine to valine fell. This relative glycine deficiency was speedier normalized by breast feeding than formula feeding (Gotthoffer op. cit. Daniel 2003). These studies support the notion that glycine deficiency during the early months of life could limit growth and as children grow up the need for glycine does not decline. Brawley et al. (2005): glycine in pregnancy and lactation

During ontogeny, sufficient quantities of high quality food alter the blood chemistry of the gestating female. The activity centers in the infant's central nervous system are altered in such a fashion that its reward and punishment centers have a high threshold, leading to the development of an individual with high motor activity, curiosity, self-discipline, social tolerance and insensitivity to stress (initiating high quality syndrome). A factor in the food of gestating females that signal to genes to switch on behaviours conducive to great individual development. If young are to be affected during geststaion so as to develop the high quality syndrome in programing them to greater activity ought to be in the spring vegetation (a factor that raises the threshold of reward and punishment centers, leading to vigorous highly mobile, very inquisitive youngsters that would not easily deterred by a painfull stimulus: in spring, newly sprouting

regrowth; also amino acid tryptophane). McNab: Raised metabolic turnover. Protein-deprived individuals were socially less active, fearful of strange objects (neophobia), performed more poorly in some learning tasks, had reduced sexual behaviour and exhibited a greater proportion of social behaviour as overt aggression. One gets the image of sensitive, fearful, overreactive, withdrawn individuals as a consequence of protein malnutrition (Zimmermann et al. 1973, op. cit. Geist 1978).

Both omega-6 and omega-3 fatty acids influence gene expression. Many chronic diseases begin in utero or early infancy and adequate dietary intake of polyunsaturated fatty acids, even prior to pregnancy is considered important. Omega-3 fatty acids have anti-inflammatory effects (inflammation associated with many chronic diseases), wheras omega-6 fatty acids do not have such effects. Furthermore, a diet supplemented with omega-3 fatty acids with fish oil inhibited adrenal activation induced by mental stress, presumably by subduing sympatho-adrenal reactivity (Delarue et al. 2003).
CHECK DL DIET-fish oil-delarue
Skilton et al. (2012): Impaired fetal growth is inversely linked to arterial wall thickening in early childhood associated with an increased risk of cardiovascular diseases in adulthood. Dietary omega-3 fatty acid supplementation in early childhood prevented the association between impaired fetal growth and arterial wall thickening, suggesting that adults which had suffered from impaired fetal growth may have a reduced risk of cardiovascular disease if having had omega-3 supplementation during childhood over the first 5 years of life.

Wissenschaftler nehmen an dass der Foetus seinen Stoffwechsel programmiert für die nachgeburtliche Welt basierend auf Aussenweltinformationen (Ernährung der Mutter; Stresseinwirkungen) während der Schwangerschaft. Eine ausgewogene Ernährung (FFGKh) ist angesagt. Die Kohlehydratkomponente unterstützt anabolische Stoffwechselprozesse und ist damit förderlich für ein gutes Geburtsgewicht und gleichzeitige Verhinderung von der Programmierung des Foetus für eine Welt mit Nahrungsmangel, wo eine Fetteinlagerungskapazität adaptiv wäre. Die Fleisch/Grünzeug-Komponente hingegen programmiert eine günstige Stoffwechselgrundumsatzeinstellung (Relativ erhöhte Einstellung für einen Stoffwechselmodus mit reduzierter Neigung zur Fetteinlagerung). Gutes Geburtsgewicht, aber Abwesenheit von vorprogrammierter Fettsucht beim Säugling ist dann zu erwarten. Simmons (2009) investigated the relationship between low birth weight and the development of disease later in life. Increased birth weights are associated with enhanced body mass indices and increased occurrence of adult obesity (Simmons 2009). Factors impacting on the intrauterine environment and in early

childhood may result in obesity through metabolic profiling. Breast-feeding seems to protect against the development of obesity in child- and adulthood (Simmons 2009). The findings of Godfrey et al. (1996) suggest that a high carbohydrate intake during early pregnancy, notably when in combination with low a low protein intake in late pregnancy (low meat more so than low dairy protein intake), results in lower placental and birth weights. Independantly thereof, lower intakes of iron and folate (insufficient levels of supplementation) were also associated with lower placental and birth weights. There is emerging evidence that maternal nutrition can induce epigenetic changes in the fetal genome resulting in metabolic programming (nutrient requirements), but also increasing risks of metabolic diseases, with consequences throughout the lifespan of the offspring (Stover 2007). Seckl (2004): Glucocorticoid or stress exposure of the fetus can have lifelong consequences in respect of low birth weight, hypertension, hyperglycemia, insulin resistance, hyperinsulinemia, and anxiety. Some of these lifelong consequences can result from premature glucocorticoid receptor-mediated chromatin remodelling in the hippocampus (Seckl 2004). Low maternal dietary protein intake during gestation resulted in offspring exhibiting glucocorticoid-dependent raised systolic blood pressure throughout life (Bertram et al. 2001). As stated by Kudielka et al. (2009), fetal programming of the HPA axis is considered as one of the mechanisms underlying the link between prenatal stress, adverse birth outcomes, such as low birth weights, and enhanced vulnerability to health disorders in later life. Evidence is increasingly emerging that stressful pre- and postnatal experiences result in lifelong impacts on HPA axis responses to stress (over-reactive and dysregulated HPA axis). From animal studies, evidence emerged for the association between prenatal stress exposure and impairments of early motor development, feminization of male sexual behaviour, increased emotionality and attention and temperament disorders (Huizink et al. 2004); notably also in reaction to prenatal intermittent noise stress exposure (Schneider et al., op. cit. Huizink et al. 2004). Serotonergic, noradrenergic and dopaminergic systems are involved in the interactions between pre-natal stress and the HPA axis (Huizink et al. 2004). In the offspring of prenatally stressed animals overactivity and impaired negative feedback regulation of the hypothalamic-pituitary-adrenal (HPA) axis are consistently observed, reflecting on a pathophysiological mechanism in the development of psychopathology. Exposure to prenatal stress seems to induce a general susceptibility to psychopathology (Huizink et al., 2004).

Turner and Thomson (2013): Fetal nutrition may also alter DNA methylation and chromatin modification, two key epigenetic processes contributing to gene expression (Reik et al. 2003, op. cit. Turner and Thomson 2013), creating differential risk for obesity (Waterland & Jirtle 2003, op. cit. Turner and Thomson 2013) and possibly energy extractionand utilization (Haig & Graham 1991, op. cit. Turner and Thomson 2013). Fetal imprinting and other epigenetic processes during development underscore the importance of fetal environments in shaping long-term body composition and metabolic health in ways that are not genetically determined. Whereas prenatal diets appear critically important in shaping long-term physiology, metabolism, and feeding behaviour, postnatal diets may also be important through the establishment and maintenanceof the human gut microbiome. Composed of an estimated one hundred trillion microbes, this microniche plays important roles in digestion, immune function and nutrient production (Guarner & Malagelada 2003, op. cit. Turner and Thomson 2013). The human infant is born with a sterile intestine and experiences rapid bacterial colonization during birth, breastfeeding, and solid food supplementation. These early exposures shape lifelong patterns of gut colonization (Guarner & Malagelada 2003, op. cit. Turner and Thomson 2013; Edwards & Parrett 2002, op. cit. Turner and Thomson 2013; Palmer et al. 2007, op. cit. Turner and Thomson 2013). Since one important functionof gut bacteria is the metabolism of indigestible polysaccharides into simple sugars and short-chain fatty acids (Guarner & Malagelada 2003, op. cit. Turner and Thomson 2013), the disruption of evlved mutualism between human populations and gut microbiota may be a contributing factor to the increasing prevalence of chronic and degenerative diseases (Dethlefsen et al. 2007). In modern environments characterized by by cheap, readily available sugary and fatty foods (Drewnowski 2000, op. cit. Turner and Thomson 2013; Nestle et al. 1998, op. cit. Turner and Thomson 2013) and psychosocial stress (Sapolsky 2004, op. cit. Turner and Thomson 2013; Sapolsky 2005, op. cit. Turner and Thomson 2013), an unchecked consumption of sugars and high fat foods are expected to have negative health consequences in this contxt. Interventions aimed at preventing metabolic diseases could also benefit from focusing as strongly on reducing sources of psychosocial stress as on controlling food intake.

Bach (2002): The administration of antibiotics to children has been suspected to increase the risk of asthma and allergy. The use of antibiotics in the first year of life increased the risk of asthma or other allergic diseases in children with a genetic predisposition to atopy (Droste et al. 2000, op. cit. Bach 2002). Antibiotics might act by decreasing the number of infectious episodes or by modifying intestinal flora. The composition of the intestinal flora differs between newborns in whom allergy develops at a later age and those in whom atopy does not develop (Bjorksten et al. 2001, op. cit. Bach 2002; Kalliomaki et al. 2001, op. cit. Bach 2002).
The transfer of maternal antiviral antibodies to newborns may have a role in the susceptibility to autoimmune diseases. Zinkernagel (2001, op. cit. Bach 2002) suggested that the decreased exposure of women to particular viruses before pregnancy may subsequently reduce the degree of protection against these viruses afforded to their newborns.
The deliberate administration of a non-pathogenic lactobacillus to pregnant women with atropy, and ultimately, to their newborns significantly decresased the incidence of atopic dermatitis in the newborns (Kalliomaki et al. 2001, op. cit. Bach 2002). Children who received antibiotics during infancy had a higher incidence of allergy and other atopic disorders who had not received antibiotics (Wickens et al. 1999, op. cit. Bach 2002).

Women with a low BMI are a greater risk for pre-term delivery and birth of low birth-weight infants (Allen et al. 1994, op. cit. Dirks & Leeuwenburgh 2006). CR should accordingly not be practiced by women prior to or during pregnancy.

Nemeroff (2004) MS ANXIETYDISORDERS-nemeroff

Cirulli et al. (2009) DL EPI-earlystress-cirulli

EPI-MATERNAL EFFECTS-INTELLIGENCE-bjorklund

Phillips et al. (2000): Low birth weights were associated with raised fasting plasma cortisol concentrations in adults. These findings suggest that the link between low birth weight and elevated blood pressure in adults is related to the prenatal resetting of the hypothalamic-pituitary-adrenal (HPA) axis to increased activity (in response to undernutrition and other stressful stimuli *in utero*), resulting in the birth of offspring with increased basal- and stress-induced glucocorticoid secretion.

Champagne (2010): There is increasing evidence for the epigenetic influence of maternal nutrition, physiology and psychological state on the developing fetus that are relevant to our understanding of how the social and environmental experiences of the mother can lead to divergent developmental pathways of offspring. Cohorts exposed prenatally to conditions of famine resulting in neurodevelopmental disorders. As found in rodents have identified specific nutritional deficits, such as prenatal protein restriction or folic acid/choline deficiency as having similar epigenetic consequences. Effects were not observed when gestational protein restriction is accompanied by folic acid supplementation (op. cit. Champagne 2010). The period of rapid cellular proliferation and differentiation that occurs during fetal development provides a critical window during which maternal gestational exposure to diverse negative impacts which lead to long-term disruptions in offspring. Evidence for an epigenetic basis of effects. Also, maternally induced epigenetic profiles emerge during the postnatal period and are sustained into adulthood (Weaver et al. 2004a).

Social and physical enrichment during the post-weaning period leads to increased synaptic plasticity, improved cognition and reduced anxiety-like behaviour (Nithianantharajah & Hannan 2006, op cit. Champagne 2010). Prenatal stress-induced reductions in social play behaviour and increases in corticosterone response to stress in rat offspring can be reversed through post-weaning environmental enrichment (Morley-Fletcher et al., op. cit. Champagne 2010). Data from clinical and

epidemiological studies are consistent in suggesting that chronic social stress plays a significant role in the development of psychopathology. Knaul 1985 Across species there is evidence for the transmission of individual differences in maternal behaviour from mother to offspring and grand-offspring (op. cit. Champagne 2010). Curley et al. 2008 EPI-curley The notion that the quality of the social environment can have a transgenerational impact is gaining considerable empirical support. The biological embedding of the quality of the social environment may have adaptive versus maladaptive consequences depending on the context of the individual (Miller et al. 2009 ALLOSTATICLOAD-miller). The induction of a defensive phenotype, based on a low socio-economic status early in life, characterized by heightened immune and HPA reactivity which may prepare an organism for conditions of threat, but long-term exposure to these defensive responses may increase the likelihood of physical and psychiatric illness.

Champagne & Curley (2009) DL EPI-rearing-champagne

No influenza vaccination

Maternal effects (age): Myrskylä and Fenelon (2012)

Breastfeeding:

Transgenerational effects: When F0 female mice are exposed to caloric restriction during late gestation, F2 grand-offspring are found to have impaired glucose tolerance and this effect is maintained even when the F1 generation is maintained on *ad libitum* food thoughout their lifetime (Zambrano et al. 2005b)

Champagne (2010). EPI-champagne

McMillen & Robinson (2005) Gestation -mcmillen

Bottini et al. (2001) PLACENTA-bottini

Gloria-Bottini et al. (2005)

Sroufe (2005) MATERNAL sroufe

Vaiserman (2011) paper copy

Edwards & Parrett (2002) GUT-edwards

Phillips (2007)

Phillip et al. (2006)

Jackson (1989) MS NEWBORN-jackson bone broth table

Skilton et al. (2012) DL Gestation

Meany (2001): EPI-meany-NB re maternal care

EPI-godfrey-fetal

Mcmillen & Robinson (2005): gestatationfetal programmingMS

Joseph and Kramer (1996).

Weaver et al. (2004b)

Weaver et al. (2004a) EPI-weaver-maternal

Kapoor et al. (2007)

Sapolsky (2004)

Paronen et al. (2000) DLautoimmunity-paronen DIABETES-COW MILK BREASTFEEDING

Vaarala et al. (1999) DL diabetes-vaarala DIABETES-COW MILK BREASTFEEDING

Sepa et al. (2005) MS MATERNAL-stress-sepa-diabetes

Badyaev & Uller (2009)

Walker (2006): IF-walker2006

Bertram et al. (2001) PRENATAL STRESS

GESTATION-seckle

MS GESTATION-barger

MS GESTATION-pistollato

CHECK all GESTATION

REPRODUCTION-prentice

MATERNAL-NUTRIENTS-reik

DIET-PROTEIN-langley-evans

EPI-gluckman-fetal-neonate

DIET-bayol-maternal diet

BODY MASS INDEX-Aune Dagfinn Aune et al. (2014) maternal BMI in ref list

Rickard et al. (2010): food availability at birth

GOOGLE FERTILITY AND EMPLOYMENT EUROPE

Refer to p 198 2.3.2c re green part

Humans have evolved a large and energetically expensive brain (Leonard et al. 2003). According to Cunnane and Crawford (2003) the fattest infants become mentally the fittest adults, implying that the impact of infant nutrition has lifelong consequences. Human newborns and exclusively breastfed babies are in a metabolic state of ketosis (Cunnane and Crawford 2003). Ketosis is a metabolic state when the body uses fat as fuel in preference to glucose (derived from carbohydrates and sugar). The body

makes ketones from fat when dietary glucose is low (fasting, low carbohydrate diet). Ketones are then used as fuel to produce energy in the brain. In the second half of pregnancy ketones supply as much as 30% of the energy required by the foetal brain, implying that ketones are essential for foetal brain development (Cunnane and Crawford 2003). After birth, newborns adapt to using their fat stores as their primary fuel source and begin to produce more ketones; converting stored fat and fat in breastmilk into ketones (Cunnane and Crawford 2003). Ketones provide them with energy between feeds and play a role as key building blocks for brain structures. Breastmilk is high in fat (55%; 39% carbohydrates, 9% protein). Exclusively breastfed babies are in a state of mild ketosis. Breastfed babies experience better cognitive performance, a lower incidence and severity of infectious diseases, lower rates of sudden infant death syndrome, certain cancers, food allergies, asthma, diabetes and obesity. Infants should be exclusively breastfed for the first six months and should be the main source of nutrition for the first year of life (World Health Organization. 2015. Breastfeeding). Human brain development during gestation and the first few years of life is enhanced, since during this phase the brain is best at processing /utilizing ketones (Prins 2008). The developing brain is vulnerable to maternal nutritional deprivation before, during and after pregnancy. Ketone bodies are breakdown products of fat oxidation. Ketones have two important roles in the brain: they provide a reliable source of brain energy between feeds and provide proportion of the lipid building blocks for developing brain cells. Healthy human infants have a large store of fat that is available to make ketones.

REFER TO P197 RE GREEN PART 232c
Cunnane and Crawford (2003): In the past 2 million years the hominid lienage leading to modern humans involved significantly larger and more sophisticated brains than other primates. According to the interpretation of cc the human brain was the product of having evolved fat babies. Body fat in human babies provides three forms of insurance for brain development: 1) a large fuel store in the form of fatty acids in triglycerides; 2) fatty acid precursers to ketone bodies which are key substrates for brain lipid synthesis; and 3) a store of long chain polyunsaturated fatty acids, particularly docosahexaenoic acid, needed for normal brain development. The role of a high quality diet in human brain development is being increasingly recognized (Leonard et al. 2003): levels of body fatness are relatively high in humans, notably in infancy; providing a ready supply of stored energy to feed the relatively large brain. The ketones which babies convert from from their fat stores and fat in breastmilk provide them with energy between feeds reqired for brain-structure development.

No CR before and during pregnancy /lactation (Dirks & Leeuwenburgh 2006) nor before 2 years of age (Samaras & Elrick 1999).

Gender role complementarity. Male protection and provisioning important for stress-free pregnancy and extended breastfeeding and presence of father effects

Magnesium and pregnancy

Seelig (1980): Lower magnesium intakes were correlated with lower birth weights. When dietary intake of magnesium is not sufficient to meet the demands of gestation maternal stores are mobilized and magnesium deficiency can develop.

Pregnancy.

Takaya et al. (2006): Review concerning the hypothesis that intrauterine Mg deficiency may induce metabolic syndromes later in life. Maternal undernutrition, including magnesium deficiency, negatively affects the health of the fetus in adult life. Magnesium, as an important cofactor in enzymes involved in carbohydrate metabolism, plays an important role in insulin action (Paolisso et al., op. cit. Takaya et al. 2006). Low serum intracellular Mg^{2+} concentrations are associated with insulin resistance, impaired glucose tolerance and reduced insulin secretion (op. cit. Takaya et al. 2006). Sufficiency of maternal Mg intake is important in respect of pregnancy outcome and infant health (Sibal et al., op. cit. Takaya et al. 2006). The risk of very low birth weights is reduced if the drinking water of the mother contains higher amounts of magnesium (Yang et al., op. cit. Takaya et al. 2006). Magnesium is used in obstetric practice to treat pre-eclampsia. Several reports claim that oral magnesium supplementation during pregnancy is safe and has positive effects on fetal health (Magnesium supplementation and positive pregnancy outcomes (op. cit. Takaya et al. 2006). Takaya et al. (2006) also cites several authors on the neural protective effects of magnesium in the prenatal context. Fetal programming of adult disease: alterations in fetal growth and development in response to the prenatal environment with long-term/permanent effects; involving *inter alia* linkages between disturbed HPA axis mediation, maternal nutritional restriction (low protein/low Mg diet), intrauterine growth retardation, associated with impaired pancreas/liver functionality (Takaya et al. 2006).

Folate/serotonin

Frühkindheit. Mutter-Kindbeziehung.

The brain is very responsive to the quality of prenatal and postnatal nutrition (op cit Geist 1978). The fetus and infant require a maternal diet rich in protein for their optimum development (op. cit. Geist1978). Optimum growth of the central nervous system is dependant on high quality nutrition, beginning with pregnancy and lasting

through lactation and beyond (op. cit. Geist 1978). Die intellektuelle Entwicklung wird maximiert durch Muttermilch (Newton 1971op cit Geist 1978).
Jentschura und Lohkämper (2014) betonen die Bedeutung reichlicher Mineralstoffversorgung während der Schwangerschaft und Stillzeit. Skilton et al. (2012): omega-3 fatty acid supplementation. Während der Schwangerschaft findet eine Entsorgung statt von vorhandenen, bislang zurückgehaltenen Schadstoffen (Abwesenheit von Menstruationsblutungen) in das Fruchtwasser hinein (Jentschura & Lohkämper 2014: Tabelle). Um solches zu minimisieren empfehlen Jentschura und Lohkämper (2014) zur Ausleitung von Säuren und Giften die tägliche Anwendung von basischen Voll- und Fussbädern und Wickeln, basische Leberwickel, basische Darmpflege und sonstige Massnahmen der basischen Körperpflege (teils wirksam als Ersatzmenses). Vermeiding jeglicher Giftstoffe (Verschiedene Bestandteile in Körperpflegemitteln wie unter anderem Aluminiumhyroxid in Deodorants und Antitranspirants; Genussgifte: Nikotin, Koffein in Kaffee und Tee) während der Schwangerschaft und Stillzeit ist von äusserster Wichtigkeit (Jentschura & Lohkämper 2014).

Folglich neuerer Erkenntnisse werden positive Resultate erziehlt wenn Ehepaare sich vor der Zeugung ihre Körper einer innerlichen Reinigung unterziehen (Rauch 1986: Tabelle). Das solcherart gereinigte mütterliche Blut als Lebensquell des Foetus während der Schwangerschaft bewirkt eine günstige vorgeburtliche Entwicklung, gesünderes Gedeihen im Leibe, sowie verbesserte Milchproduktion während der Stillzeit (Rauch 1986).
Weinstock ?
Bewusste Schlackenlösung (ob mit Homöopathica, Salzsole, Kräutertees, Obstessig oder durch Fasteneffekte) darf grundsätzlich nur ausserhalb der Schwangerschaft und Stillzeit praktiziert werden (Jentschura& Lohkämper 2014).

ENDOCRINE DISRUPTORS re EE lit
Skinner et al. (2010): print

Brawley et al. (2004) MS GLYCINE-pregnancy-brawley
Zambrano et al. (2005a) GESTATION-zambrano-maternal
REARING COSTS-sear

Stillphase. FFGKh-Ernährung: effiziente Freistellung mütterlicher Energie- und Nährstoffresourcen an das Kind während der Stillzeit). Keine FFG-Ernährung.
Full breast feeding (not artificial substitutes) maximizes the intellectual development of children (Newton 1971a op cit Geist 1978). Säuglinge können Muttermilch besser verwerten als jegliches Ersatzprodukt. Muttermilch repräsentiert die optimale Säuglingsernährung. Ein optimales Gleichgewicht besteht zwischen den Bestandteilen: Aminosäuren, Fett, Kohlehydrate, Mineralien und Vitaminen. In Muttermilch kommen auch Anti-Körper vor zum zusätzlichen Immunschutz für den Säugling.

Sellen (2007): Mismatch between optimal and actual infant feeding practices is widespread in contempory populations and presents a major public health challenge (Huffman & Martin 1994, op. cit. Sellen 2007; Quandt 1985, op. cit. Sellen 2007; Sellen 2002, op. cit. Sellen 2007; Underwood & Hofvander 1982, op. cit. Sellen 2007). The proportions of newborns exclusively breastfed for six months, receive timely and appropriate complementary foods, and continue to breastfeed into their third year, is low in Western contemporary societies; even though overwhelming evidence indicates that such a pattern is optimal for healthy, term infants and also for low low-birth-weight infants. Current international recommendations (Dewey 2003, op. cit. Sellen 2007; Dewey 2005, op. cit. Sellen 2007; Dewey 2002, op. cit. Sellen 2007; World Health Organization 1979: WHO/UNICEF Meeting on Infant and Young Child Feeding: Statement and Recommendations, op. cit. Sellen 2007; World Health Organization 2001: Rep. A54/ Info.doc./4, op. cit. Sellen 2007), based on clinical and epidemiological data (Dewey 2003, op. cit. Sellen 2007; Kramer & Kakuma 2002, op. cit. Sellen 2007), are consistent with the evolved pattern of infant and young child feeding practices predictive of optimal growth and development of healthy newborn humans in favourable environments (Garza 2006, op. cit. Sellen 2007; Sellen 2001b, op. cit. Sellen 2007; Sellen 2006b, op. cit. Sellen 2007). The evolved template for human infant and young child feeding accordingly includes (I) initiation of breastfeeding within an hour of birth; (II) a period of exclusive breastfeeding followed by by the introductionof nutrient-rich and pathogen-poor complementary foods at about six months of infant age; (III) introduction of high-quality family foods, usually prepared from a variety of raw sources using some form of processing, heat treatment and mixing; (IV) continued breastfeeding at least until the third year; and (V) a package of responsive caregiving throughout the period of nutritional dependency; particularly during the transition to complementary feeding. Humans evolved to begin consuming complementary foods at about six months of age (Sellen 2007, op. cit. Sellen 2007). Clinical and epidemiological evidence shows that human infants have not evolved to make efficient use of other foods before six months (Dewey et al. 2001, op. cit. Sellen 2007; Kramer et al. 2003, op. cit. Sellen 2007) and suffer deficits and increased morbidity if not exclusively breastfed (Cohen et al. 1994, op. cit. Sellen 2007; Kramer & Kakuma 2002, op. cit. Sellen 2007). The frequency of suckling and volume of milk consumed do not necessarily diminish after six months in health babies, and as the complementary feeding phase comtinues until the third year of life, breast milk remains an important, source of nutrients and immune protection. (**AS: Epigenetically transmitted maternal patho-information-engrams may become exposed to the immune systems of babies through breast**

milk consumption and partially erased from the biocybernetic system of the body through active immune interaction. This requires verification, but if relevant, would implicate further significant health benefits of extended breastfeeding, notably in the context of recursive systemsecological healing: 2.1.2).
It was estimated that breastfeeding beyond two years was the norm in between 75 % (Nelson et al. 2005, op.cit. Sellen 2007) and 83 % (Barry & Paxson 1971, op.cit. Sellen 2007) of small-scale societies and that the modal age at weaning was c. 30 months (Sellen 2001a, op.cit. Sellen 2007; Sellen 2001c, op.cit. Sellen 2007). (AS: Section Table). Within relatively broad limits, human lactation performance seems to be well-buffered fom fluctuations in maternal condition, nutrient supply (e.g. Rasmussen 1992, op.cit. Sellen 2007) and physical activity; provided that healthy fat depletion (of adequate fat stores accumulated during pregnancy) and nutritionally adequate complementary feeding is applicable. For normal-term and preterm babies, the lower bound for safe complementary feeding is around six months, as determined by constraints on the evolution of physiological features relating to the growth and maturation of infant systems; affecting immune, feeding and digestive competency.

Milton (1999): Childhood nutrition. Another important aspect of meat-eating concerns the increasing importance as evolution progressed, of higher-quality, volumetrically concentrated foods for infants and children. Protein quality is of great importance in rapidly growing young animals which are actively depositing new body protein (Lozy et al. 1980, op. cit. Milton 1999). Due to the increased ratio of metabolic requirements to gut capacity in homeotherms (Kleiber 1975, op. cit. Milton 1999); Demment & Van Soest 1985, op. cit. Milton 1999), eating a diet high in bulky plant material could pose virtually insurmountable probems for small children, with their high energetic and nutrient demands (Liebermann 1987, op. cit. Milton 1999), as well as large brain relative to body size. (**AS: Breastfeeding should ideally provide for an appropriate nutrition of infants in this context and maternal nutrition during lactation should *inter alia* include the nutritional components listed below**). Raw meat, organs, brains, viscera, and bones are concentrated sources of iron, calcium, iodine, sodium and zinc, vitamin A, many B vitamins, vitamin C and other essential micronutrients, not to mention high quality protein and fat (Lieberman 1987, op. cit. Milton 1999; Carpenter 1994, op. cit. Milton 1999; Milton, 1993, op. cit. Milton 1999).

(Paronen et al. 2000). DL AUTOIMMUNITY-paronen RE BREASTFEEDING.

Table 2.6b Breastfeeding
McDade (2003): Breastfeeding can be understood as a partial solution to the competing life hidstory challenges of rapid growth and immunological naivete. Breastmilk delivers the appropriate balance of macro- and micronutrients for rapid brain and body growth through the first 4-6 months of life (Institute of Medicine 1991, op. cit. McDade 2003; Pierse et al. 1991, op. cit. McDade 2003). High concentrations of nonspecific immune defences such as lactoferrin, lysozyme, and complement proteins inhibit pathogen colonization and growth in the neonatal gastrointestinal and respiratory tracts; and pathogen-specific defences are provided in the form of secretary IgA; providing antimicrobial, anti-inflammatory and immunomodulating properties for the immune system of the neonate (Goldman 1993, op. cit. McDade 2003). The mother shares her immunologic experience with

the infant, thereby conferring some specific immunity which could not be otherwise attained timeously by the infant. Exclusive breastfeeding generally does not continue beyond infancy since by about six months maternal milk production has reached an upper limit. Supplemental foods then become necessary to meet the expanding requirements for protein, calories and micronutrients for the fast-growing infant (Institute of Medicine 1991, op. cit. McDade 2003).
McDade et al. (2014): Elevated concentrations of C-reactive protein (CRP), a biomarker of inflammation, predict increased cardiovascular and metabolic disease risk in adulthood. Compared with individuals not breastfed, CRP concentrations were 20.1 %, 26.7 %, 29.6 %, and 29.8 % lower among individuals breastfed for less than 3 months, 3-6 months, 6-12 months and greater tha 12 months, respectively. Apparently, consumption of breast milk in infancy has lasting effects on inflammation by shaping regulatory pathways during sensitive periods of immune development (McDade 2012; Field 2005, op. cit. McDade et al. 2014). Effects of breastfeeding, through programming of relevant metabolic pathways, are also associated with reduced risk of overweight later in life (Harder et al. 2005, op. cit. McDade et al. 2014). Breastfeeding according to appropriate recommendations are thus anticipated to reduce levels of chronic inflammation in adulthood and result in lower riskfor chronic degenerative diseases of ageing.

BREASTFEEDING PLUS
McDade-breastfeeding
BEASTFEEDING-CHRONIC DISEASE-kelishadi-2014
BREASTFEEDING-victoria-pdf
BRESTFEEDING-hanson-IMMUNOLOGY
BREASTFEEDING-IQ-caspi
BREASTFEEDING-akobeng-coeliac disease

MS LACTATION-fleischer

MS LACTATION-greer

LACTATION-cisco-2015

American Academy of Pediatrics (2012): Policy statement on breastfeeding.DLbreastfeeding

Mutter-Kind Immuninteraktion.

Surplus mortality and morbidity in children likely related to nutritional deficits associated with premature weaning. Exclusive breastfeading for 4-6 months, followed by continued partial breastfeeding into the second year of life promotes infant and child health (Filteau 2000, op. cit. Kemkes-Grottenthaler 2004).

Heinrichs et al. (2002): In animal studies it had been found that lactation was associated with a marked blunting of stress responses to physical and psychological stress. In their review the available data for women suggested that breast-feeding supresses the HPA axis stress response to physical and psychosocial stress; providing some transient stress protection to the breast-feeding mother, which may plausibly also benefit stress protection of the newborn.

Mothering. Sapolsky (2004): Frequent licking and grooming by rat mothers increases the number of hippocampal glucocorticoid receptors in their pups, leading to tighter regulation of stress hormone levels. DNA methylation of the glucocorticoid receptor gene and acetylation of histones early in life provides a mechanism for these permanent changes in stress responses. As adults such rats have tighter regulation of the secretion of a class of stress hormones (glucocorticoids), resulting in lower and post-stress levels. Weaver et al. (2004) show how a facit of mothering style leads to a cascade of molecular and cellular changes/alterations, resulting in lifelong changes in the nature of the stress response.

Joseph and Kramer (1996). Weaver et al. (2004), Mirescu et al. (2004)

Fish et al. (2004)

Fragmented, unpredictable and unattentive maternal care during the early years of life (especially baby care) has substantial negative impacts on the developing child. Responsive parenting (taking cues from child) most effective when parents are fully engaged and present (Molet et al. 2016): Refs therein

Sroufe (2005) MATERNAL sroufe

Meaney (2001) EPI-meaney-NB

Motherhood and career

As has been outlined, reproduction is very demanding on the energy metabolism in human females (Jasienska 2003). Any demands placed on female physiology resulting in an increase of basal metabolism, such as increased physical activity, results in energy costs at the expense of reproduction. Increased basal metabolism also interferes negatively with fat accumulation during pregnancy (of notable importance for lactation). Such increased basal metabolism of females increases their vulnerability to conditions of energy deficits, inducing reproductive suppression as an adaptiv response (Jasienska 2003).

Career stress: in competitive-performance sympathetic mode
Shielding of prenatal and postnatal offspring against population density-related stress
Television Knaul (1985): p 335, 340-342, 346/347 Google
Auditory noise stress: p355/356, 358-359, 360, 361, 362-364, 365-368, 369-372-376, Google
Vermeiding jeglicher Giftstoffe (Verschiedene Bestandteile in Körperpflegemitteln wie unter anderm Aluminiumhyroxid in Deodorants und Antitranspirants; Genussgifte: Nikotin, Koffein in Kaffee und Tee) während der Schwangerschaft und Stillzeit ist von äusserster Wichtigkeit (Jentschura& Lohkämper 2014).
Bewusste Schlackenlösung (ob mit Homöopathica, Salzsole, Kräutertees, Obstessig oder durch Fasteneffekte) darf grundsätzlich nur ausserhalb der Schwangerschaft und Stillzeit praktiziert werden (Jentschura & Lohkämper 2014).
Ketone: McCarty et al. (2015)AUTOPHAGY
Auch Babys und Kinder sollten basisch Baden (Jentschura & Lohkämper 2014).
Special precautionary measures in order to ameliorate career stress of working mothers so that occupational stress effects during gestation and mothering (lactation) are minimized (predominance of the parasympathetic state of the nervous system must be achieved).

Kindheit.
MS-CHILDFHOOD-INFLUENCES-gilman
MS-CHILDFHOOD-wickrama
MS-CHILDFHOOD-fox
MS-CHILDFHOOD-hertzman
DL-CHILDFHOOD-richards
DL-CHILDFHOOD-kajantie
DL-CHILDFHOOD-peck
MS-CHILDFHOOD-reiss
Obesity EPIE-metabolic syndrome ?
Myopia Kurzsichtigkeit: Davis (1972); Manifestation of stress. Associated with undersupply or faulty absorption of Ca (lense muscle tension), rapid growth, inadequate diet, allergies. When the adrenals are exhausted, fluids pass from the blood into the tissues, and because of the eyes of the young are still slightly elastic, the

increased pressure forces the eye ball to elongate slightly. Cordain et al. (2002b) MS cordain myopia **MS EPI-bell-twin-myopia**

Association between uric acid, high IQ, myopia and gout (Sofar & Emery 1981). Section 2.4.1.7c

Ramessur et al. 2015 MS: Myopia EPIE-adrenal fatigue

Tonsillektomie (Thonon 1983).

Cognitive competence

Bei zu hoher Patho-Engrammbelastung (niedrige Kampf-Flucht Reaktionsschwelle: 2.3.2) ist die Effizienz geistiger Arbeit herabgesetzt. Aufnahme, spontane Bearbeitung und fliessende Wiedergabe von Information (thinking on your feet) ist gestört (Internalisierungsblockade). Mit einer niedrigen Kampf-Flucht Reaktionsschwelle schaltet das Gehirn spontan/unbewusst um in den Kampf-Flucht Modus (vor allem unter Stress) wenn konfrontiert mit neuer Information. Damit ist die rationelle Verarbeitung der neuen Information vorerst blockiert (being in a state of sympathetic overarousal: Gedgaudas 2011). Erst später (delayed) wenn die Information integriert wird im Nicht-Kampf-Flucht Modus (in parasympathetic mode) kann eine effektive geistige Verarbeitung dann stattfinden. In diesem Rahmen sind auch verschiedene Formen von Lernstörungen (allgemeiner subklinischer Art, ADHS, Legasthenie und andere) zu betrachten (*Information Processing Response Dysregulation Syndrome*). Anxiety syndrome disorders *vide* Scott (2011) similarly are included in this context.

Information Processing Response Dysregulation Syndrome (IPRDS).

Auf Grund einer niedrigen Kampf-Flucht Reaktionsschwelle dominiert der sympathikone Funktionsstatus zu Lasten parasympathikoner Funktionalität.

As explained (2.3.2), high epigenetic patho-information-engram loadings are associated with compromized functional metabolic efficiency (low vitality status) and low fight-flight reaction thresholds. New information (such as representaed by a food item or new information on the mental level) is then initially considered as an enemy by the body and subconsciously responded to in fight mode (sympathetic arousal); preventing proper information processing, which requires the body to be in parasympathetic mode (refer also to Miller et al., 1999 *re* Fragile X Syndrome). This is the basis of allergic reactions to information (food allergens or psycho-allergic

responses: irritability, aggressive responsiveness, relatively low-intensity daily stressors are over-experienced, over-reacting emotionality). Sympathetic nervous activity at times of perceived stress/emergency results in the secretion of adrenal medullary hormones that act on autonomic effector sites as to mimic, as well as to potentiate, the effect of widespread sympathetic discharge. Slowed, delayed destruction of these hormones have the effect of prolonging sympathetic excitation (Cannon, op. cit. MacLean 1990). Information processing (food digestion, cognitive processing) can only take place efficiently if and when in the parasympathetic mode; not in fight-flight alarm reaction mode. Responding to information in a fight-flight mode (on the basis of a low fight-flight reaction threshold due to reduced vitality arising from epigenetic pathoinformation-engramload accumulation: primary causality) can result in subclinical cognitive inefficiencies and is typically associated with clinically defined disorders such as ADHD, dyslexia and others, forming a group of disorders here termed ***Information Processing Response Dysregulation Syndrome*** (IPRDS: including both subclinical and clinical cognitive inefficiencies). Whereas relatively smaller (increasing) percentages of people in populations experience clinical disorders, subclinical cognitive inefficiencies may apply to the majority of people in populations with accumulated patho-information-engram loadings (such as in contemporary Caucasians generally).

ADHD (ADHS: Aufmerksamkeits-Defizit-Hyperaktivitäts-Störung) is part of the *Information Processing Response Dysregulation Syndrome* (IPRDS). Der Zusammenhang zwischen Allergien und Hyperaktivität ist seit langem bekannt und bestätigt (Rochlitz 1989). Damit lässt sich die Hyperaktivität bei Kinder als eine Reaktion auf Allergene im Alarm- und Anpassungsstadium (*vide* Selye 1978) erklären (Rochlitz 1989). Solcherart Anfälligkeit ist bei einer niedrigen Kampf-Flucht Reaktionsschwelle zu erwarten (2.3.2); als eine Art von psychoallergischer Reaktion auf Reizüberflutung. ADHD is the most common neurobehavioral disorder presenting in children and such children represent a group at risk in respect of their further emotional and social development (Mousain et al. 2011).

These findings underpin the links between the anxiety disorder syndrome (ADS), neurological disorders (IPRDS), central nervous hyperexcitability, allergies, low fight-flight reaction thresholds; ultimately linked to metabolic functional inefficiencies as a result of accumulated (epigenetic) patho-information-engram loading.

Das Vorkommen von Legasthenie und Lernschwäche bei Kindern ist ansteigend (Jentschura & Lohkämper 2014). Lernhilfen sind angesagt; sowie Gehirnintegrationsübungen nach Rochlitz (1989). Aber die besagten Lernstörungen sind Symptome deren grundsätzliche Ursächlichkeit (ultimate causality) bei einer Pathogen-Engramminformationsbelastung (Funktionsinsuffizienz) zu finden ist (). Auf Grund einer niedrigen Kampf-Flucht Reaktionsschwelle dominiert der sympathikone Funktionszustand und es kommt damit zu einer spontan-kurzfristigen Ausschaltung parasympathikoner Funktionalität, dass heisst, zu einer momentanen geistigen Verarbeitungsblockade im Ansturm neuer Information (Internalisierungsblockade). In a state of subconsciously perceived stress, new information is subconsciously interpreted as an intrusive insult; prompting the fight/flight response (MacLean 1990: Sympathetic mode: Bewältigung von Umgebungsanforderungen, Mobilisierung interner Überlebensressourcen, Agression) zu Lasten parasymphatikoner Funktionalität (MacLean 1990: Parasympathetic mode: promotion of a stress-free mental state, promoting digestion and elimination, involving the activation of bladder and gut functions; promotion of storage of sugar, fat and protein; preparing the organism for rest and sleep).

Auf der Grundlage solcher Belastung (epigenetic procursive patho-information-engram load: primary causality) ist auch generell ein Magnesiummangel zu erwarten (secondary causality). Sircus (2014): Magnesium acts as a natural guide or valve in the brain synapses that regulates influx of calcium into postsynaptic channels from presynaptic neurons in parts of the brain that are involved in mood and behaviour (e.g. hippocampus). With inadequate magnesium (calcium toxicity), this function becomes altered and irritability, anxiety, depression, ADHD, mania, hypomania, bi-polar disorder, hyperexcitability, and perhaps some psychoses, result (Table 2.5.1.3b: The Magnesium Factor). Durlach et al. (2000) describe the pathophysiolpgy of central nervous hyperexcitability due to magnesium deficiency (see also Mousain-Bosc et al., 2004: Symptoms of hyperexcitability such as aggressivity, impulsivity, scholar inattention were reduced after 1-6 months of Mg-Vit B6 supplementation treatment). Mousain-Bosc et al. (2006a) berichteten über die Wirkung von Magnesium-Vitamin B6 Supplementierung auf ADHS Symptome bei Kindern. Während der Supplementierungsperiode (erhöhte intraerythrozytäre Mg^{2+} Werte) waren Hyperaktivität, Hyperemotionalität und Agressivität bedeutend reduziert und Aufmerksamkeit in der Schule erhöht. Similarly positive results were obtained in the

case of autism (Mousain-Bosc et al. 2006b). Curtis & Patel (2008) review nutritional and environmental approaches in the treatment of autism and ADHD.

Ferner ist des öfteren eine Verpilzung anwesend (secondary causality; ultimately a reflection of metabolic dysfunctionalities due to patho-information-engram loading, resulting in a favourable terrain for fungi). Diese Pilze sondern Stoffwechselgifte ab wie Acetaldehyd und Aflatoxine. Schwedische Forschungsergebnisse haben diese Toxine als ursächlich für Legasthenie erkannt (Jentschura & Lohkämper 2014). In diesem Zusammenhang empfehlen Jentschura und Lohkämper (2014) eine Entpilzung durch Entsäuerung und Zuckerverbot. Legasthenie und verwandte Störungen eines gestörten Kampf-Flucht-Verhaltens (Psycho-Allergie; Aggressivität, Hyperaktivität, Passivverhalten, Depressionen) sind symptomatisch verbunden mit Mykosen (Jentschura & Lohkämper 2014); insbesondere *Candida albicans* (Rochlitz 1989).

Legasthenie wird zunehmend als Integrationsstörung des Gehirns erkannt (Rochlitz 1989). Dies gilt auch für Störungen im allergischen Formenkreis. Acetalhyd/ Formaldehyd sind von besonderer Schädlichkeit. Acedalhyd stört, unter anderem, die Rezeptoren für Acetylcholin, den wichtigsten Überträgerstoff im Corpus callosum (Rochlitz 1989).

EPIE-ADS 2.1.3.1

Nemeroff (2004): Emerging literature suggests that traumatic experiences early in life increase the risk of mood and anxiety disorders in genetically predisposed persons. Long-lived alterations in the corticotropin-releasing factor (CRF) system and stress responses underpin this vulnerability.Women with histories of abuse and current depression exhibit the greatest dysfunctionalities in the hypothalamic-pituitary response system. Surrogate parenting/anti-depressant treatment. Re ADHD: Nigg et al. (2010). This type of interplay early in life could modify ADHD risk and/or its later consequences (Mill & Petronis 2008). Such epigenetic effects can be transmitted across generations and potentially also be reversed (Thapar et al. 2013).

Fortschreitende Rekursionsheilung ist hingegen notwendig um diesen Zustand, as generally for the anxiety disorder syndrome (Scott 2011) sowie andere IPRDS Störungen, grundlegend **ursächlich** zu heilen und damit auch eine **epigenetische Vererbung zu verhindern.**

Adrenal fatigue

Under present-day conditions of stress experienced in Western societies, adrenal fatigue and related forms of hypocortisolism are manifesting widely in any given population (Wilson 2014). Chronic exposure to stress results in chronic engagement of the fight-flight mode and sympathetic nervous system (Head & Kelly 2009). In response to chronic activation of the hypothalamic-pituitary-adrenal (HPA) axis by stress, cortisol levels are sustained at relatively high levels to cope with the demands of such stress levels. Such high sustained levels then lead towards the development of metabolic syndrome and associated diseases later on (such as late onset diabetes, heart disease, cancer: op. cit. Wilson 2014). Elevated levels of cortisol may generally have inhibitory effects on the reproductive, growth hormone and thyroid axes (op. cit. Anderson). However, as expected according to the General Adaptation Syndrome (Selye 1978), a stage of exhaustion will be reached after prolonged stress activation of the HPA axis and cortisol levels will drop and become unresponsive to stress stimuli, resulting in stress-induced adrenal dysfunction (Anderson 2008). Adrenal fatigue is generally a subclinical condition featuring typical patterns of fatigue (early morning fatigue, midmorning low, mild to severe afternoon lows, improved energy after 18:00 h, more refreshed in the morning if able to extend usual sleeping time with about two hours) and other signs and symptoms such as exhaustion over much of the day, with reduced productivity, symptoms of hypoglycaemia, difficulty of focusing and concentrating, irritability and a genera feeling of being overwhelmed (op. cit. Wilson 2014). Treatment primarily involves stress minimization, appropriate exercise and nutraceutical management of adrenal dysfunction (Anderson 2008; Head & Kelly 2009; Wilson 2014). Therapeutical substances include complex B-vitamins (especially pantothenic acid), vitamin C, magnesium citrate (400 mg before bedtime) and adaptogens to balance the HPH axis; Siberian ginseng (*Eleutherococcus senticosus*), Ashwagandha (*Withania somnifera*), Maca (*Lepidium meyenii*) and Licorice (*Glycyrrhiza glabra*). Based on the clinical experience by Wilson (2014), subjective improvements can be expected within 4-6 weeks. Depending on severity of the adrenal fatigue condition full recovery may take anything between 6 months and two years. In terms of diet, **Wilson (2014) recommends the combination of protein, unrefined carbohydrates and good fats in every meal. The protein must be from an animal source as it turned out that animal protein was an essential part of the dietary recovery protocol for adrenal fatigue** (Wilson (2014). Ongoing persistance states of adrenal dysfunction requires life styles promoting sustained recursive self-healing ().

Crucial components in this context involve appropriate treatment (catalysm of functional insufficiencies due to PIE-loading), a Peri-Arctic-diet/lifestyle (Table 2.5.1.5e); including intermittent and/or annual extended fasting (2.1.2; 2.1.3.3).

Anderson (2008) OK
Wilson (2014) ADRENALFATIGUE
Head & Kelly (2009)

Kinderkrankheiten.
Entscheidend ist dass (fieberhafte) Erkältungs- und Infektionskrankheiten, inbesondere die sogenannten Kinderkrankheiten, völlig und rekursionsunterstützend ausgeheilt werden durch natürliche Behandlung unter ärztlicher Aufsicht (Rauch 1967, 1986). Siehe auch **2.3.3 Gesundheitspflege**.

Ernährung förderlich für einen erhöhten Stoffwechselumsatz (Rekursionsentschlackung). Kein Fasten im Kindesalter und den Entwicklungsjahren (Buchinger 1987).
Fieber indiziert eine gute Abwehrlage (Carus op.cit. Külken 1985) Tabelle Cancer patients, for example, lack fever reactions in their years prior to the emergence of clinical cancer ().

Many parents, themselves living a successful life and relatively healthy, are crudely awakened to the reality of finding themselves confronted with their children turning out less mentally and socially competent, and less healthy. This then is the expected outcome of transgenerational procursive accumulation of epigenetic patho-information-engram loading (2.1.2a/2.1.3). This implies that recursive healing considerations are of crucial relevance for all (prospective) parents.

practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

b) Adult-phase health considerations

Ernährung.

Beide sich abwechselnde Ernährungsphasen sind demnach notwendig für den fortgesetzten Verlauf von Rekursionsheilung zu optimaler Gesundheit und Leistungsfähigkeit. Besondere Erwägungen gelten für die Ernährung während der Schwangerschaft und Stillzeit.

Cooking:

Steaming best conserved flavonoid and individual hydroxycinnamonoyl derivatives in broccoli, while high-pressure and conventional cooking resulted in leaching losses. Microwaving resulted in high losses (ranging between 74-97 %) of the tested compounds (Vallejo et al. 2003).

Exercise

DIET-HORMESIS-gomez-pinilla
EXERCISE-HORMESIS-radak

Daily life style rhythm

Late breakfast/early dinner, intermittent fasting, exercise, afternoon naps (see Traditionally Healthy Living populations) Maimonides ex

Gesundheitspflege.

Medical Disclaimer

All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

Jentschura & Lohkämper (2014) listen die Schadstoffrückstaufolgen von dem Gebrauch der Verhütungspille (unter anderem Giftstau, Gewichtszunahme, Wasserstau).

Progressive Abnahme der Kinderzahl über Folgegenerationen, vor allem in begabten, erfolgreichen Familien in Europa. Eine Gegensteuerung des genealogische Aussterbens Europas erfordert rekursionseffektive Heilungsmassnahmen und Lebensstile.

Im Rahmen erfolgreicher Rekursionsheilung ist es extrem wichtig dass alle akut fieberhafte Erkrankungen und Entzündungsprozesse, unter ärztlicher Aufsicht, vollkommen zur Ausheilung gebracht werden. Viel Schlaf, eine reichliche Flüssigkeitszufuhr (Mineralwasser, Kräutertees, Gemüsesäfte) und Darmreinigung durch Kamilleneinläufe. Fortzusetzen bis zum Ausklingen jeglicher Fieberschübe. Hensel (1980) betont den therapeutischen Wert bei Fieber (> 40°C) von physikalischer Kühlung welche nur die Temperatur senkt aber andere für die Fieberwirkung wichtige Funktionen (unter anderem: Stoffwechselsteigerung und pathoinformationslöschende Immuninteraktionen) erhält (keine Anibiotika, Antipyretika oder Schmerzmittel).

Die Ursache vieler degenerativen Erkrankungen ist die Unterdrückung der körpereigenen Krankheitsabwehr (Reckeweg 1986). Vor allem durch die Unterdrückung von akut fieberhaften Erkrankungen durch stark wirksame Pharmaka (Anti-Biotika; fiebersenkende, entzündungshemmende, schmerzunterdrückende Mittel), und damit einer Blockierung der Ausheilung, kommt es zur Belastung des Abwehrsystems und der Stoffwechselfunktionen; und letztendlich zu degenerativen Erkrankungen (*inter alia* Reckeweg 1986, Schleicher 1991) Fieberkontrolle mit lauwarmen Hals- und Wadenwickeln ist einer Fieberunterdrückung mit Antibiotika und Schmerztabletten vorzuziehen (unter fachärzlicher Aufsicht).

Haut als Organ (Reckeweg ?)

Rauch (1967): Infektionskrankheiten

Rauch (1986): Darmreinigung/Darmsanierung

Fasteneffekte bei Fettleibigkeit und Magersucht (Buchinger 1987) Clarify: fasting nd body condition types.

Mit aktiven Rekursionsheilungsbestrebungen, beziehungsweise ein rekursionsunterstützender Lebensstil, sollte so früh wie möglich im Leben begonnen werden; nicht erst nachdem Gesundheitsstörungen eingetreten sind.

Transgenerational recursion healing:

- Peri-Artic-Diet-Lifestyle
- Active PIE loading elimination (extended fasting, function-catalysis, Mennerich principles, fever)
- Intergenerational health considerations (pre-conception conditions, pregnancy, lactation, early childhood) Gender-differentiated complementary roles for fitness maximization.

Table 2.6c Components of Transgenerational Recursionhealing

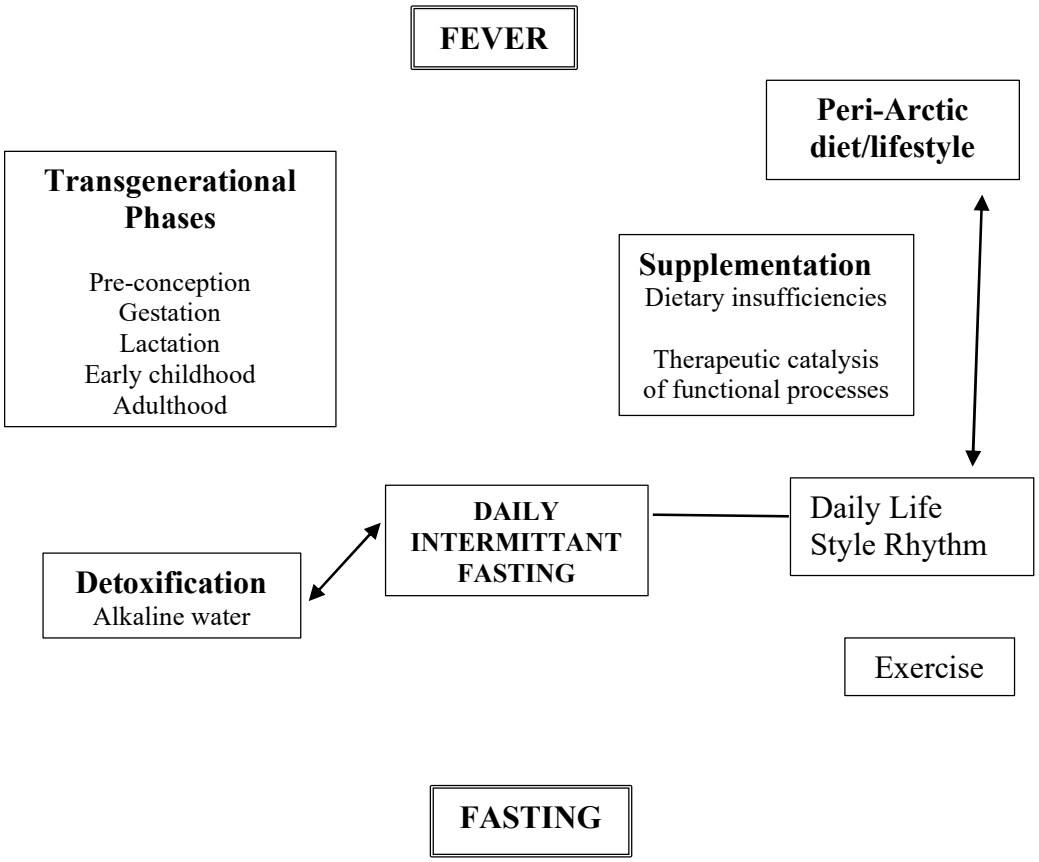


Table 2.6d Lifestyle imperatives for recursive healing (Systemsecological Healing)

Transgenerational project
Childrearing (pre-conception, pregnancy, breastfeeding, childcare)
Peri-Artic-Diet-Lifestyle
Low density stress refugia/circumstances

Medical Disclaimer
All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

3. EUROPE UNDER DEMOGRAPHIC INVASION IN THE ERA OF GLOBALIZATION

3.1 Life history survival strategies

3.1.1 Globalisation: a first-time, fateful era in human history

For the first time in the history humankind have their numbers reached an extent that world-wide overpopulation has become a reality. The sustainability of systems-functionality in the spheres of economics, finance and ecology is threatened (Laszlo 2008). Starvation, increasing unemployment, destruction of the environment, ousting/displacement of native populations from their homeland habitats, widespread economic dysfunctionality and therewith associated inter- and intra-state conflict; climate effects (unpredictable climate change effects and impacts), povery, starvation and conflict (scientists predict the increasing prevalence of uprisings, civil war and war for scarce resources: Knaul 1985), international migrations and intra-state displacements (an estimated 65 million displaced persons globally *vide* UNHCR 2016), as well as escalating urbanization. An estimated 795 million of 7.3 billion people globally are suffering from chronic undernourishment (2014-2016; FAO: The State of Food Insecurity in the World). Less than 5% of the population occuring in developed regions and 12.9% in developing regions suffer from undernutrition (779.9 million: Africa: 232.5 million, 20.1% of the population of Africa; Asia: 511.7 million, 12.1%; Latin America/Caribbian: 34.3 million, 5.5%; Oceana: 1.4 million, 14.2%). Third world countries have the highest starvation rates and yet also the highest rates of population growth. It is furthermore irrelevant whether it would be technically feasible to produce enough food for the burgeoning populations of the world. Food production and transport remain subject to the laws of logistics and economic viability; which means that sufficient buying power of product recipients must be available. It is no longer possible to deliver or sustain middle class prosperity to the entire population of the world (Hormann 1985). The rich become richer relative to the poor, not only as a result of higher wealth creation and wealth monopolization capacities of the former, but increasingly so due to wealth dilution among the latter. The combination of increasing population densities and declining economic efficiencies, as experienced

during the era of globalization, is inevitably and unavoidably manifesting in wealth dilution in middle class and poor population segments.

Limits to growth do not only apply to the economy, but also to human population numbers. Lutz & Qiang (2002): The global human population reached one billion by c. 1800; after another 130 years (until 1930) two billion was reached. The six billion mark was reached in 1999. The growth rate peaked at 2.1 % in the late 1960s and then progressively declined; nevertheless, mid-range population projections foresee a further population increase to 8 to 10 billion by the end of the 21st century. Total fertility rates (TFR: average number of children per women under a period perspective) declined modestly in most parts of the world, with Africa lagging with still having had above six children per women on average through the late 1980s. Forecasted regional population sizes for the years 2000 and 2100 (Lutz et al. 2001, op. cit. Lutz & Qiang 2002), 2000/2100 in millions: World 6055/8414; North Africa 173/333; Sub-Saharan Africa 611/1500; North America 314/454; Latin America 515/934; Central Asia 56/106; Middle East 172/413; South Asia 1367/1958; China region 1408/1250; Pacific Asia 476/654; Europe 813/607 (Western Europe 456/392; Eastern Europe, including European part of the former Soviet Union, 357/215). Europe: 13.4% of world population (2000) to 7.2 % by 2100 (2.3.4f).

As Demeny (2011) notes, resource constraints (including environmental constraints), in the face of a global human population heading toward nine billion by mid-century, are to be seen as highly problematic. Optimists see all countries progressing towards further economic growth being achievable and that this could even reverse the growth in global population numbers. However, this view of world economics and population dynamics is dismissed as unreasonably optimistic, if not naïve (Daly 2008; Dorius 2008). These authors, *inter alia*, recognize that the twenty-first century is being characterized by the combination of growing material consumption per capita and further increases in population numbers which are bound to be unsustainable in the face of biophysical limits of the globe. This suggests that the twenty-first century would be characterized by increasing domestic economic and social problems, political instability and international conflict (Demeny 2011). The unfolding of this scenario can already be observed.

Der Verhaltensforscher Konrad Lorenz (Nobelpreis 1973) identifizierte acht systemfunktionelle Gleichgewichtsausrastungen der heutigen Menschheit, insbesonders bezüglich dem überzivilisierten Teil der heutigen Menschheit (Lorenz

1978): Überbevölkerung, Verwüstung des Lebensraumes, der Wettlauf mit sich selbst, Wärmetod des Gefühls (Lorenz 1986: Generationskonflikt, Werteverfall, Sinnentleerung), genetischer Verfall, das Abreissen der Tradition, Indoktrinierbarkeit und Kernwaffen. Emerging socio-psychological conditions in the western world 'Wie im alten Rom' (Sichelschmidt 1973); consistent with the predictions by Spengler (1923: Table 1.1b; 1.1) predictions 2000+ Konzentrierung von Macht und Finanzresourcen zu Gunsten von bereits mächtigen und finanzstarken internationalen Gruppierungen (Multinationale Konzerne und Dominanz kosmopolitischer Win-lose Plutokratien) erreicht ungeahnte Ausmasse. Global profit-driven resource exploitation by multinational corporations; largely in disregard of the interests of local populations and the environment.

Survival of human population groups (ethnic entities) and representation of their offspring into the future in the face of selection during the course of evolution required/requires that its members had access to resources (land as resource base), sufficient competence for efficient resource use and accumulation (food storage for periods of food deficits); in combination with the capacity to defend their resources against intruders (evolution-competence). Ongoing human population increases have reached unsustainable proportions in this era of globalization. Sink areas where population surpluses from source populations could find refuge for survival no longer exist to any extent. The proportion of humans suffering relative resource shortages has increased disproportionately relative to those relatively wealthy (wealth creation capacity). Population groups differ in their capacities to keep wealth creation rates in alignment with their population sizes/growth rates. In this context, those that achieve this alignment are termed wealth-competent and those that do not, wealth-deficient, respectively. Wealth-deficient population groups are thus here defined as population groups no longer capable of creating sufficient wealth to adequately cater for themselves within their own country. Wealth-deficient countries are usually entangled in a demographically-driven poverty trap (2.3.4g); placing these countries on a socioeconomic-psychological boom to bust trajectory (2.3.5a). During initial phases along this trajectory (boom phase) levels of population density and resource competition are relatively low and psycho-social harmony prevails. With progression towards the bust phase, as the relation between population density stress and per capita wealth becomes successively more unfaviourable, competition for livelihood resources intensifies, poverty and psychosocial intolerance levels increase, increasing ideological

polarization manifests, increased vulnerability to emerging disease erpidemics, crime rates and civil unrest increase and the incidence of violent conflict escalates; often culminating in population displacements and civil wars (2.3.5a). Under these circumstances then/now manifesting in this era of globalization, waves of migrations from wealth-deficient populations towards wealth-competent countries are evident (scramble competition for resource monopolisation by the former *versus* interference competition, i. e. territoriality, for resource defence by the latter). The demographic invasion pressure towards wealth-competent-population areas will continue to escalate (2.3.4f). Unless wealth-competent populations can maintain their territoritality (requiring evolution-competent leadership), their survival as viable populations is in jeopardy (by being displaced into minority status and/or through assimilation). The global activities and impacts of the (remaining) wealth-competent populations will be greatly diminished in the post-globalization era and wealth-deficient populations will become subject to the unblunted forces of natural population regulation (war, famine, disease). Human population densities will then be much reduced globally.

In this era of globalization, for the first time in the history of humankind, we have an emerging situation where demographic and socio-economic constraints globally induce intra- and intercontinental chronic mass migrations (refugee migrations) from poorer regions/countries to wealthier ones. Unless wealthier countries can maintain their border integrity, resident populations will be wiped out in the medium to long-term future. Their 'sacrifice' will however not be able to pre-empt a global implosion of human population densities through systemic population regulatory mechanisms (famine, diseases, escalation of violent competition for scarce resources). Europe is endangered the most due to the lack of evolution-competent leadership (Table 3.3) and its vulnerable demographic status (2.3.4; 3.1.3).

Weltweitverbreitete Migrationen eskalieren. Wenn die Mehrheit (global gesehen) ihre Überlebensbedürfnisse nicht mehr befriedigen kann, wird sie sich die notwendigen Resourcen mit Gewalt nehmen (Bundesministerium für wirtschaftliche Zusammenarbeit. Hrsg. Durch Partnerschaft Probleme lösen. Bonn, Deutschland); und zwar dort wo sie (noch) vorhanden sind; vornehmlich in der Ersten Welt, speziell Europa. Dieser Zeitpunkt ist jetzt angebrochen (3.1.3: Demographic colonization of Europe). **Thus, in this era of globalisation, we have an existential conflict of interests of unprecedented proportions between masses of people seeking a better life through migration and the longer-term survival of residents in targeted,**

relatively wealthier countries. Zum grossen Teil aus Eigenverschuldung der europäischen Staatsführungen ist Europa (Deutschland) als das schwächste Glied zum Ziel für solcherartige Migrationen erkannt worden. According to the information available to those seeking a better life elsewhere (media, electronic media), Europe appears as *Paradise*; but they are inadequately informed regarding the socio-economical problems of targeted countries (e. g. unemployment, poor work prospects, skills requirements in order to make a living in the country of destination), escalating intolerance to migrants by residents as the numbers of the former continuously increase, inconveniences/harshness of a cold climate, legal entry requirements and the risks associated with migration. The decision in favour of migration is generally not the best choice for such prospective migrants when taking all short-term and long-term factors into consideration (such as events of economic collapse and potential of mounting inter-group conflict in the target countries). Those that migrate most often become victims of criminal expoitation by human traffickers; for some with deadly consequences. Paradise seekers (economic migrants) that attempt to force themselves into Europe in conflict with entry requirements essentially embark on an illegal venture (demographic invasion). They enter targeted countries on the implicit assumption that there are livelihood opportunities in excess of the requirements of residents (even implying that such livelihoods are owed to them). In the longer-term, what is supposed to happen in times of economic downturns or collapse (invariably to be expected to occur over time)? Economic migrants thus arrive at the doorstep of Europe with unrealistic expectations, most having made bad life choices based on false or incomplete information; many even with an aggressive invasion/infiltration mentality.

Europas Führende geben sich der defaitistischen Meinung hin dass derartige Migrationsströme ohnehin nicht zu kontrolieren sind, bzw. aufgehalten werden können. Solcherart Position ist falsch und reflektiert eine Mentalität nach welcher sich die Betroffenen der Herausforderung einer Problemlösung nicht stellen wollen (Problemflucht; Abwesenheit von evolutionskompetenter Führungspotenz *vide* Tabelle ; und Bruch der Amptseide-oath of office).

Im übrigen läuft das Migrantenproblem bereits an seit über drei Jahrzehnte (Schade 1974, Hormann 1985). Es wäre also genug Zeit gewesen relevante Strategien zu entwickeln basierend auf einem Grundverständniss der Situation im Langzeitkontext.

Geschichtlich betrachtet kamen Migrationen periodisch vor; generell in die Richtung zu Regionen gekennzeichnet durch Bevölkerungs- bzw. Machtvakuen (Kolonisierung). Derzeit finden chronische Massenmigrationen statt, von Ländern (Drittweltländer, auch Zweitweltländer) geprägt durch Armut und damit einhergehendem Konkurrenzkonfikt, in die Richtung zu auch überbevölkerten aber reicheren Länder (Erstweltländer). Dritt- und Zweitweltländer waren impaktiert durch Kolonisierung, während heute Erstweltländer (insbesondere Europa) mit demografischen Invasionen konfrontiert werden. Die friedliche Koexistenz der Völker ist nunmehr globalübergreifend gefährdet.

According to a key **systems-ecological law the peaceful co-existence** among people can only be maintained if **ethnic entities** are not placed under circumstances of mutual **existential competition and mutual threat** or perceived threat.

Zerfallsphase einer Spät-Zivilisation im Zeitalter der Globalisierung. Schicksalsentscheidende Epoche für Europa. Schleichender Genocid der aufnehmenden Gastvölker (fehlende Territorialitätsintegrität)
-Unterschiedliche Lebensstrategien. Hormann (1985)

3.1.2 Life strategies: reproduction, survival and migration strategies

Reproductive fitness as driving force of evolution defines the biological/evolutionary success of individuals. In order to maximize reproductive fitness individuals must maximize the proportion of individuals carrying their own genes in succeeding generations. Inclusive fitness arises as an individual contributes to the success of other individuals in proportion to their genetic relatedness (Geist 1978). To maximize reproductive fitness an individual (groups of related individuals) should minimize expenditure on maintenance in order to conserve maximum resources for reproduction, maintain physiological homeostasis (health) and provide for access to and defence of scarce resources essential for reproduction (Geist 1978). The associated strategy involves resource accumulation (storage) and defence of the resource accumulations through territoriality. Such resource accumulations produce pull factors for invasions due to the associated relative resource surpluses. In contrast, in countries such as China

there would be an absence of pull factors due to the absence of resource surpluses because of prevailing resource use saturation (niche saturation through high population densities of maintenance types: Geist 1978).

The best invasion strategy is to disperse widely (dispersal types) and building up population numbers as opportunities arise. Resource accumulations must be defendable against invasion of competitors (territoriality), otherwise such accumulations become a liability in that they create pull factors for invaders. Pre-emption of any resource surpluses can be achieved by maximizing the number of individuals (maintenance types) per unit of exploitable resource, giving maximum coverage of the landscape (Geist 1978). K-S Reproduktionsstrategie

Rolle von Territorialität bei wohlfahrtserzeugender-und lagernder Taktik (weniger, aber stresstolerante Nachkommen) versus opportunistisch Resourcennutzung/Konsum und Umsetzung in viele stressresistente Nachkommen. The role of territoriality for periartic-European populations: defense of stored wealth (re nutrition/energy costly metabolic performance mode) and space in the face of sensitivity of reproduction and health to population density stress (notably in respect of social harmony, reproductive success and healthy offspring). SECTION BELOW TABLE KNAUL 1985 Territoriality as buffer to transient resource shortages (economic down-turns/collapse) and for the regulation of population density stress. To achieve this, territoriality must be maintained in the face of migrant invasions.

At already relatively high population densities, poorer nations/continents sustain relatively high population growth rates (r-Selection reproduction strategy) whereas richer nations/continents have low or negative population growth rates (K-Selection reproduction strategy). Die ärmsten Länder/Kontinente (r-Selektion) haben nachhaltig höhere Populationszunahmen.

Die Aufrechterhaltung eines genetisch-fixierten Dispersalphenotyps erfordert einen Resourcenüberschuss (in excess of need), eine Situation welche in begrenzten Territorien nur erhalten werden kann wenn die Zahl der Nachkommen relativ eingeschränkt ist (Geist 1978).

Geist (1978): Initially the dispersal phenotype of the colonizers have the advantage over competitors in the area colonized (as occupied by maintence phenotypes) because it is more plastic than the maintenance phenotype of the colonized competitor. By disturbing the delicate balance of coexistence of the colonized it can gain resources at their expense, thereby broadening its ecological niche. This then leads to a saturation phase of the colonizing population in which plastic adaptable dispersal phenotypes in large numbers fill and probe all potential opportunities of a landscape. The invader ought to maintain a dispersal phenotype over many generations, even when the area has been colonized, because of the inherent plasticity of this phenotype (allowing such individuals to continue adjustments to competition and other environmental contingencies). The maintenance phenotype characterizes the holding phase of a population; and as such must be designed to preclude any opportunity for interspecific competitors to expand at their expense. This can be achieved by removal of all resources within the ecological niche, i.e. by maximizing the number of individuals per unit of exploitable resource so as to maximize coverage of the landscape. This is facilitated by reducing individuals to the smallest possible body size. Diversification supports ensuring that all possible resources are actually utilized. Also ensuring the removal of a maximum of resources is achieved as and when the maintenance phenotype can feed/feeds on lower quality food resources (pre-emption of all possible resources). Maintenance phenotypes should select against genetically distant individuals in mate choice in order to reduce heterosis, which is bioenergetically expensive. Such costs may be charged against the costs of reproduction, consequently lowering reproductive fitness. In a tightly packed community each species keeps the other in check by depriving it of critical resources, or of access to them, with minimum expenditure. Competitive abilities are refined by specializing in exploiting resources. The success of such specialized individuals depends on a narrow margin of resources acquired and saved from maintenance for reproduction. It follows that a penalty will be paid by the individual should it mate with a conspecific of a genotype shaped elsewhere and introduced by dispersal. In densely packed communities, this should lead to the rapid isolation of genetic pools adapted to local situations. Therefore, densely packed communities will be communities of specialists and loosely packed communities would involve generalists. From this it is predicted that generalists will not disperse into tightly packed communities of specialists, since they would face several specialists in their respective niches that collectively would deprive them of the resources needed for existence. The converse, i.e. the invasion of specialists into communities of generalists is however quite possible. (**AS: the invasion of specialists into communities of genetically-fixed dispersal-type generalists, such as occurring in Western Europe**).

Resource monopolization strategies/scenarios (largely following Geist 1978).

- **Selection under tropical-type conditions**. Resource monopolization through dispersal and opportunistic use of relative resource surplus aggregations and efficient conversion (Umsetzung) into many stress resistant offspring (low maintenance settings). Propensity towards the redistribution of wealth. Communal sharing of scarce resources (in Africa: *Ubuntu*, Mabovula 2011). A

life strategy based on the reproduction of many stress-resistent offspring (**Table 3.1.2a**: r-Selection reproduction-strategy), even under conditions of relative resource scarcity, is adaptive in the sense of inclusive fitness under tropical-type conditions. (Table **3.1.2a**).

- **Selection under temperate/arctic-type conditions: <u>Dispersal types</u> *vide* Geist (1978): K-selection reproduction strategy. Resource defense through territoriality)**. Accumulation of resource surpluses (wealth), storage thereof and defence through territoriality. Wealth creation efficiency. During colonization of the cold and periglacial zones by *Homo sapiens* attributes of the dispersal phenotypes were genetically fixed in populations exploiting highly variable habitats (seasonal superabundance of forage resources in summer extended over winter by hunting and energy storage). (Dispersal phenotypes: strong development and genetic fixation of i.a. the cortex, fat storage, relatively large body size, capacity for adaptive problem solving competence and planning according to a long-term time horizon). To perpetuate dispersal phenotypes in a finite environment requires resources in excess of need (for high *per capita* investment in offspring: K-Selection reproduction strategy: Table **3.1.2a**). This can only be maintained by keeping the number of offspring relatively low (birth control; reproductive rate sensitive to population density).
- **Selection under temperate/arctic-type conditions: <u>Maintenance types</u> *vide* Geist (1978): K-selection reproduction strategy; relatively high population densities. Resource defense through livelihood saturation)**. Pre-emptive resource use saturation. Low invasibility. Land saturation: pre-emption of resource surpluses (z.B. China). Under conditions of relative resource scarcity due to intra-group competition (high maintenance costs). Under such conditions natural selection favours individuals increasingly more capable of maximizing the amount of resources they can spare from maintenance for reproduction (relatively small body size). Maintenance phenotypes maximizing abilities to compete for resources needed for reproduction (Geist 1978).

As outlined by Geist (19878), under conditions of resource scarcity we have selection for phenotypes able to cope with high intra-group population densities (intra-group competition); either by maintenance (Mongolids: Asian scenario) or K-phenotypes

(Caucasoids: variable, but seasonal superabundance or deficits; resource shortages via intra-group competition: European scenario).

European scenario

In order to cope with the harsh and variable northern environments (conditions of periglacial existence) it was essential and adaptive to maximize physical, intellectual and social development. It is accordingly expected that attributes of dispersal phenotypes required during colonization of the cold zones (a phenotype that is most likely to deal with the the diverse and unexpected) became genetically fixed in species exploiting such highly variable environments (Geist 1978). Plasticity of metabolic performance is geared to cope with such circumstances (Section **2.5.1.1**; Table **2.5.1.1a**). Periglacial populations of humans maximised physical and intellectual development (well-developed physique of adults, large body size: requiring physical exercise and excellent nutrition). The required rearing quality depended on a favourable social milieu, since ontogenetic growth is much affected by the type of home life children experience (Geist 1978). Maximum physical and intellectual development requires the constant availability of resources that can be invested in ontogenetic development and expensive intellectual and social development (Geist 1978). Associated requirements are supported by the periarctic metabolic performance mode (Section 2.5.1.1; Table 2.5.1.1a). Excellent nutrition must be readily available from conception onward (high per capita investment in relatively few offspring; K-reproduction strategy: Table **3.1.2a**). To maintain conditions with resource availabilities (nutritional and space; absence of density stress *vide* Knaul 1985) adequate in fulfilling realtively high needs for reproductive success requires keeping the number of offspring relatively low (Geist 1978). A **K-reproduction strategy** (Table 3.1.2a) and defence of sustained resource adequacy and accumulated resources underpinning high *per capita* resource-level security (K-S reproductive strategy) through **territoriality** are paramount for long-term survival. **Ethnic-linked territoriality** represents the entity of ecolutionary fitness maximization under such circumstances.

Asian scenario

European Paleolithic populations lived in more productive areas and more benign climates than did the Asian and Beringian ones (Geist 1978). The last major groups of

people to evolve were probably the classic Mongolians who are products of the cold ice ages of interior Asia. It is therefore expect that the evolution of people in these areas resulted in better adaption to cold and promoted large brain sizes (Geist 1978). The larger brain sizes are expected to be the product of neotony; since the more neotonous the population the better the chances for extended growth and body organs. Mongolians show the typical neotoneous features such as large brains and reduced secondary sexual characteristics and reduced sexual dimorphism (enlarged brain size a product of extended ontogenetic growth). Phenotypes are expected to invest in diverse mechanisms of maintenance (Geist 1978). A phenotype that maximises abilities to compete for resources needed for reproduction with body size adjusted to no larger than necessary for efficient reproduction is adaptive. Under conditions of intense competition for available resources, particularly when associated with high density of conspecifics/intra-group competition, individuals are expected to intensify their competence to deal with a few or only one strategy of resource exploitation (Geist 1978). Reductions of diversity of behaviours and settling in on a few which have a high return in energy and nutrients relative to the amounts invested (maximised individual *specialization*). Reduced body size is then adaptive so that only tissues are prioritized for development that maximise the adaptive success of individuals in a population of intense intra-group competition (Geist 1978). Land/resource/niche saturation eliminates pull factors for migrations by foreigners (resource niche pre-emption).

Table 3.1.2a Reproduction Strategies		
(Both of the two here differentiated reproductive strategies and associated life history traits are characterized by evolutionary superiority under the conditions of their selection. Any differences in value systems associated with particular strategies are to be respected. Value judgements would be inappropriate)		
Reproduction strategies under r- and K-Selection	**r-Selection Reproduction Strategy**	**K-Selection Reproduction Strategy**
	r-S Reproduction-strategy	K-S Reproduction-strategy
Reproduction tactics (Table 2.2.2a)	Many offspring Early onset of reproduction Short birth intervals	Relative fewer offspring Later onset of reproduction Longer birth intervals
Reproductive investments (Table 2.2.2a)	High numbers of stress-resistent offspring (low *per capita* investment)	Anzahl der Nachkommen niedrig im Vergleich zur Ressourcenverfügbarkeit (Hohes *per capita* Investment)
Reaction dynamics under conditions of resource deficits (Section 2.3.1.1)	Capacity to survive under conditions of resource scarcity and to maintain some reproductive success	Survival and maintenance of reproductive success requires favourable condtions of resource availability
Productivity performance (P performance = Productivity	Transient peaks of productivity Pr > Pt	Sustained productivity performance over time

rate (Pr) x (Pt): sustainability of productivity rate over time)	(Table 2.5.1.1a)	Pt > Pr (Table 2.5.1.1a)
Dynamics of resource monopolization	Consumption opportunism in the present	Long-term wealth accumulation
Dynamics of resource allocation	Resource channeling (*Wealth redistribution*)	Resource accumulation (*Wealth creation*)
Resource acquisition and defence	*Scramble competition*	*Interference competition* (Resource territoriality)
Reaction to *per capita* resource shortages and population density stress	Maintenance of reproductive performance (Section 2.5.1.1)	Restriction of reproductive output (Decline of birth rates under population density stress) (Section 2.5.1.1)

Survival- and migration strategies

When subject to selection under temperate-type conditions (cold seasonality) the peri-artic metabolic performance mode is superior in terms of fitness (2.5.1.1). Generationsübergreifende Wohlfahrtsanhäufung um das Überleben und die Fortplanzungsbasis relativ weniger Nackommen (hohes *per capita* Investment) zu gewährleisten und Schutz durch Territorialität. Diese Strategie der Wohlfahrtsanhäufung zieht feindliche Invasionen an und ist demnach nur evolutionsadaptiv wenn Resourcenschutzterritorialität gehandhabt werden kann.

When subject to selection under tropical-type conditions the tropical metabolic performance mode is superior (2.5.1.1). Zeiträumliche Ressourcenaufspürung (resource tracking) und gleichzeitige Umsetzung in viele stressresistente Nachkommen (Investment in Vielzahl der Nachkommen; niedriges *per capita* Investment). Reaktion auf Ressourcendefizite: Ressourcenmonopolisierung durch Migration (Stressresistenz) auf der Suche nach relativen Ressourcenanhäufungen und Nutzung dieser.

3.1.3 Demographic colonization of Europe

Colonization is an age-old phenomenon where people from one area with relatively high population densities or military prowess and with expansionist vigour invade other areas in order to monopolize inadequately defended/indefensible resources belonging to the people of the targeted areas. Demographic colonization represents a process where migrants from poorer countries infiltrate targeted wealthier countries in order to

monopolize resources (seeking a better life) actually belonging to the people (and their successive generations) of the targeted countries. Demographic colonization has as its outcome a progressively increasing proportion of the population of a country represented by foreigners relative to the native population. It results from migratory penetration into the target country by those seeking a better life (intentional) and disparately high reproductive outputs by non-natives within a country. Refugees from active war situations, in as far as they remain in the guest country, also contribute to the colonization effect.

Coleman (2006): The main finding of the analyses conducted indicate that the ancestry of low-fertility Western European countries is being radically and permanently altered by high levels of immigration from areas of remote geographic origins, with distinctive ethnic and racial ancestry. The estimates and projections related to seven European countries (covering 183 million people in 2005, about half the population of Western Europe: Austria, Germany, Denmark, Netherlands, Norway, Sweden, Great Britain); but were similarly relevant to most of the other European countries with low fertility and high immigration. The analyses confirm that 1) in some industrial countries a rapid change is already apparent in the composition of their populations according to national or ethnic origin aring from from the direct and indirect effects of immigration in the last few decades and 2) projections based on plausible assumptions imply, within the conventional time scale of projections, a substantial alteration of the composition of populations, which if continued in the longer term would lead to the displacement of the original populations into minority positions (termed third demographic transition). If current trends continue, the majority population of indigenous origin in most European countries would be replaced towards minority status relative to populations of recent immigrant or mixed origin. The author concludes that any population with subreplacement fertility maintaining a constant or growing population through immigration will acqire a population of predominantly, eventually entirely, of immigrant origin. In any population with average fertilitybelow replacement, any one minority population with a higher growth rate must in the long term become numerically dominant (Steinmann & Jäger 2000, op. cit. Coleman 2006). The original population is transformed irrespective of whether the growing new populations retain a strict separation of identity or become mixed. The ultimate outcome of replacement is unaffected by whether immigrant populations adopt domestic low fertility rates quickly, slowly or not at all (Coale 1986, op. cit. Coleman 2006).
According the United Nations report on replacement migration (UN 2000, op. cit. Coleman 2006), an average net immigration of 1.4 million migrants per year would be required to the European Union to preserve overall population size, population workforce size and age structure in low fertility European countries. This would preserve the working age population at the level of 1995 up to 2050 (EU-15). The figure of 1.4 million immigrants is close to the actual average net immigration since 2000. If continued that would produce a population of 108 million immigrants and their children post-1995 by 2050; representing 26 % of the EU total population in 2050 (the projected figure not even including existing immigrant populations which had accumulated before 1995). Immigration has become the driving force behind demographic change in many European countries; either by preventing or moderating population decline or

restarting population growth. The natural increase of non-European foreign-origin populations is often greater than that of the indigenous populations due to a more youthful age structure and higher age-specific fertility rates of the former. Summary projections for selected Western European countries for percentages of foreign population numbers in relation to the total country-specific population sizes (2000/2050): Austria 9.3/28.0, England and Wales 11.3/36.1, Denmark 8.7/14.8, Germany 9.9/23.6, Netherlands 17.5/29.7, Norway 7.5/23.5 and Sweden 15.9/32.3.

Substantial migration streams into Northern, Western and Southern Europe occurred after 1990 and this immigration is associated with an increasing proportion of births in Europe being attributed to immigrants (Frejka et al. 2008).

Fertility levels (TFRs) of women with national citizenship compared to women with foreign citizenship (2009-2010-2011; Eurostat 2013): Belgium 1.74/2.53; Bulgaria 1.52/2.84; Czech Republic 1.53/0.73; Denmark 1.84/1.73; Germany 1.34/1.59; Estonia 1.64/1.37; Greece 1.36/2.57; Spain 1.33/1.64; Italy 1.31/2.14; Cyprus 1.45/1.59; Latvia 1.30/1.17; Lithuania 1.61/3.87; Hungary 1.28/1.26; Malta 1.34/3.36; Netherlands 1.76/2.11; Austria 1.31/2.06; Switzerland 1.41/1.84; Portugal 1.30/2.06; Slovenia 1.51/3.01; Finland 1.84/2.16; Slovenia 1.51/3.01; Finland 1.84/2.16; Sweden 1.89/2.51; Iceland 2.19/1.99; Norway 1.87/2.41. United Kingdom (native-born/foreign-born women; 2009/2010) 1.84/2.49.

According to Sobotka (2009) the European Union had a net migration gain of 22 million during the period 1985-2008; which amounts to one million per year on average, strongly accelerating after 2000. Total population increases (1985-2008; in millions) and percentages of population growth due to migration: EU-15 (member states as in 2003) 36.1/69, EU-12 (new members) -2.0/0, EU-27 34.2/66; Western Europe 16.4/35, Nordic countries 2.5/56, Southern Europe 13.3/84, Austria, Germany, Switzerland 6.3/100, central-eastern Europe 0.0/0, Southeastern Europe -2.7/0, Eastern Europe (excluding Russia) -5.1/0, Russia -0.6/0.

Coleman (2009): During the course of what has been termed the third demographic transformation, far-reaching demographic changes are unfolding in Europe. Immigrants are arriving in unprecedented numbers, re-shaping the structures and composition of European populations. Migration tilts the balance between population growth and decline. Populations are becoming more diversified in terms of languages, ethnic composition and religion. If recent trends continue, the self-identity and physical appearance of people in Europe will be changed. For the most part, public opinion is opposed to high levels of immigration and associated changes in the character of their

neighbourhoods; but other stakeholders, with economic and ideological agendas favour immigration, dominate the public/media narrative. It follows from basic rules of demography that populations with sub-replacement fertility and subject to a regular net inflow from foreign populations, will diminish as a proportion of the total population, and be eventually replaced by immigrant-origin populations. Western countries, as subject to sub-replacement fertility and positive immigration, face that outcome unless birth or migration rates change (Coleman 2009).
Around the year 2000, in western European populations, foreign-origin populations comprised between 8-18 % of the total population; projected to reach 20-30 % in 2050, given the continuation of ongoing migration inflows. In France, for example, 23 % of births were to foreign women in 2006, 25 % in Germany and approximately 24 % of births to immigrant women in England and Wales. In most of Europe, except in Eastrn Europe, annual contributions to the populations from foreign immigration are approaching the annual contributions from all births. In 2007, net immigration to Spain exceeded the total number of births by 44 %; and in eight other European countries net immigration aamounted to at least half the number of annual live births (from 50 % in Sweden to 93 % in Switzerland). Overall, the weighted average for western Europe was 44 %.

Lanzieri 2011 (EUROSTAT 2011): Migration has been the main driver of population growth in many Europrean countries. In some countries natural growth has become negative and migration counterbalanced the otherwise declining populations, sustaining population growth. At the beginning of the third millennium, migration into the European Union reached considerable levels, rapidly modifying the composition of the populations of member states exposed to large migratory flows; affecting their population composition and national identity.With net migration of 59 million, the projected population of the EU by the end of 2060 was estimated at 505 and 414 million, with and without migration respectively (representing a difference of 91 million).

The projected share of persons with foreign background in the total population in selected years and broad age groups for EU countries is outlined in Table 3.1.3a. Total fertility rates (TFR) and mean age at childbirth (MAC), by group of country of birth or citizenship, are detailed in Table 3.1.3b.

Table 3.1.3a Projected share of persons with foreign background in the total population in selected years and broad age groups for EU countries
(ex Lanzieri 2011: EUROSTAT 2011)

[a] Model 4	2021		2041		2061	
Age grouping	Total	0-14 y	Total	0-14 y	Total	0-14 y
EU	19.2	23.6	26.4	29.8	34.6	42.8
Nordic Europe and North-western Europe						
Sweden (SE)	24.3	30.3	31.2	33.7	39.0	46.8
Denmark (DK)	18.4	23.4	26.7	27.7	36.1	42.8
Netherld (NL)	19.3	23.3	24.5	23.8	30.9	37.4
Belgium (BE)	26.3	38.3	36.5	46.9	48.4	65.5

Britain (UK)	22.0	25.1	30.7	32.0	39.5	44.6
Ireland (IE)	29.9	33.4	37.5	39.1	45.1	50.4
France (FX)	17.6	17.3	19.3	16.6	21.8	24.0
Finland (FI)	11.6	15.3	15.7	16.1	20.2	23.7
Average	**23.4**	**29.0**	31.2	33.9	**39.8**	**47.9**
Central-Northern Europe						
Germany (DE)	22.9	29.7	33.0	38.7	45.1	58.0
Austria (AT)	27.8	38.4	40.3	50.9	54.2	69.6
Average	**25.3**	**34.0**	36.6	44.8	**49.6**	**63.8**
Southwestern Europe						
Greece (EL)	23.0	30.2	32.6	40.6	42.5	55.1
Italy (IT)	18.4	28.5	29.0	38.7	40.1	55.5
Spain (ES)	28.8	36.7	38.7	46.7	49.0	61.0
Portugal (PT)	19.4	29.8	29.7	39.6	40.7	56.7
Average	**22.4**	**31.3**	32.5	41.4	**43.1**	**57.1**
Baltic/Eastern Europe						
Latvia (LV)	16.5	8.9	12.2	7.7	10.5	12.0
Lithuania (LT)	11.8	9.5	14.5	15.2	19.6	25.4
Estonia (EE)	17.7	9.9	14.1	10.6	13.8	16.2
Poland (PL)	6.2	5.5	5.9	5.0	7.4	9.5
Czech R (CZ)	12.7	13.4	18.9	20.8	26.5	33.0
Slovakia (SK)	9.2	7.3	9.4	7.2	11.1	13.0
Slovenia (SI)	20.3	20.0	26.4	30.7	34.8	45.6
Hungary (HU)	9.4	10.7	13.1	14.5	17.9	22.9
Bulgaria (BG)	6.4	11.0	9.6	16.0	15.1	28.0
Romania (RO)	5.0	5.1	5.7	5.2	7.3	9.3
	11.5	10.1	13.0	13.3	16.4	21.5

[a] Model 4: Involves a comprehensive appraisal of the full contribution of migrants by including in the base population available estimates of the irregular foreign resident population and of the stock of second generation migrants and also incorporates differential fertility of migrants and their descendants (Lanzieri 2011: EUROSTAT 2011)

For Western European countries (Table 3.1.3a: northern, central and southern Europe), the current shares of foreigners of the total populations (c. 22-25 %) and of juvenile cohorts (< 14 years: c. 31-34 %) are already of a magnitude signifying circumstances threatening the continued coexistence in multicultural societies as xenophobic sentiments are progressively mainstreaming. From a systemsecological perspective further progession of shifting population compositions towards 2060 (of population totals: c. 40-50 %; < 14 year cohorts: c. 45-65 %), as projected by Lanzieri 2011 (EUROSTAT 2011), can inevitably only have one or both of two outcomes: existential civil war along ethnic/religious frontlines or/and the genetic replacement of of native populations (genosuicide).

Table 3.1.3b Total fertility rate (TFR) and mean age at childbirth (MAC) by group of country of birth or citizenship (ex Lanzieri 2011: EUROSTAT 2011)						
	TFR 2007	TFR 2007	MAC 2007	MAC 2007	TFR 2060	TFR 2060
	Native	Foreign	Native	Foreign	Native	Foreign
Nordic Europe and North-western Europe						
Sweden (SE)	1.82	2.20	30.9	29.9	1.83	2.07
Denmark (DK)	1.86	1.76	30.5	30.9	1.86	1.79
Netherld (NL)	1.71	1.85	31.0	30.1	1.76	1.85
Belgium (BE)	1.58	3.04	29.0	20.1	1.68	2.60
Finland (FI)	1.82	2.04	30.1	29.5	1.83	1.97
Average	**1.76**	**2.18**	30.3	28.1	**1.79**	**2.06**
Central-Northern Europe						
Germany (DE)	1.33	1.68	30.0	29.2	1.52	1.72
Austria (AT)	1.25	1.90	29.7	28.6	1.47	1.88
Average	**1.29**	**1.79**	29.8	28.9	**1.49**	**1.80**
Southwestern Europe						
Greece (EL)	1.33	1.99	30.8	26.7	1.52	1.94
Italy (IT)	1.28	2.40	31.7	28.0	1.49	2.19
Spain (ES)	1.33	1.79	31.8	28.2	1.52	1.81
Portugal (PT)	1.28	2.15	29.6	29.4	1.49	2.04
Average	**1.30**	**2.08**	31.0	28.1	**1.50**	**1.99**
Baltic/Eastern Europe						
Lithuania (LT)	1.35	1.44	27.9	28.1	1.53	1.59
Estonia (EE)	1.64	1.57	28.7	28.1	1.72	1.67
Slovenia (SI)	1.38	1.53	30.0	28.3	1.55	1.65
Hungary (HU)	1.32	1.26	28.8	28.6	1.51	1.48
Bulgaria (BG)	1.41	2.65	26.6	28.9	1.57	2.35
Average	**1.42**	1.69	28.4	28.4	**1.58**	1.75

Foreigners to Europe have consistently higher total fertility (TFR) rates than native populations, currently and as projected towards 2060 (Table 3.1.3b); notably applicable to Western European countries and typically associated with lower maternal ages at childbirth in the csase of foreigners. A persistence of TFRs below replacement levels are also evident for Eastern European countries, reinforcing continued population shrinkages in these countries (2.3.4f).

Demographic transitions (2.3.3e: Demographic transitions) and the colonization of European land by non-Europeans through migration and disparate reproductive rates represents a deadly combination threatening the long-term survival of European populations. Regarding the final phase (> 2000) of the disintegration of the Occident

('Abendland': Western civilization), Spengler (1923) stated a '*Paralysis and impotence also of the imperial machinery facing younger peoples (Völker) eager for spoil, or foreign conquerers'* (1.1).

3.1.1 Population groups differ in their capacities to keep wealth creation rates in alignment with their population sizes/growth rates. In this context, those that achieve this alignment are termed wealth-competent and those that do not, wealth-deficient, respectively. Wealth-deficient population groups are thus here defined as population groups no longer capable of creating sufficient wealth to adequately cater for themselves within their own country.

The important role of territoriality for periartic-European populations is clear: defense of stored wealth (re nutrition/energy costly metabolic performance mode) and space in the face of sensitivity of fertility to crowding (notably in respect of social harmony, reproductive success and healthy offspring).

This should further be assessed in the light of:

The persistence of low fertility of European populations (2.3.4a); population replacement (2.3.4b); dysgenic reproduction (2.3.4c); parental age effects (2.3.4d); population ageing (2.3.4e); population declines of Europe (2.3.4f) and the latitudinal poverty gradient in evidence (2.3.4g).

The demographic colonization of Europe has five main negative consequences, threatening its survival:

1) Long-term genetic displacement of European native populations
2) Escalation of inter-ethnic/inter-religeous conflict (then also involving/dragging into conflict of minorities which have hitherto been living in harmony with native populations)
3) Intensified competition for livelihood opportunities (particularly consequential in phases of economic stress or collapse)
4) Increased population density stress (space as a fitness msaximizing resource due to the fertility-suppressive effects of population density: demographic transition 2.3.3e).
5) Threatening the peaceful coexistence of ethnic/religeous groups world-wide.

3.2 Migrant invasions

Two types of refugee streams can be differentiated: actually war-induced (for safety and escape from war-induced destitution) and chronically poverty-induced (flight from poverty and often associated conflict/crime). Migrants of the former type may possibly show some inclination for returning to their countries of origin after conditions have normalized in their home countries. For migrants of the latter type, livelihood conditions are expected to remain better in the long-term in the countries to which they have migrated than in their countries of origin. Inclination of such refugees to return to their home countries is not to be expected. As both components of poverty and conflict are increasingly concurrently evidenced in an contemporary overpopulated world (2.3.4g) and the numbers of refugees/migrants and potential migrants involved are vastly increasing (2.3.4f), the asylum concept in its present form is no longer situation-relevant; and therewith not only outdated, but suicidal. International law (codified in UN 1951 Refugee Convention and subsidiary instruments) qualifies the right of sovereign states to setting rules of admission to its territory by obligating states to admit and provide asylum to refugees. Refugees were defined as persons outside their country owing to a well-founded fear of persecution for reasons of race, religion, nationality, membership in a particular social group, or political opinion. The concept of asylum was not intended to include migrants seeking escape from poverty or general crime. As noted by Demeny (2016), the definition was formulated in resrictive language indicating that it was intended to apply in rather exceptional cases, thus only involving relatively few candidates. It certainly did not make provision for granting political asylum to *ca* one million Syrians during 2015 and allowing them into Germany (Europe) as excercised by the German government. Such a broad reading of the Convention was clearly untenable, notably since the escalating occurence of such large refugee contingents are to be anticipated. In the mean time, migrant influx into Europe continues (mainly across the Mediterranean Sea). The underlying push factors are likely to persist or even increase in intensity. These include demographic, economic and safety factors (Demeny 2016): cumulative changes in relative population numbers between the EU and its broad non-European neighbourhood (); the persistent and widening levels of average income between the EU and potentially migrant-sending countries; and, the deterioration in the safety situation in numerous states in the Middle East and Africa (civil wars). In a broader context, increasing population numbers and

associated poverty in third world countries represent a demographic time bomb on a global scale. Responses of European leaders to this crisis have been confused and ineffective. A specialised report of the Commission (titled: The demographic future of Europe – from challenge to opportunuity) made a forecast of the population of the EU in 2050 of slightly less than 2 percent below the 2005 population. Such a forecast was calculated by assuming net immigration of 40 million to the EU, roughly a million per year over the next four decades (Demeny 2016). Subject to an ideology favouring multiculturalism and economic opportunism, the leaders of Europe and the EU fail to understand and recognise the long-term fundamental crisis confronting the European people. They have no strategy in response to this crisis based on a multigenerational time horizon. As phrased by Demeny (2016): "the road leading to what may in effect amount to collective national and civilizational suicide is taken unhurriedly, step by step".

Die Führungen Europas verstecken sich hinter der Asylgesetzgebung um das fortgesetzte Einströmen von sogenannten Asylbewerbern ihren Bevölkerungen gegenüber zu rechtfertigen, aber die Mehrzahl der Flüchtlinge die bisher hereingelassen wurden und werden sind gar keine Asylanten (verbleiben aber des öfteren trotzdem im Land), sondern Wirtschaftsflüchtlinge. Und wo verbleiben die diejenigen dessen Asylantrag abgehnt wurde? Vor allem Deutschland hat sich als Migrantenmagnet etabliert: relativ hohe Wohlfahrtslage, aber niedrige evolutionskompetente Führungspotenz (niedriges Selbserhaltungsbewusstsein und schwaches Territorialitätsbewusstsein) und eskaliert die Migrantenproblematik damit auch für andere Europäische Länder.

Das Konzept/Model der Integration unterstellt dass die Fremdgruppen wenig Wert legen auf ihre kulturelle, religiöse und/oder ethnische (genetische) Identität (Assimilationswilligkeit). Dies ist eher nicht vorgegeben. Perceptions of separate identity and holding on to traditions of many minority groups tend to persist beyond the immigrant generation; reinforced by residential segregation and difficulties with education and integration into the workforce (Coleman 2009).

In vielen Ländern der Welt leben ethnisch/religiöse Minderheitsgruppierungen langfristig unassimiliert zusammen (über hunderte von Jahren und länger). Integrationsfähigkeit/-willigkeit ist demnach nur bei einer kleinen, wirtschaftlich erfolgreicheren Minderheit einer Fremdgruppe zu erwarten. Das Integrationsmodell ist systembiologisch unrealistisch. Wenn durch fortschreitende Eindringung von

Migranten eine gewisse Mindestzahl dieser überschritten wird kann/wird eine Integration ohnehin nicht mehr stattfinden. Systemökologisch ist eher abzusehen dass sich eine langfristige innerstaatliche Balkanisierung einstellt, mit allen damit verbundenen Konfliktproblemen.
Auch wird angeführt dass bei Geburtenschwund und damit einhergehender Veralterung des Gastvolkes das Hereinnehmen von Fremdvölkischen wirtschaftliche Vorteile mit sich bringen würde. Results from a demography-based model however shows that immigration by itself cannot counteract ageing in the European Union since the number of immigrants needed to compensate for the increasing number of retired people would be far too high and that no country could afford the social and political costs of such a process (Coleman 2009; Alonso 2009; Grant et al. 2006; Saczuk 2003). In the report by the United Nations on replacement migration (United Nations 2000; determined for 2000-2050) it was concluded that the potential of immigration to substitute domestic births was limited (Kohler et al. 2006). In the report it was furthermore concluded that, if retirement ages remain the same as currently, increasing the size of the working population is the only short- to medium term option to reduce declines in the support ratio; but such a policy could not reverse the process of ageing (Kohler et al. 2006). Such a policy option would, however, require the influx of nearly 19 million migrants into Europe (10 million into Germany); amounting to 376 and c. 200 thousand per annum, respectively. Such numbers of migrants with relatively higher fertility rates introduced into countries with below-replacement fertility rates (especially Germany) would threaten the longer term survival of resident populations through genosuicide. Kurz- bis mittelfristige wirtschaftliche Vorteile werden angestrebt durch langfristigen Genosuizid, da die nachwachsenden Generationen dann längerfristig vorwiegend nicht mehr europäischen Ursprungs wären (ein völliger Zusammenbruch evolutionskompetenten Verhaltens in den Gastländern).

According to systemsecological laws, ethnic heterogenization of ethnic territories (countries) represents a fundamental existential evolutionary threat at various temporal scales and constitutes the foremost obstacle to the long-term peaceful coexistence of ethnic entities.

With continuing influx of migrants, escalating inter-ethnic conflict becomes a system-ecological inevitability; transcending proximate political influences. Harmony and

peaceful coexistence in any multi-ethnic country depends on the persistence of a state of equilibrium in political power, demography and wealth between the ethnic goups involved. However, such states of equilibrium do not last over the long-term; most importantly because most foreign population groups represent demographic time-bombs. Dynamic shifts (favouring a particular ethnic group/groups), due to numerous driving factors are bound to occur, resulting in changes of relative political power (diminishing power of group-specific self-determination, notably of the original residents), population numbers and wealth (access to livelihood resources). Such shifts generally represent threats to other ethnic groups living in the same country and are certainly perceived as such in direct relation to the progressive extent of the shifts experienced. Progressive demographic shifts can only have one of two outcomes (or both): the slower reproducing group is eventually genetically displaced (driven to extinction through assimilation) or the progressive escalation of existential inter-ethnic conflict over the long-term. This then eventually leads to annihilation of the weaker group(s) or spatial segregation (re-territorialization). Consider groups X and Y living in the same area. Both groups start off with a population ratio of 50:50; thus each group with 25 pairs each. If for group X, due to sensitivity of reproduction to population density stress or high epigenetic patho-information-engram accumulation (EPIE loading), two pairs only produce 3 children; whereas group Y produces 4 children per pair, the X:Y population ratio would have shifted to 12:1600 in the 5^{th} generation. Such a shift is realistically irreversible (Knaul 1985). From a perspective concerning evolutionary survival, multi-ethnic territories are fundamentally flawed; and a prominent cause of violent intra-national strife globally, escalating with progressing globalization. The general notion is that extreme right-wing groups must be prevented from spreading their ethnocentric perspectives becoming mainstream in order to safe-guard peaceful co-existence. However, escalating ethnic survivalist anxieties becoming mainstream sentiments cannot be effectively induced by extremists in the absence of experienced threat by the population. Mainstreaming can only and will result from increasing proportions of foreigners in a country, as facilitated under liberalistic policies (lack of evolutioncompetent leadership). Two fundamental human emotional mindsets are in conflict: compassion (for suffering refugees) and instinctive survivalist fears. Irrespective of any politically opportunistic exploitation of such sentiments in the short-term, over the long-term, systems-ecological dynamics will inevidably progress. With increasing numbers of inflowing migrants, compassion fatigue will set in,

followed by the progressive mainstreaming of survivalist reactions. The only way to pre-empt ensuing existential conflict playing itself out in the future, is by preventing any further influx of foreigners (in some cases it may already be too late to pre-empt escalating civil conflict. Refer to 3.1.3).

Integration als Vorstufe zu Assimilation würde ohnehin auf Genosuizid der Gastvölker in Europa hinauslaufen. Der Geburtenschwund (Section 2.3.3; Schade 1974; Meves 1984), vor allem bei westeuropäischen Völkern, muss im ursächlichen Zusammenhang gesehen werden von, einerseits, einem niedrigen Vitalitätsstatus (hohe Pathogeninformations-Engrammbelastung; Zivilisatose) und andererseits durch die Blossstellung an hohen Populationsdichtestress (Knaul 1985). Eine kinderbejahende Einstellung (Ja zur Familie) setzt Lebenskraft voraus (Psychagogin Meves 1984: Analytische Kinder- und Jugendlichenpsychotherapeutin). Des weiteren, die Deutschen in Deutschland als Beispiel, leben bereits seit längerem unter Zuständen von relativ hohem Populationsdichtestress und damit verbundener negativer Rückkoppelung zwischen Populationsdichte und Geburtenrate (Knaul 1985: Das biologische Massenwirkungsgesetz). Demograpic transition. SCHADE HORMANN Eine gleichzeitig einhergehende höhere Geburtenrate der Fremdvölkischen impliziert eine längerfristige Abnahme des Bevölkerungsanteils der Deutschen in Deutschland (Umvolkung/Genosuizid). Dieselbe demografische Dynamik gilt auch für andere europäische Völker. Eine Entwicklung mittel- bis langfristiger Umvolkung (Transformation) von staatstragenden Völkern zu Minderheiten in den Gastländern in Europa ist damit im vollem Gange.

Das Hereinlassen von aussereuropäischen Migranten ist langfristig gesehen humanitär kontraproduktiv und verantwortungslos:

- Ethnische Heterogenität eines States impliziert dass evolutionär konkurrierende Gruppenentitäten im selben Land vorkommen (demografischer Wettlauf). Progressive genetische Umvolkung.
- Innerstaatliche Balkanisierung. Bei der Existenz von bedeutend unterschiedlichen Fremdgruppen mit zahlenmässiger Signifikanz ist eine räumliche Absonderung in Enklaven oder Ghettos systemökologisch vorprogrammiert.
- Friedliche Koexistenz kann nur gehandhabt werden wenn keine der unterschiedlichen Rassen- oder Volksgruppen sich durch die Anderen bedroht

fühlen, bzw. werden; was unweigerlich Eintritt wenn die Zahl der eingeströmten Fremden eine gewisse Mindestzahl überschreitet. Spätestens in Zeiten wirtschaftlichen Notstands (welche langfristig mit Sicherheit eintreten) kommt existentieller Konflikt zum Ausbruch.

- Zunehmende Migrantenanhäufungen führen unweigerlich zu weiterer religiöser und ethnischer Polarisierung. Eskalierende Xenophobie als Hauptstromsentiment ist unausweichlichlich bei steigender und fortgesetzter Migranteneinströmung (Friedensgefährdung).
- Nicht nur Angehörige der Gastvölker sondern auch Minderheiten, welche bereits geraume Zeit mit ihren Gastvölkern in Harmonie leben, werden dann in bürgerkriegsartige Konflike verwickelt.
- Solcherart ethnisch und religiös heterogenisierte Länder bieten fruchtbaren Boden/geignete Umstände für Fremdmächte (ausser und überstaatlichen Ursprungs) diverse religiöse oder ethnische Gruppen gegeneinander zu polarisieren und auszuspielen (*divide et impera*). Socherart gesteuerte win-lose Polarisierungen (z. B. Islam *versus* Christentum) sind bereits in vollem Gange. Die Neutralisierung solcher *divide et impera* Manipulationen erfordert win-win Führerschaft auf allen Seiten.
- Talententzug zu Kosten der Ursprungländer. Da die letztentlich erfolgreich Migrierenden zum Teil überdurchschnittliche Kompetenzen besitzen im Vergleich zu deren Ursprungpopulationen (dispersal phenotypes: Opportunistisch-wagemutige Individuen - resourceful opportunism mit relativ erhöhter Problemlösungsfähigkeit wenn konfrontiert mit unerwarteten und verschiedenartigen Situationen einer Migration ins Ungewisse *vide* Geist 1978), werden den Urspungländern gerade jene Kräfte entzogen welche besonders wichtig wären für Problemlösungen vorort (brain drain).
- Weitläufige Proliferation von Elendsvierteln (slum proliferation) in den Gastländen. Da die Mehrzahl der Migranten kurzfristig bis langfristig in den Gastländern nicht wirtschaftlich konkurrenzfähig/wirtschaftlich integriert sein werden ist eine landweite Wucherung solcher Elendsviertel vorprogrammiert (mit zunehmendem Kriminalitätspotential). ADD LIT RE ELLIS
- Fragmentation/Destruction of the European Union (EU). The EU was and is failing to protect Europe from the dangers of progressively escalating invasions

by non-European migrants. Individual European states are likely to reclaim their sovereignty in order to deal with this situation in the best interests of their own people. Europe needs an EU of sovereign states, not a plutocratic, cosmopolitan and democratically-dysfunctional (*vide* Achen & Bartels 2016) construct of a 'United States of Europe'.

- The European Union is seen by many as a supranational structure to contain win-lose nationalism over the long-term. However, the only way to achieve this would be by accommodating nationalist (ethnic survivalist) concerns through win-win evolution-competent leadership.

Die generelle Reaktion zu solchen Erläuterungen ist um dass als Angstmache abzutun. Da stellt sich die Frage nach der wievielsten Million von nach Europa eingeströmten Flüchtlingen (über eine Million in 2015; primarily into Germany) die europäischen Führungskräfte vorhaben Angst zu bekommen. Nach welchen Zeithorizont versuchen die europäischen Staatsführungen ihre Führungverantwortlichkeit zu vollziehen? Die Meinung von einer relativ hohen und zunehmender Anzahl gemässigt links- bis mitte Wählenden mit Besorgnis über das Einströmen von aussereuropäischer Flüchtlingen wird inkriminiert als rechtsradikal (concerned moderate right and centre to left conservative voters now all designated as far-right, i. e. extremists) und damit ignoriert. Diese und andere Vorgehensweisen (Meinungsmanipulation durch die Medien die als Kampfinstrumente angewandt werden; Verdrängung ideologisch unliebsamer Wissenschaftserkenntnisse z.B. der Genetik) stellen eine Dysfunktionalisierung dar des demokratischen Prinzips (eine Bestätigung dass es im klassischen Sinne funktionierende Demokratien wohl gar nicht gibt, sondern nur Pluto-Demokratien, bzw. Plutokratien: 1.1, 1.2). Bei weitem die Mehrzahl europäischer Ehepaare wünscht sich eigene Kinder. Das heisst, die Genetik ist für diese von grosser Bedeutung; bewusst oder unbewusst. Dieses wird ignoriert in dysfunktionellen Demokratien (bzw. Pluto-Demokratien). DEMOCRACY Achen & Bartels (2016) Democracy is perceived as the rule of the people in the interest of the people. This is no longer achieved in the case of Western democracies (plutocracies).

Populationen mit einer r-S Reproduktionsstrategie (Lebensstrategie) handhaben relativ hohe Geburtenraten (Populationszunahmen) selbst unter Armutszuständen. Das Problem mit dieser Lebenstrategie ist dass Wirtschaftswachstumsraten der Bevölkerungszunahme hinterher hinken. Die *per capita* Armut nimmt progressiv zu (Armutsfalle; poverty trap; boom-bust

demography). Wirtschaftswachstum ohne Geburtenkontrolle führt zu mehr Menschen in Armut. Zunehmend mehr Menschen geraten in Not. Jährlich werden Millionen potentielle Flüchtlinge geboren die ein besseres Leben in Europa erwarten. The population sizes of potential refugees in third world countries exceed those of population sizes of Europe and increase by millions annually. Their problems can surely not be solved by allowing them to enter Europe. The European political leadership does not seem to understand this in the relevant spatiotemporal context. Während echte Kriegsflüchtlinge nur kurzfristigen Schutz gegen akute Kriegsfolgen anstreben sollten, sind solche mit einer Zielvorstellung eines langfristig besseren Lebens im Gastland (Wirtschaftsflüchtlinge) teil einer resourcenmonopolisierende Invasion (ein nicht-militärischer Agressionsakt), gerichtet gegen die Ziel-Gastlandländer, und für diese mit denselben, oder selbst noch gefährlicheren, langzeitigen Konsequenzen wie eine militärischausgeführte Invasion haben würde). Selbst wenn Europa solche Flüchtlinge weiterhin aufnehmen würde hätte das langfristig keine positiv-humanitäre Wirkung (Tropfen auf den heissen Stein). Aber die europäischen Völker würden damit Genosuizid begehen. Einen Beitrag zur Lösung der Notlage in den Drittweltländern könnte Europa nur leisten durch Herstellung eines Zustandes gleichlaufender Angleichung zwischen Bevölkerungszahlen und wirtschaftlicher Effizienz (Wirtschaftwachstum) vorort. Ein Nachhaltigkeits-gleichgewicht zwischen Wirtschaft und Demografie kann nur existieren wenn Bevölkerungszahl/Zuwachs im Einklang miteinander stehen. Es ist unklar ob solcherart Zustand realistisch erreichbar ist da Geburtenkontrolle im Gegensatz steht zu den Lebensstrategien und Fortpflanzungsstrategien vieler der betroffenen Völker (3.1.2; 3.1.3). Im grösseren zeit-räumlichen Rahmen, wenn nachhaltige, im demografisch-wirtschaftlichen Gleichgewicht, autarke Systeme sich nicht in den Drittweltländern etablieren, werden natürliche Regulationsmechanismen unweigerlich zum Zuge kommen (Krankheit, Konflikt, Hungersnot). Nach dem ehernen naturgesetzlichen Prinzip der Evolution können dann nur Gruppen überleben die ihre Resourcen auch effektiv verteidigen können. Im Klartext, wenn Europa seine Territorialität nicht handhaben kann wird es untergehen.

Inwischen dämmert es auch manchen europäischen Führungen dass eine Zulassung fortschreitender Migranteneinströmungen keine nachhaltige Problemlösung darstellt. Weder für die Gastländer noch für die Migranten. Im Gegenteil, eine bürgerkriegsartige Explosion wird mittelfristig heraufbeschworen. Dabei hat sich das

Migrantenproblem schon seit über drei Jahrzehnten angebahnt (Schade 1979; Hormann 1985). Aber wirklich Verstanden haben die europäischen Führungen die Lage noch immer nicht. Wege werden gesucht zur legalisierten Einwanderung nach Europa um die Flüchtlingsfrage zu lösen (Problemausweitung anstelle von Problemlösung). Ohne strategische Grundlage wird im Krisenmanagement herumtaktiert. Furthermore, the internal power dynamics and overriding value systems as experienced in pluto-democracies, are not conducive for effective containment of criminal networks such as drug cartels or human trafficking networks (1.1). Fortschreitende Einwanderung nach Europa, illegal oder legal, kann nicht nachhaltig den Bedürfnissen des Volkschutzes und des Völkerfriedens entsprechen. An understanding is required that, in reality, multi-ethnic/multicultural states are evolutionary unstable and are unavoidably subject to inherent systemsecological dynamics manifesting over the long- term; any destructive trends progressively becoming intractable to politically-based countermeasures.

Innerhalb der Gastländer haben sich zwei Interessenlager formiert: Verpflichtung zu international-solidarischer Humanität und der damit einhergehenden Hilfeleistungen (auch durch die Aufnahme von Flüchtlingen) gegenüber den langfristigen Überlebensinteressen der europäischen Völker. Eine Win-win Lösung für einen solcherartigen Gegensatz kann nur gefunden werden wenn die Realisierung beider Positionen widerseitig vertragbar ausgeführt wird. Dabei würde es hilfreich sein wenn die Vertreter beider Seiten der Kontroverse ihre Positionen professionell und nicht im ideologischen Win-lose Modus vertreten würden. Humanitäre, international-solidarische Hilfeleistungen an Kriegsflüchtlinge (z. B. von Syrien) ist durchaus angebracht auf zeitbeschränkter Basis. Dies darf aber nicht geschehen durch das Hereinlassen von Flüchtlingen welches zu einer langfristigen ethnisch-religiösen Heterogenisierung der hilfeleistenden Länder führen würde. Mit solcher Heterogenisierung ist eine Polarisierung diverser Gruppen langfristig vorprogrammiert (ausgedehnte generationsübergreifende bürgerkriegsähnliche Auseinandersetzungen) mit extrem kontra-humanitären Folgen für alle Beteiligten. Verantwortliche, evolutionskompetente *Win-win* Staatsführung ist angesagt, nicht emotionale Selbsbefriedigung.

3.3 Evolution-competent leadership requirements

Globally, the country with the highest content of evolution-competent leadership and behaviour of its population is Israel (though compromised by ongoing win-lose strategies); that with the lowest such competence is Germany, being most prone to genosuicide. The evolution-competence exhibited in Israel is compromised by win-lose pursuits, and could be fundamentally enhanced if the objective of safe-guarding long-term survival was pursued though Win-win strategies (1.3). This would then be associated with kharmically-positive higher levels of *Invincibility* (*vide* Sun Tzu *The Art of War*).

Achen & Bartels (2016) The re-functionalization of Democracy
Electronic mass surveillance leads to self-censuring by the people, constraining the expression and communication of free opinion; particularly of opinions deemed politically incorrect. This is fundamentally counter-democratic.

Table 3.3 Evolution-competent Leadership Potency (refer also to Table 2.3.2c)	
• Inner guidance by an aristocratic-type value system	***In honour bound to the protection imperative***
• Prioritisierung von Volksinteressen als genetisch-basierte Entität	Maintenance of ethnic-linked territoriality (ethnically homogeneous states). Ethnic homelands v*ide* Israels Führungselite.
• Handhabung des Territorialitätsprinzips	Territorialität als unersetzbares (indispensible) Element in der Überlebensstrategie von wohlfahrtsakkumulierenden Völkern (3.1.3).
• Elitäre Führungsplicht (*noblesse oblige*): Respekt für und Inachtnehmung auch von nicht medieninduzierten bzw. -reflektierten Volksmeinungen und Anliegen (Einbeziehung relevanter Erkenntnisse über Grundanliegen der Volkserhaltung).	Refunctionalisation of the democratic principle: Responsiveness to concerns of the people. Volle und inklusive Nutzung relevanter wissenschaftlicher Erkenntnisse durch die Staatsführungen
• Langzeitperspektive (Generationen)	
• Kharmapositive Win-win Strategien	(Sun Tzu: Art of War): Von Bismarck/Gandhi/Mandela Salah Ed-Din

Untergang des Abendlandes? Mit zunehmender Patho-Information-Engramm-Belastung kranken die Europäer dem Untergang entgegen. With the continuing decline of health and vitality of the European people due to the continuing accumulation of patho-information-engram loadings a stage of irreversible evolutionary incompetence will inevitably be reached. ('*Unless we change direction, we shall end up where we are headed*' Altes chinesisches Sprichwort"/Old Chinese proverb) (2.?). Ein niedriger Vitalitätsstatus erlaubt kaum evolutionskompetentes Verhalten und evolutionskompetente Führungspotenz ist nurmehr spärlich vorhanden. Dieses macht sich am stärksten bemerkbar in westeuropäischen Ländern; etwas weniger im östlichen Europa (siehe Mennerich 1979). Wenn Europa im Zeitalter der Globalisierung nicht seine Territorialität handhaben kann wird es vernichtet werden. Das Überleben Europas ist damit abhängig von wieviel evolutionskompetente Führungspotenz (in honour bound to the protection imperative) sich noch in Europa realisieren kann/wird.

Ausklang

With the continuing decline of the health and Ausklang
Die erörterten systemökologischen Perspektiven zur Ursächlichkeit der Aufstiegs-Niedergangsabfolge mit Bezug auf Europa, wie dargestellt durch Oswald Spengler und auch kontemporär beobachtet und belegt, sind gedacht als Beitrag zu einem besseren Verständnis dieser schicksalsschweren Entwicklungen.
Contributions to invincibility (Sun Tzu: The Art of War) in order to promote evolutionary competence of European people. For those of you who are concerned about the future survival of European people, now is not the time to engage in win-lose conflicts. Now is the time to build *Invincibility*. Recursive healing in the family; inner strenghthening to allow for mastery of life in a win-win mode (respecting both your own position and that of perceived opponents). Live according to your value system and support leaders with an aristocratic value system (in honour bound to the protection imperative).

If the insights shared in this book are found useful by readers in pursuit of fundamental healing, and if this book convincingly conveyed the message that adopting win-win strategies in mastering life is superior, the author would consider this book to be a successful contribution towards the survival of European genetically differentiated ethnicities and other ethnicities worldwide (under the imperative of biodiversity conservation).
Irdische Leben: konkrete Potentialrealisierung (entwickelt sich innerhalb dem vorgegebenen Potentialrahmen)

Medical Disclaimer
All information in this book is intended for educational purposes only. The insights presented in this book were carefully considered and checked by the author and editors. However, no guaranties can be undertaken or accepted. It is neither intended nor implied that any advice in this book represents a replacement for professional medical advice, treatment or care. Any information in this book should not replace visits to medical professionals, especially in the case of pre-existing illnesses. In general, applications of information presented in this book should take place under the guidance, instructions, agreement or care of a medical professional (especially also in respect of selection and dosages of therapeutic substances). By reading relevant text sections of this book, practitioner-patient relationships are not established. Any liability of authors or editors and persons acting on their behalf for personal or any other forms of damage is excluded.

Life History Strategies	
Fundamental systemsecological trade-off: Biological systems capable of functioning at high process rates under surplus resource conditions tend to have lower capacities for sustained functional efficiency under conditions of fluctuating and generally low resource availabilities. This translates into a trade-off between maximum use of abundant resources (generally transient: current) for production (growth and reproduction) and investment in basic long-term survival processes (somatic maintenance: including self-healing processes). Adaptation to feast-famine rhythm. Under constant feast conditions self-healing processes (*inter alia* autophagy) are compromised.	AS AS
EPI Environmental insults producing increased stress vulnerability and other dysfunctionalities potentiate subsequent stress in pregnancy with consequent transmission of the phenotypes of vulnerability to the next generation (Drake & Walker 2004). EPI-drake Drake & Walker (2004) CHECK MORE Epigenetics: The historic prevalence of energetic constraints imply the likelihood of adaptive mechanisms to buffer early development from associated insults to mothers and foetuses. The centrality of epigenesis to development furthermore confirms the role of environment in co-determining phenotype.	AB AB
DTB-Doblhammer (2000) in ref check REPRODUCTION-klindworth-krummhorn EVOLUTION-voland-NB LHS-bielby-FAST-SLOW LHS-INEQUALIY-bowles-2010 LHS-EVOLUTION-kaplan LHS-INTELLIGENCE-rushton LHS-walker-2006b BODY SIZE-walker-2008 LHS-figueredo-2004 LHS-figueredo-2006 GENETICS-ebstein-human-personality LHS-GENES-BRAIN-figueredo-2006	

STRESS-de kloet Elenkov ANS-elenkov-sympathetic	
INTEGRATIVE PALEO-DIET Latner, J. D. & Schwartz, M. (1999). The effects of a high-carbohydrate, high-protein or balanced lunch upon later food intake and hunger ratings. *Appetite* 33: 119-128.	
OXIDATIVE STRESS-mokhtari	
Wu et al. (2009): Culturing autophagy deficient cells in the presence of the antioxidant N-acetylcysteine (NAC) resulted in a reduction of ROS levels (Wu et al. 2009). Data suggests that antioxidant treatment of autophagy-impaired cells is beneficial in preventing the glucose intolerant phenotype within pancreatic β cells. It is known that pancreatic secretion of insulin is sensitive to changes in the cellular redox state and mitochondrial functionality. In the context of impaired autophagy, the in vivo use of antioxidants interrupted the vicious cycle of mitochondrial generated ROS inducing further mitochondrial damage. Such observations suggest that antioxidant targeted therapy might be of benefit for conditions where deficiency or impairment autophagy is involved (Wu et al. 2009).	
CR-sohal-forster CR-moatt in ref Brunet et al. 2004 MITOCHONDRIA-de benedictis-longevity MITOCHONDRIA-rose-longevity MITOCHONDRIA-niemi-longevity	
Figueredo et al. (2006) Figueredo et al. (2004) STRESS-ellis-2006-NB	A
AUTOPHAGY-mizushima	
LHS-COVITALITY-figueredo-2006a	A
Bruce & Wingfield	
Immune function	

LHS-mcdade-life 2003 DTB-mcdade-2017	
HUMAN WELL-BEING-fredrickson EPI-HEALTH DEVELOPMENT-halfon NBNB IN REF	
Dribe et al. (2017): **Dribe et al. (2014, 2017)**: The progressive fertility decline during the late 1800s and early 1900s has been associated with changes following the transition from an agricultural-based economy to an industrial economy; characterised by a sustained mortality decline, increased levels of urbanization, expansion of education and increasing female employment (op. cit. Dribe et al. 2017; Brown & Guinnane 2002). The fertility decline was led by the upper and middle classes. Dribe et al. (2017) posed the question whether this pattern was due to socioeconomic factors first affecting the upper and middle classes or whether it was related to diffusion of innovations/ideational changes from upper to lower social strata. Prominent in the literature was the view that higher social status was linked to higher fertility before the fertility transition which changed to a negative association between social status and fertility as the fertility transition progressed (e.g. Borgerhoff Mulder 1998; Voland 2000; Kaplan & Lancaster 2003). This reversal occurred during or even before the demographic transition began (e.g. Skirbekk 2008). Dribe et al. (2017) present a more differentiated perspective on the interplay between socioeconomic status and fertility. They presented the results of investigation of selected case studies focusing on socioeconomic and/or educational differentials in fertility before, during and after the transition. Both parity-specific stopping and prolonging birth intervals were involved in the fertility transition. Upper and middle classes acted as forerunners, while farmers were late in the transition. Farmers and unskilled labourers generally lagged behind in the progression of fertility decline.	

Dribe et al. (2017) differentiated between four transition phases: pre-transition (PT) as a phase before any signs of fertility decline, early transition (ET) when the fertility decline had started, but had not spread to the whole population, and during the late transition phase (LT) a general decline of fertility had been ongoing. During the post-transition phase, fertility evened out at low levels, usually around replacement levels (SDT: second demographic transition). Transition phases and associated total marital fertility levels at ages 20-49 (in parentheses) for the case studies represent some variation, the explanation of which provided some more insights regarding the nature of the demographic transition (Data not available for some phase/study site combinations). Scania (Sweden): Pre-transition (PT) 1815-1879 (8.2), Early transition (ET) 1880-1909 (7.7), Late transition (LT) 1910-1934 (4.8), Post-transition 1935-1968 (3.1). Utah (USA): PT 1850-1879 (na), ET 1880-1919 (7.8), LT 1920-1969 (4.4). Alghero (Sardinia/Italy): PT 1866-1915 (7.6), ET 1916-1935 (6.9). Saguenay (Canada): PT 1842-1929 (8.9), ET 1930-1959 (7.2), LT 1960-1971 (3.7). Stockholm (Sweden): PT (na), ET 1878-1909 (6.6), LT 1910-1926 (3.8).

Scania, Sweden: Data from five rural parishes. High fertility levels in the pre-transition phase are closely associated with short time spans between marriage and the start of childbearing. Compared to the other three study populations Scania had the lowest mean marriage to first birth intervals (Mean marriage to first birth interval/inter-birth interval 1.06/2.69 years during the pre-transition phase, progressively increasing to 1.34/3.05 in the late transition phase (Dribe et al. 2017). Elite and middle class families had higher fertility in the pre-transition period, their fertility started to decline in the 1880s, earlier than in lower status groups (Dribe et al. 2014). Low skilled and unskilled workers of Scania and Utah had lower higher-order birth rates (restricted family size) compared to farmers; suggesting some socioeconomic harshness during pre-transition and to some extent also early transition phases. This contrasted the situation in Alghero and Saguenay during the pre-transition phase when low/unskilled workers had similar or relatively higher values of higher-order births than higher socioeconomic groups; suggesting that socioeconomic constraints did not limit their family sizes disproportionately.

This changed during the early transition phase when low/unskilled workers tended to have mostly lower levels of high-order births than farmers in Scania, Utah and Saguenay (again suggesting socioeconomic constraints on family size). Farmers and unskilled workers consistently lagged in the fertility decline, notably also during the late and post-transition phases.

Utah, USA: Mean marriage to first birth interval/inter-birth interval were determined for the Utah study population as 1.21/2.01 years during the pre-transition phase, progressively increasing to 2.14/3.46 in the late transition phase (Dribe et al. 2017). Declining fertility was due to longer intervals from marriage to births, longer birth intervals and early stopping. This was found to be the case for all socioeconomic groupings. However, whereas unskilled families in Utah had relatively long intervals from marriage to birth (notably during pre- and early transition phases) compared with short intervals in Scania and Alghero, longer intervals were experienced by the higher status groups in Alghero. Sharp fertility declines relating to both first- and higher-order births between early and late transition phases (fertility decreases of 30-50 % and even more so regarding higher-order births). However, the fertility decline started earlier and proceded more quickly regarding white collar families (delayed age at marriage and longer time between marriage and first birth: Dribe et al. 2014). Highest fertility levels were recorded for farming families.

Alghero, Sardinia/Italy: There were no signs of fertility transition for the cohorts born before 1912 and analyses showed more or less pre-transitional fertility patterns (natural fertility: absence of deliberate fertility control) until the 1930s (Breschi et al. 2014). The fertility decline between the pre- and early transition phases was relatively small (marital fertility at ages 20-29: 7.6 to 6.9). Regarding the total population no indications of family limitation were found (parity-specific control). Mean birth intervals from marriage to first births were comparatively long (1.41/1.64 years) during the pre- and early transition phases compared with those of other study populations. Limitations of number of births as adaptation to resource availability levels was based on controls of marriage behaviour, i.e. late marriage of foregoing marriage. Child survival was generally higher in the upper classes

Saguenay, Quebec/Canada: Analyses of rural parts of Quebec in the Saguenay-Lac-St. Jean region. Onset of fertility transition relatively late in comparison with regions of Western Europe and the United States of America. This was linked to the ruralness of the region and remoteness from the influence of urban centers. The population was also French Catholic and had relatively low levels of education. Mean marriage to first birth interval/inter-birth interval were determined as 1.22/1.98 years during the pre-transition phase, progressively increasing to 1.41/2.25 in the late transition phase (Dribe et al. 2017). Interbirth-intervals were relatively short, notably also since such were retained at a late stage of the fertility decline (1960-1971). Farmers had relatively high/higher fertility rates during pre-, early and late transition phases.

Stockholm, Sweden: A marked decline in total marital fertility to 3.8 recorded for the late transition phase which was already reached relatively early during (1910-1926; Dribe et al. 2017). Early onset of birth control and more rapid decline of fertility than for the rest of Sweden (forerunner of overall fertility decline in Sweden: op. cit. Dribe et al. 2017). The fertility decline of low/unskilled workers lagged behind higher and skilled socioeconomic groups during the early and late transition phases.

Patterns of fertility decline were similar across populations, with pronounced decreases experienced from early to late transition phases regarding fertility parameters linked to first- and higher order births. Fertility levels were about 30-50 % lower in the late transition phase; with larger decreases in respect of higher order births. Fertility declines in Alghero (1916-1935) and Saguenay (1930-1959) started much later than in Scania (1880-1909), Utah (1880-1919) and Stockholm (1878-1909). Spacing of births is an important part in fertility transitions. Generally, time between marriage and first birth increases and higher-order birth intervals become longer during the transition. Higher occupation families generally tend towards relatively longer birth spacings in comparison lower socioeconomic groups; with farmers tending to sustain shorter birth spacing.

Families with higher occupations (elite groups, professionals, managers) led the fertility decline in all study populations (Scania, Sweden;

Stockholm, Sweden; Utah, USA; Alghero, Sardinia/Italy and Saguenay, Quebec/Canada). Already during the early transition phase higher occupation families experienced the lowest rates of marital fertility (forerunners of the decline). Farmers and unskilled worker families sustained relatively higher fertility rates. From the early to late transition phases, all socioeconomic status groups experienced declining fertility. Thus, higher-occupation families appear early in the transition compared with lower socioeconomic status groups, with converging to lower fertility of lower socioeconomic status as the transition progressed. However, although also having experienced fertility declines over the later transition phases, families headed by farmers and unskilled workers retained relatively higher fertility rates into the post-transition phase (based on higher order births) than other groups (approximately 30 % higher). (**AS: experienced lower levels of procursive impacts resulting in patho-information-engram accumulations due to uninterrupted transgenerational affluence/population density stress: intra- and transgenerational continuity of resource abundance and progressively higher impacts of urbanization effects**). The generally reported or assumed reversal of a fertility advantage of higher socioeconomic status during pre-transition phases to relatively lower fertility in subsequent transition phases is often not detected because such reversal could have occurred further back in time not covered by the available data (Breschi et al. 2017).

Breschi et al. (2014). Breschi et al. (2014) investigated marital fertility patterns for the Sardinian population of Alghero for the period 1866-1935. Pre-transitional fertility variations were linked to cultural and biological factors (breastfeeding, age-related lower coital frequency and temporal sub-fecundity due to nutritional deficits). The total marital fertility rate $TMFR_{24-29}$ was 7.7, mean age at last birth was rather late (over 39) and birth intervals were comparatively short (less than 2.5 years). For the population of Alghero, as Sardinia in general, marriage behaviours (late marriages or constraining factors in respect of marriage access) rather than reproductive behaviours (such as limiting total number of births) were instrumental in adapting to available resource levels (op. cit. Breschi et al. 2014). Differences in marital

fertility according to socio-economic groupings were detected: for the small minority of non-manual workers marital fertility started to decline, especially after 1885. In Alghero, children born to the upper classes experienced substantially lower mortality rates than those of the poorer classes.

Sardinia experienced the slowest and most gradual fertility transition in Italy (Livi bacci 1977, op. cit. Breschi et al. 2014). Initially having relatively low levels compared to other Southern regions, Sardinia had the highest fertility levels in Italy during the 1950s (TFRs: National average: 2.3; Southern regions: 2.3; Sardinia: 4 children per women). Contrasting this, Sardinia currently has the lowest fertility levels in Italy (Santini 2008, op. cit. Breschi et al. 2014). The system of family formation and reproductive behaviour which prevailed in Sardinia differed from the Mediterranean model (low female marriage age and high fertility) by resembling the north-western European model: late marriage and requiring spouses to have accumulated sufficient resources to sustain a self-sufficient household (AS: resembling a more K-selected reproduction strategy). Marital fertility was relatively high around 1861; with first signs of reduction after 1939-1945. From 1862 to 1962, marital fertility only fell by about 15 %, the national level of Italy by 50 % and in northern and central regions by around 70 %. Later age at marriage and restricted marriage rates in response to resource level constraints controlled fertility in Sardinian populations during the 1800s, persisting to about 1950. A moderate decline in marital fertility, but a more pronounced decrease in general fertility was recorded towards the end of this period. Variability in marriage-fertility dynamics in Sardinia is taken to be associated with socioeconomic context factors such as pastoral, mining or coastal activities (op. cit. Breschi et al. 2014). In Alghero, various socioeconomic groupings were represented, including a large presence of farmers and shepherds, thereby providing the opportunity for a differentiated investigation of the unusual progression of the Sardinian fertility transition (Sardinia has become post-industrial without ever being fully industrialised: Bottacci 1999, op. cit. Breschi et al. 2014). Standards of living for lower socioeconomic groups were generally low. Farmers represented a separate socioeconomic group in Alghero due to their numerical relevance and their closer relationship

with rural populations of the interior of Sardinia (with the occurrence of Blue Belt populations as characterised by notable longevity: Table 2.5.1.2b).

There seems to be general agreement that the relationship of socioeconomic status and fertility changed over the course of the fertility transition (Skirbekk 2008; Cummins 2009, op. cit. Breschi et al. 2014): individuals of higher socioeconomic status had relatively high number of children before the onset of the fertility transition, but then acted as forerunners of declining fertility during the transition. (AS: LHS-modes PM before the transition and shifting Pm to pM during the decline phase: lowering fertility due to Pm decline and increasing pM: declining mortality). Over the period 1866-1905, total marital fertility, mean age at marriage and mean age at last birth of five year marriage cohorts remained largely unchanged/stable (representing a natural-type of fertility schedule), resembling a pre-transitional stage. Furthermore, the results of Breschi et al. (2014) revealed that the non-manual group (higher occupations/lower to medium skilled) had the lowest total marital fertility rate averaging at 6.6; average values were higher for lower socioeconic groups (Manual workers: unskilled, low skilled, farmers, skilled), reaching 8.0 for farmers. Associated evidence indicated that some fertility control was operative in the non-manual group. In Alghero, as in the rest of Sardinia, neonatal/infant mortality was notably low compared with the rest of Italy. A link to extended breastfeeding, sometimes lasting over a year, was implicated (op. cit. Breschi et al. 2014).

Large amounts of research on the European fertility transition has as yet not resulted in any consensus regarding precise causes and mechanisms of the underlying demographic processes. According to Carlsson (1966, op. cit. Breschi et al. 2014) fertility control took place when conditions for innovation (emergence of new attitudes triggered by new knowledge) or adaptation (adjustment behaviour to new circumstances) are being realised.

EVOLUTION-pigliucci-2009
EVOLUTION-PLASTICITY-2005

Jablonka & Lamb (2007): GXE-keller 2014 EVOLUTION-FITNESS-bouchard	
Darnaudery-pdf Beauchaine BREASTFEEDING PLUS McDade-breastfeeding McDade et al. (2014): in print BREASTFEEDING-anderson-cognitive development BREASTFEEDING-CHRONIC DISEASE-kelishadi-2014 BREASTFEEDING-victoria-pdf BRESTFEEDING-hanson-IMMUNOLOGY BREASTFEEDING-IQ-caspi BREASTFEEDING-akobeng-coeliac disease CHILDHOOD ADVERSITY-heron	
AUTOPHAGY-CANCER-wu-2012	
GRAINS-INFLAMMATION-esposito-2006 WHOLE GRAIN-esposito INFLAMMATION-esposito INFLAMMATION-METABOLIC SYNDROME-esposito-giugliano-2006 H65dietary fiber FIBRE-king	
EVOLUTIONARY SYNTHESIS-pigliucci-2007 NBNB in ref PLASTICITY-belsky-pluess 2013 NB PLASTICITY-pluess-belsky-2013- vantage sensitivity NB PLASTICITY-pluess-belsky-2012 actually 2011 PLASTICITY-CHILDCARE PLASTICITY-belsky-pluess-2009 Pettay et al. (2007) LHS SES HISTORY EDUCATION-GENETICS-keltikangas GENETICS-ENVIRONMENT-keller	
BREASTFEEDING-IQ-caspi AS high SES types with genetically higher plasticity supporting genetically-based performance capacity/competence realization under favourable conditions.	

PLASTICITY-belsky-pluess 2013 NB
PLASTICITY-pluess-belsky-2013- vantage sensitivity NB
PLASTICITY-RESILIENCE-belsky-pluess
PLASTICITY-pluess-belsky-2012 actually 2011
Pluess & Belsky (2011):

PLASTICITY-CHILDCARE
PLASTICITY-belsky-pluess-2009

DEVELOPMENT PROGRAMMING
Ex Belsky & Pluess (2009): Fetal programming. Is it the case that prenatal stressors compromise later development, as prevailing thinking presumes, or do these prenatal experiences promote plasticity and thereby the openness of the organism for future experiential input, positive or negative in character? Is there prenatal programming of postnatal plasticity? (Pluess & Belsky 2011).

Epigenetic findings by Oberlander et al. (2008) showed that maternal suppressed mood in pregnancy predicted increased methylation of the human glucocorticoid receptor gene *NR3C1*, which itself forecasts elevated cortisol stress reactivity at age 10 months; thereby identifying one of the biological mechanisms that may be central to fetal programmingof postnatal plasticity (consistent with the biological-sensitivity-to-context thesis of Boyce & Ellis 2005). Thus it can be concluded that, on the basis of fetal programming research, plasticity is a function of experience as mch as a function of genetics. The fetal programming process is accordingly characterized by GxE interaction (Gluckman & Hanson 2005).

GXE-oberlander-2008

DEVELOPMENTAL PROGRAMMING-gluckman-hanson-2014 act 2008
DEVELOPMENTAL PROGRAMMING-gluckman-2006 2005
EARLY LIFE EVENTS gluckman-2007
DEVELOPMENTAL PROGRAMMING-gluckman-2011
DEVELOPMENTAL PROGRAMMING-EPI-vaiserman
DEVELOPMENTAL PROGRAMMING-EPI-vaiserman-2015-NB
Gluckman-2 2005
GLUCKMAN-HANSON IN PRINT

GXE-belsky-2013
PLASTICITY-belsky-pluess 2013 NB
PLASTICITY-pluess-belsky-2013- vantage sensitivity NB
PLASTICITY-pluess-belsky-2012 actually 2011
PLASTICITY-CHILDCARE
PLASTICITY-belsky-pluess-2009

EPI-skinner-2010 Miller et al. PREGNANCY-dl giudice-fetal programming CHILDCARE-pluess-belsky-2009	
McDade p46	
ALLERGIES-hurtado LACTATION-sellen NB Ben-Shlomo & Kuh (2002) Crimmins & Finch (2006) print	
OXIDATIVE STRESS-metcalfe-2010 NB RELIGION-baumard-LHS GINGER HOT TEA IN THE MORNING Aryurvedic remedy for for digestive and liver support Apple cider vinegar **Dockerty et al. (2001)**: LHS-bogin-2007 CHECK	A
Ryff & Singer (1998): Optimal allostasis, sustained over time, entails the the cumulative long-term pattern of resistance to catecholamine depletion (sympathetic nervous system activity), rapid return of cortisol levels (HPA axis reactivity) to normal operating range following stress exposure; and maintenance within optimal operating ranges of other remaining markers (e.g. blood pressure, waist-hip-ratio).	
Halton & Hu (2004): Convincing evidence that a higher protein intake increases thermogenesis and satiety compared to diets of a lower protein content. High protein meals lead to a reduced subsequent energy intake. Latner, J. D. & Schwartz, M. (1999). The effects of a high-carbohydrate, high-protein or balanced lunch upon later food intake and hunger ratings. *Appetite* 33: 119-128.	

Serotonin deficiency: depression, anxiety, irritable bowls, inflammation of the colon, hormonal imbalances (particularly estrogen/progesterone imbalances), premenstrual symptoms, unhealthy cravings for alcohol and carbohydrates, common mental emotional difficulties and notably insomnia (INSOMNIA: Two capsules of 500 mg tryptophan just before retiring; 1000 mg dosage). Tryptophan supports sleep best when accompanied by small doses of niacinamide (amide of B3) and pyridoxyl 5-phosphate (vit B6). Both tryptophan and niacinamide metabolism requires pyridoxyl 5-phosphate (vit B6). Tryptophan supports neurotransmission throughout the entire body. For normal tryptophan metabolism: niacin, pyridoxyl 5-phosphate (vit B6), glutamine. Taurine and tyrosine combination (Parkinson).	
Widespread disorders of of human psychobiology in Western industrialized countries: serotonin deficiency syndrome (Table sleep; IPALEO DIET; INTERMITTANT FUNCTIONAL CATALYSIS) Depression, common anxiety, sleep disturbances, obsessive compulsive actions, fear, anger, over-arousal, violence, aggression, suicidal tendencies.	
Braverman Preferred serotonergic drug: L-tryptophan	
Q10 Navarro-yepes	
DTB-LONGEVITY-REPRODUCTION-mueller LHS-low-BOOK NB DTB-fogel-economics LHS-mode pM > Pm population density stress/overburden of psychological procursive insults LHS-mode pM REPRODUCTION- jasienska (2009) NB LIFE HISTORY-bateson DT-Newson (2009) LONGEVITY-REPRODUCTION-doblhammer Wendt Bulgarian/Russian centenarians THL populations and protein consumption: meat vs dairy products. SEASONALITY refer to section CR effects Homozygosity effects	

Demographic transitions	
Gloria-Bottini et al. (2005) DELAYEDCHIDBEARING FERTILITY-DECLINING-skakkebaek-2006 FERTILITY-bachrach CHECK DEMOGRAPHIC TRANSITION-haaga CHECK DL DEMOGRAHIC TRANSITION-coleman-third DL DEMOGRAHIC TRANSITION-lesthaeghesurkyn DL DEMOGRAPHIC TRANSITION-newson-2007 DEMOGRAPHIC TRANSITION-newson-2009 DL LIFE HISTORIES-sear- DL DEM TRANS-lesthaege DL DEM TRANS-bongaerts DL DEM TRANS-hirschman DL DEM TRANS-brewster Gloria-Bottini et al. (2005) DELAYEDCHIDBEARING Knaul (1985); population density effects, role of female vs males p 437-450-454 DL DEMOGRAPHIC TRANSITION-rindfuss MS DEMOGRAPHIC TRANSITION-rindfuss-1996 DL DEMOGRAPHIC TRANSITION-reher-2011-NB DL DEMOGRAPHIC TRANSITION-newson ref DL DEMOGRAPHIC TRANSITION-castles CHECK DL DEMOGRAPHIC TRANSITION-lesthaeghe DL DEMOGRAPHIC TRANSITION-coleman DL DEMOGRAPHIC TRANSITION-lesthaeghe-2009 PAPER DO DL DEMOGRAPHIC TRANSITION-lesthaeghe-surkyn DO DL DEMOGRAPHIC TRANSITION-goldscheider CHECK DL FERTILITY EVOLUTION-davis DL DEM TRANSlam; DL DEM TRANS-fertility DL DEM TRANS-hirschman CHECK DL DEM TRANS-brewster CHECK Gloria-Bottini et al. (2005) DELAYEDCHIDBEARING FERTILITY TRANSITION FERTILITY-EUROPE-frejka FERTILITY TRANSITION-frejka-2 FERTILITY TRANSITION-koytcheva CHECK FERTILITY TRANSITION-123-sigle-rushton-educatio FERTILITY TRANSITION-FRANCE-toulemon CHECK FERTILITY TRANSITION-sobotka-toulemon-family CHECK FERTILITY TRANSITION-GERMANY-dorbritz CHECK dorbritz x3 FERTILITY TRANSITION-kneale-education CHECK FERTILITY TRANSITION-henz-gender roles CHECK GERMANY	

FERTILITY TRANSITION-james-education CHECK FERTILITY TRANSITION-nauck-germany-japan NB CHECK GERRMANY FERTILITY TRANSITION-bourgeois-pachet CHECK FERTILITY TRANSITION-vanbavel CHECK FERTILITY-preston DTB-OFFSPRING-NB CHECK	
FERTILITY-DECLINING-skakkebaek-2006 FERTILITY-DECLINING-grant-2006 FERTILITY-DECLINING-lutz-2006 FERTILITY-DECLINING-kohler-2006 FERTILITY-bachrach FERTILITY-EARLIER-HERMAN-GIDDENS-2006 DEMOGRAPHIC TRANSITION-SECOND-van der kaa DEMOGRAPHIC TRANSITION-casterline DEMOGRAPHIC TRANSITION-haaga DL DEMOGRAHIC TRANSITION-shenk DL DEMOGRAHIC TRANSITION-lesthaeghesurkyn DL DEMOGRAPHIC TRANSITION-newson-2007 DEMOGRAPHIC TRANSITION-newson-2009 DL LIFE HISTORIES-sear- AGEING-RUSSIA-gavrilov Mulder (1998) DL DEMOGRAPHIC TRANSITION-mulder DL DEM TRANSlam; MS DEM TRANS-vandekaa DL DEM TRANS-fertility DL DEM TRANS-lesthaege DL DEM TRANS-bongaerts DL DEM TRANS-hirschman DL DEM TRANS-brewster DL DEM TRANS-femalestatus Gavrilov & Gavrilova **Life history trade-off relationships**.	

Demographic transition.

DL DEMOGRAHIC TRANSITION-shenk

FERTILITY-GERMANY-heiland

DL DEMOGRAHIC TRANSITION-dribe

DL DEMOGRAHIC TRANSITION-lesthaeghe-2010

DL DEMOGRAPHIC TRANSITION-rindfuss

MS DEMOGRAPHIC TRANSITION-rindfuss-1996

MS DEMOGRAPHIC TRANSITION-santow

DL DEMOGRAPHIC TRANSITION-reher-2011-NB

DL DEMOGRAPHIC TRANSITION-newson ref

DL DEMOGRAPHIC TRANSITION-imhof

DL DEMOGRAPHIC TRANSITION-castles

DL DEMOGRAPHIC TRANSITION-lesthaeghe

DL DEMOGRAPHIC TRANSITION-lesthaeghe-1983

DL DEMOGRAPHIC TRANSITION-coleman

DL DEMOGRAPHIC TRANSITION-lesthaeghe-2009

DL DEMOGRAPHIC TRANSITION-lesthaeghe-surkyn

DL DEMOGRAPHIC TRANSITION-goldscheider

DL LIFE HISTORIES-sear-

Mulder (1998) DL DEMOGRAPHIC TRANSITION-mulder

DL DEMOGRAPHIC TRANSITION-sobotka

DL FERTILITY EVOLUTION-davis

DL DEM TRANSlam;

MS DEM TRANS-vandekaa

DL DEM TRANS-fertility

DL DEM TRANS-lesthaege

DL DEM TRANS-bongaerts

DL DEM TRANS-hirschman

DL DEM TRANS-brewster

DL DEM TRANS-femalestatus

FERTILITY TRANSITION

FERTILITY-EUROPE-frejka

FERTILITY TRANSITION-frejka-2 FERTILITY TRANSITION-koytcheva FERTILITY TRANSITION-FRANCE-toulemon FERTILITY TRANSITION-sobotka-toulemon-family FERTILITY TRANSITION-GERMANY-dorbritz FERTILITY TRANSITION-kneale-education FERTILITY TRANSITION-henz-gender roles FERTILITY TRANSITION-james-education FERTILITY TRANSITION-nauck-germany-japan FERTILITY TRANSITION-bourgeois-pachet FERTILITY TRANSITION-vanbavel	
MED sofi	
Oberritter (2010) soucres BMI (kg/m^2): normal body weight 18.5-24.9; overweight 25.0-29.9; obese grade 130-34.9; obese grade 2 35.0-39.9; obese grade 3 > 40	
Fertility-Europe-kneale British cohorts Fogel (2004) Nobel Prize winner for Economics in 1993 Basten et al. (2013). In respect of the ongoing transition to low fertility some features thereof are often highlighted: expanding education, rising income, the rise of gender equality, female labour force participation, ideational changes, consumerism, urbanization, family disintegration, economic uncertainty, globalization, modern conception, and other contrasting or complementary forces. The authors consider/contend that rising education levels, especially regarding women, is the most important factor contributing to global fertility trends in the past decades, particularly in respect of the	**D**

decline of fertility in higher fertility countries, and the postponement of parenthood to higher childbearing ages in more affluent countries with low fertility.

Billari (2009).

ADAPTOGENS

Bird et al. (2010). Allostatic load

Savini et al. (2013). Obesity is characterised, by *inter alia*, elevated levels of reactive oxygen or nitrogen species. Inadequacy of antioxidant defences in obese individuals may be due to lower intakes of antioxidant- and phytochemical-rich foods (foods and vegetables) or an increased requirement for such antioxidant substances. The authors describe the meaning of obesity as a state of chronic oxidative stress and the potential for interventions to improve redox balance. Based on Caucasian mortality data, a BMI of 30 kg/m^2 or higher indexes obesity and more than 25 kg/m^2 implicates overweight. (Perez-Escamilla et al. 2012, op. cit. Savini et al. 2013). Obesity involves excessive fat accumulation in the context of a positive energy balance associated with the interaction of several factors including diet (increased intake of energy-rich foods and decreased intake of food rich in micronutrients and bioactive compounds), decreased physical activity, nutritional and hormonal status early in life; as well as genetic, environmental, cultural and economic factors (Winter et al. 2013, op. cit. Savini et al. 2013; Drewnowski 2009, op. cit. Savini et al. 2013). Oxidative stress and inflammation are apparently interlinked in obesity; with ROS triggering the release of cytokines, which in turn enhance ROS production (Bryan et al. 2013, op. cit. Savini et al. 2013). Systemic oxidative stress and inflammation is accordingly considered key factors in the pathogenesis of obesity and obesity-related diseases (including atherosclerosis, insulin resistence, type 2 diabetes, and cancer: Dandona et al. 2005, op. cit. Savini et al. 2013; Crujeiras et al. 2013, op. cit. Savini et al. 2013).
One of the strategies to lower oxidative stress involves an antioxidant-rich diet. A diet with abundant fruit, vegetables, whole grains, fish, olive oil and fermented dairy foods assists in reduction of the incidence of metabolic diseases (Sofi et al. 2010). Supplementation of single individual compounds does not seem to have much health-supporting effects; but health-supporting effects as observed require the cumulative effects of multiple nutrients of diets containing such compounds.
At low concentrations ROS/RNS (reactive nitrogen species) are involved in a diversity of biological effects, such as intracellular signalling and immune-mediated defence against pathogenic microorganisms; whereas at high levels these reactive species can damage DNA, lipids and proteins, leading to tissue injury and cell death (Halliwell 2001). Involved in minimizing free radical cytotoxicity are also endogenous antioxidant

compounds such as urate, glutathione, ubiquinone and thioredoxin. Some proteins act as antioxidants (ferritin, transferrin, lactoferrin, caeruloplasmin) by binding and sequestering transition metals which may start oxidative reactions.
Redox imbalance is considered to play a key role in cancer etiology. Main determinants in carcinogenesis involve inter alia energy balance, hyperinsulinemia oxidative stress and chronic inflammation. There is a strong correlation between increased risk of cancer/worst cancer outcome and BMI (overweightness, obesity) and fat distribution (Fujihara et al. 2012, op. cit. Savini et al. 2013; Calle et al. 2003, op. cit. Savini et al. 2013). Existing evidence that oxidative stress may cause DNA damage, resulting genomic instability (associated with activation of oncogenes and/or inactivation of tumor suppressor genes). Altered gene expression may result from direct action of oxidative DNA modifications or mediated by epigenetic alterations. ROS has been shown to disrupt epigenetic patterns by producing carcinogens which induce hypermethylation and/or by regulating histone modifications and miRNA expression; thereby affecting tumorigenesis and cancer progression (Crujeiras et al. 2013, op. cit. Savini et al. 2013).
Potential strategies to reduce oxidative stress (redox state modulation).
1) ***Weight loss and physical activity***. Weight reduction in obese individuals decreases oxidative damage and inflammation. Lowering energy supply activates proteins of the sirtuin (SIRT) and Forkhead box (sub-group O: FoxO) families (Crujeiras et al. 2008). Sirtuins transcriptionally improve metabolic efficiency, strengthen antioxidant defenses and dampen inflammatory activities (Galli et al. 2011). FoxO proteins modulate transcription of genes in respect of energy homeostasis, cell survival and inflammatory responses (Salminen et al. 2011, op. cit. Savini et al. 2013). The combination of a hypoenergetic diet and regular exercise potentiates the beneficial effects on redox balance (Rector et al. 2007, op. cit. Savini et al. 2013; Montero et al. 2012, op. cit. Savini et al. 2013; Strasser 2012, op. cit. Savini et al. 2013; De Lemos et al. 2012, op. cit. Savini et al. 2013). Regular physical activity acts as a natural antioxidant and anti-inflammatory strategy for preventing obesity-associated complications (improves glucose-insulin homeostasis, endothelial function and antioxidant defenses).
2) ***Dietary patterns and macronutrients***.

EPI-ALLOSTASIS-badanes
EPI-ALLOSTASIS-chyu
EPI-ALLOSTASIS-mcewen-2016 in text
ALLOSTASIS-mcewen-2010
ALLOSTASIS-EPI-darnaudery

SLEEP-chen
SLEEP-owens

Straub et al. 2010. In ref

Choi purine rich foods
OBESITY-stenvinkel
URIC ACID-zhang-magnesium
URIC ACID-de oliveira-BMI
URIC ACID-abdullah-body condition
URIC ACID-bedir-leptin
URIC ACID-Kanellis-inflammation
URIC ACID-baillie-hypoxia
URIC ACID-Ruggiero-inflammatory markers
URIC ACID-johnson-CR

URIC ACID-kutzing-firestein
URIC ACID-yao-purine metabolism
OXIDATIVE STRESS-alonso-testosterone
OXIDATIVE STRESS-ALVAREZ-evolution
OXIDATIVE STRESS-martinon-inflammasones
OXIDATIVE STRESS-johnson

Immune System Disregulation (ISD) syndrome

OXIDATIVE STRESS-kim
OXIDATIVE STRESS-Mattson-cheng-neurohormosis
OXIDATIVE STRESS-sareila-
OXIDATIVE STRESS-halliwell-biochemistry
OXIDATIVE STRESS-chatterjee
OXIDATIVE STRESS-hekimi-ageing
OXIDATIVE STRESS-serafini-NB
OXIDATIVE STRESS-serafini
OXIDATIVE STRESS-stedile

Hekimi (2011). Also put in ref
Howes (2006). also re SUPPLEMENTATION

References: oxidative stress/autophagy
OXYGENSTRESS-sanz-2004 CR in ref
OXIDATIVE STRESS-berlett
OXIDATIVE STRESS-johnson-UA
OXIDATIVE STRESS-glantzounis-UA
OXIDATIVE STRESS-johnson-CR
OXIDATIVE STRESS-buchowski-CR
OXIDATIVE STRESS-oliviera-UA

OXIDATIVE STRESS-puddu-UA **OXIDATIVE STRESS-alvarezlario** **OXIDATIVE STRESS-george-UA-allopurinol** **OXIDATIVE STRESS-catoni-NB** **OXIDATIVE STRESS-chen-antioxidant** **OXIDATIVE STRESS-aitken-spermatozoa** **OXIDATIVE STRESS-cao-spermatozoa** **OXIDATIVE STRESS-bromfield-NB** **OXIDATIVE STRESS-aitken-spermatozoa** **OXIDATIVE STRESS- aitken-1999** **OXIDATIVE STRESS-harshman** **OXIDATIVE STRESS-raberg-immunity** **OXIDATIVE STRESS-von Schantz NB** **OXIDATIVE STRESS-zera** **OXIDATIVE STRESS-alonso-alvarez-testosterone** **ANITIOXIDANT-velioglu** **OXIDATIVE STRESS-halliwell-NBx3** **OXIDATIVE STRESS-halliwell-NBNB** **OXIDATIVE STRESS-koskenkorva-frank** **EPI-MALE FERTILITY-jenkins** **EPI-EARLY LIFE** **EPI-laurent-stress** **BERRIES-** **AUTOPHAGY-OXIDATIVE STRESS-lee-NB** **AUTOPHAGY-OXIDATIVE STRESS-filomeni-NB** **AUTOPHAGY-OXIDATIVE STRESS-kiffin** **AUTOPHAGY-wu and wu-pdf** **AUTOPHAGY-giordano also My Documents** **NUTRITION-DISEASES-ruiz-nunez NB** **NUTRITION-LIFESTYLE-ruiz-nunez-pdf** **NUTRITION-thorburn NB, also re fibre** **LHS-belsky-childhood** **LHS-brumbach** **ALLOSTATIC LOAD-beauchaine** **ALLOSTASIS-hastings** **ALLOSTASIS-juster-2010** **STRESS-flinn** **STRESS-miller-childhood** **STRESS-nettle** **MATERNAL-champagne**	

FAMINE-INCREASED

DTB- lesthaeghe-NB

BOOK ULTRAMIND SOLUTION HYMAN

HOWES

Pischinger (1989).

Nettle

URIC ACID-sautin
URIC ACID-CHOI-2004
URIC ACID-min-min-
De Oliveira & Burini (2012).

Coleman (2004). The concept of the Second Demographic Transition (SDT) was jointly developed by Van de Kaa (1987) and Lesthaeghe (1987). The model recognizes and describes a syndrome of substantial and unprecedented progress of cohabitation, lone parenthood, childbearing outside of marriage and low fertility observed since 1960, and the retreat from marriage and traditional norms of sexual restraint. These trends have been consolidated in the 1990s.

Surkyn & Lesthaeghe (2009
Miettinen et al. (2014) NB
DT-frejka-CENTAL
DT-frejka-family size NB
Dribe et al. (2014) NB
DT-huijts-childnessless
INTELLIGENCE-EDUCATION-FERTILITY
FERTILITY-EDUCATION-heiland

FERTILITY-kohler-Education also DEM TRANS FERTILITY-GENETICS-rodgers INTELLIGENCE-nisbett	
Kaplan & Lancaster (1999) op cit Kaplan & Lancaster (2003) Kaplan & Gangestad (2004) A	
LHS-rogers-1990 Rogers (1990) BC	

1. Notizen	
AFRICAN ORIGIN-eswaran	
	ADS
Toynbee (1946)	
Growth (mimesis-resonance with elite) **Genesis of civilizations** The possibility that man achieves civilization, not as a result of superior biological endowment or geographical environment, but as a resposponse to a challenge in a situation of special difficulty which rouses to make a hitherto unprecedented effort. An essential difference between civilizations as we know them is the direction taken by mimesis or imitation. Mimesis is a generic feature of all social life (both in primitive societies and in civilizations). In primitive societies, as we know them, mimesis is directed towards the older generation and towards dead ancestors who stand, unseen but not unfelt, at the back of the living elders, reinforcing their prestige. Custom rules and society remain static. On the other hand, in societies in process of civilization, mimesis is directed towards creative personalities who command a following because they are pioneers. Society is in dynamic motion along a course of change and growth. Alternating rhythm of static and dynamic, of movement and pause and movement, has been regarded by many observers in many different ages as something fundamental in the nature of the universe. In their pregnant imagery the sages of the Sinic Society described these alternations in terms of yin and yang – Yin the static and Yang the dynamic. In the Chinese	

formulaYin is always mentioned first, and, within our field of vision, we can see that our breed, having reached the ledge of primitive human nature 300 000 years ago, has reposed for ninety-eight percent of that period before entering on the Yang-activity of civilization. It seems obvious that the positive factor which, within the last 6 000 years, has shaken part of mankind out of the Yin state of primitive societies 'on the ledge' into tha Yang state of civilizations 'on the cliff' must be sought either in some special quality in the human beings who made the transition or in some special feature of the environment in which the transition has taken place or in some interaction between the two. It is clear that if the geneses of civilizations are not the result of biological factors or of geographical environment acting separately, they must be the result of some kind of interaction between them. By the light of mythology we have gained some insight into the nature of challenges and responses. We have come to see that creation is the outcome of an encounter, that genesis is a product of interaction. Quest: Search for the positive factor that has shaken part of mankind out of the 'integration of custom' into the 'differentiation of civilization' within the last 6000 years.'Conception of 'Challenge-and-Reponse'. Thus, our

In the thirteenth and fourteenth centuries the task of Westernizing the last remaining Continental barbarians was carried on no longer under the leadership of hereditary monarchs who, like Charlemagne and Otto I, had assumed the Roman Imperial title, but through the instrumentality of two new institutions: the city state and the militant monastic order. The Hansa towns and the Teutonic Knights, between them, advanced the bounds of Western Christendom from the Oder to the Dvina.

MS saxon wars. Charlemagne-THEOCRACY ? CLERICTOCRACY 1090-1400 Papacy 1400-1648 interdenomial religious wars (al religious type wars are strongly win-lose: Theocracy-Papacy-Thirty years war) MS Thirty years war

Growth of civilizations.

The problem now confronting the Western Society was how to change over from an agricultural aristocratic to an industrial democratic way of life without adopting the city-state system. The feudal institution of a periodical representative and consultative assembly was well fitted for its original purpose of serving as a liaison between the Crown and its subjects. On the other hand it was originally not at all well fitted for the task to which it was successfully adapted in seventeenth-century England - the task of taking over the functions of the Crown itself and gradually superceding it as the mainspring of political authority. It is no mere paradox to say that the strength of English monarchy in the second, or medieval, chapter of the history of Western Christendom made possible its supercession by parliamentary government in the third chapter. No other country in the second chapter experienced such authorative and disciplinary control as that exercised by William the Conqueror, the first and second Henrys, and the first and third Edwards. Under these strong rulers England was welded into a national unity long before anything like it was achieved in France or Spain or Germany.

Prussian aristocracy The descendants of medieval colonists who occupied (Brandenburg, Pomerania and Eastern Prussia) these 'bad lands' have payed an exceptional part in the history of our Western Society. It is not only that in the nineteenth century they mastered Germany and in the twentieth led the Germans in a strenuous attempt to provide our society with its universal state. The Prussian also taught his neighbours how to make sand produce cereals by enriching it with artificial manures; how to raise a whole population to a standard of unprecedented social efficiency by a system of compulsory education and of unprecedented social security by a system of compulsory health and unemployment insurance. Stein, Hardenberg, Humboldt to Bismarck Prussian professional value system and its mimesis (e. g. Prussian ethics: sense of duty and justice, diligence, integrity, incorruptibility, reliability).

	Too light
RE PAPAL Christendom. Toynbee (1046):The creative spirits of the Roman Church (who) set themselves in the eleventh century to rescue our Western Society from a feudal anarchy by establishing a Christian Republic. Hildebrand and his successors succeeded in creating the master institution of Western Christendom. They won for Papal Rome an empire which had a great hold on the human heart and which on the mere material plain embraced vast tracts of Western Europe beyond the Rhine and the Danube. These Papal conquests were based on a combination of ecclesiastical centralism and uniformity with political diversity and devolution; and, since the superiority of the spiritual power over the temporal power was a cardinal point in its constitutional doctrine, this combination made the note of unity predominant without depriving the adolescent Western Society of those elements of liberty and elasticity which are indispensable conditions of growth. But the very reason why in this age a majority of the princes and city states of Western Christendom accepted the Papal supremacy with so little demur was because the Pope was not then under suspicion of attempting to trespass on the domain of the secular power. The Papacy was able to be creative because it threw itself without hesitations or reservations into the task of giving leadership and expression and organization to an adolescent society society's awakening desires for a higher life and a higher growth. The fall of the Hildebrandine Church is as extraordinary a spectacle as its rise; for all the virtues which had carried it to its zenith seemed to change, as it sank to its nadir, into their own exact antithesis. Gregory VII (Hildebrand) and his successors persisted in the use of force until victory on this non-spiritual plane became an end in itself. It was at the moment of triumph, in the third year of his reign as Pope Gregory VII, that Hildebrand extended the field of battle to the debatable ground of Investiture. MS Investiture controversy. On this issue of Investiture Hildebrand staked the whole of the moral prestige which he had won for the Papacy and his hold upon consciousness of the Plebs Christiana in Henry IV's Transalpine dominions was strong enough, in conjunction with the strength of Saxon arms, to bring the Emperor to Canossa. Yet, although Canossa may have dealt the Imperial dignity a blow, the sequel was not an end but a resumption of the struggle. Fifty years of conflict had produced a breach between the Papacy and the Empire too wide and too deep to be closed by any politic compromise on the particular issue over which the conflict had originated. The outcome of the great war between the thirteenth-century Popes and the Hohenstaufen was the usual outcome of all wars that are fought out to the bitter end. The nominal victor succeeded in dealing the death-blow to his victim at the cost of sustaining fatal injuries. As result of the deadly struggle of 1227-1268, the Papacy had sunk to the level of weakness to which it had reduced the Empire. The sixteenth century saw the process completed. CLARIFY Schism: 1379-1415. It was now certain that the local secular princes would inherit, sooner or later, within their respective territories, the whole of the administrative and financial organization and power which the Papacy had been gradually building up for itself.	
The disintegration of civilizations.	
It is that disintegration of a broken-down civilization which declares itself in the 'secession of the proletariat' from a band of leaders who have degenerated into a 'dominant minority'. We tried to obtain a clearer view of the nexus of cause and effect between the loss of the leading minority's faculty of creation and the loss of the faculty for attracting the majority by charm rather than by force. It is not surprising to find that mimesis fails when the leaders' creativity gives out. This link of mimesis has always been precarious by reason of a treacherous duality – the revenge of the unwilling slave – which is part of the nature of any mechanical device. The outstanding criterion of disintegration is the schism of the body social into three factions: Dominant minority (militarists, exploiters, legists/administrators maintaining the universal states), internal proletariat (existence of an 'intelligentsia' recruited from the internal proletariat as an agent of the dominant minority) and external proletariat () and schisms of the soul. Standardisation/uniformity through	

disintegration. We have seen dominant minorities uniformly working out philosophies and producing universal states; internal proletariats uniformly discovering 'higher religions' which aim at embodying themselves in universal churches and external proletariats uniformly mustering war bands which find vents in 'heroic ages'.	
Toynbee (1957)	
Thirty Year War The Thirty Years' War was a series of wars in Central Europe between 1618-1648. It was one of the longest and most destructive conflicts in European history, as well as the deadliest European religious wars, resulting in eight million casualities. Initially a war between various Protestant and Catholic states in the fragmented Holy Roman Empire, it gradually developed into a more general conflict involving most of the great powers. These states employed large mercenary armies, and the war became less about religion and more of a continuation of the France-Habsburg rivalry for political European pre-eminence. Religious beliefs affected ideas of the legitimacy of the political status of rulers. The war began when the newly elected Holy Roman Emperor, Ferdinand II, tried to imose religious uniformity on his domains, forcing Roman Catholicism on its people. The war altered the the previous political order of European powers. The rise of Bourbon France, the curtailing of Habsburg ambition and the ascendancy of Sweden as a great power created a new balance of power on the continent, with France emerging from the war strengthened and increasingly dominant in the latter part of the 17th century.	
Mercenary pillaging, famines, plagues, great population losses, destruction of civilian lives and property by cruel and greedy mercenary soldiers. Major outbreak of whitch persecutions. Marks the period as the peak of European whitch-hunting phenomenon.	
The arangements agreed upon in the Peace of Westphalia were instrumental in laying the legal foundations of the modern sovereign nation-state. It was the large major religious war in mainland Europe, ending the large-scale religious bloodshed accompanying the Reformation, which had begun over a century before. England and Brandenburg-Prussia, shy participants in the conflict, finally managed to get themselves on the European stage, increasing their strengths over time. 18th century Europe had another political reconstruction in which they had a greater role. The episode ended with the Seven Years' War.	
Feudalism	
(The feudal system first appears in definite form in the Frankish lands in the 9th and 10th century. The powerful surrounded themselves with men who rendered them service, particularly military service in exchange for protection. More and more, this service-and-protection contract came to involve granting of a *beneficium*, the use of land which tended to become hereditary. Local royal officers and great landowners increased their power and forced the king to grant them rights of private justice and immunity from royal interference. By these processes feudalism became fixed in Frankish lands by the end of the 10th century. Feudalism spread from France to Spain, Italy and later Germany and Eastern Europe. In England the Frankish form was imposed by William I (William the Conqueror) after 1066, although most of the elements of feudalism were already present).	
Vierhaus (1984) Absolutismus	
Allerdings ist die Politik von Fürsten, die absolute Herrschaft in Anspruch zu nehmen, die dynamischte politische Kraft der Zeit gewesen. Ansätze der Ausübung solcher Gewalt schon vor der Mitte des 17. Jahrhunderts. Monarchischer Absolutismus keineswegs zuende nach 1763. Vierhaus (1984) considers the term Absolutism as era descriptor to cover the time period between the end of the thirty years war and the seven year war (1648-1763 in central Europe, sensu stricto).	**P 10**
Thirty Year War (1618-1648): much devastation caused by pillaging, poorly or unpaid mercenary soldiers in the final phase of this war. Pest 1636-1640.	**P 16**

Substantial population reductions. In dieser Situation ist es von grosser und folgenreicher Bedeutung gewesen dass die Landesherren und ihre Regierungen wirtschaftspolitisch aktiv wurden. Es setzte eine Phase des Merkantilismus und Kameralismus ein, einer politischen Praxis, die mit der Förderung der Wirtschaft vor allem die Stärkung der Staatsmacht anstrebte. Das 16. Jahrhundert hatte, aufs Ganze gesehen, steigenden Wohlstand gebracht. Am stärksten ist die merkantilistische-kameralistische Politik in Brandenburg-Preussen zur Wirkung gekommen wo die wirtschaftliche Entfaltung in den Dienst der staatlichen Machtsteigerung, der Rüstung und der Sozialdisziplinierung gestellt worden waren.	
Vierhaus (1984) Der ältere norddeutsche Adel war Landadel; auf dem ländlichen Güterbesitz beruhte die Landstandschaft, die Zugehörigkeit zur Ritterschaft. In der Hierarchie der politischen Ordnung hat der Adel seine Rolle als Herrschaftsstand in vielfältiger Form wahren können. Zwar hat der Absolutismus die überkommenen intermediären Gewalten weitgehend ihrer autonomen Rechte und Funktionen entkleidet; als strukturell soziale und mittelbar politische Ordnungselemente aber hat er sie konserviert.	
(Absolutismus Die absolute Monarchie ist eine Herrschaftsform bei der ein Adliger das Staatsoberhaupt ist, den Staat nach aussen und innen repräsentierent. Im Absolutismus ist folglich eine einzige Person der Träger der Staatsgewalt. Der Absolutismus war zwischen den Ende des *Dreissigjährigen Krieges* (1618-1648) und der *Französichen Revolution* (1789) die verbreiteste Herrschaftsform in Europa Diese Herrschaftsform kristallisierte sich vor allem zwischen dem Übergang vom Mittelalter zur Früher Neuzeit heraus, und ist dann vor allem im Barock und der Aufklärung die bestimmende Form der Herrschaft. Wobei es mitunter schwierig ist die Monarchien im Mittelalter vom fogenden Absolutismus abzugrenzen.) Der wesentliche Unterschied ist, dass das Spätmittelalter vom Feudalismus geprägt war. Im Feudalismus erhielt ein Grundherr von einem höhergestellten Adligen ein Stück Land (inklusiver der Bewohner) und schuldete dem Adligen dafür Kriegsdienste. Er wurde so zum Vasallen des Adligen. Der Grundherr erhielt die wirtschaftlichen Nutzungsrechte, wobei ihm die Bewohner, welche das Land bewirtschafteten Arbeitsdienste schuldeten und zur Naturalabgabe verpflichtet waren (Zehnt). Der Monarch stand in diesem feudalen System an der Spitze: er vegab Land an die Konvasallen, die es dann an Untervasallen aufteilten, die es wiederum von unfreien Bauern bearbeiten liessen. Der König selbst war hierbei – dem Verständnis im Mittelalter folgend – selbst ein Vasall, da er Gott untergeordnet war und war somit das Oberhaupt aller anderen Vasallen, hatte aber keinen unmittelbaren Zugang zu seinen Untertanen, die von ihren Grundherren abhängig waren und diesem die Treue schworen. Das Land der Vasallen wurde zunehmend der erbliche Besitz der Vasallen. Das Feudalsystem führte damit Schrittweise zum Verfall der königlichen Macht. Somit verloren die Monarchen Macht an den Adel. Das änderte sich im Absolutismus. In seiner vollen Ausprägung entstand der Asolutismus im Frankreich des 17. Jahrhunderts und löste hierbei das Feudalsystem ab. Die Macht wurde auf den Monarchen konzentriert, wohingegen der Einfluss des Adels stufenweise beschnitten und dann vollständig neutralisiert wurde. (Ludwig XIV, Frankreich). Kardinal Mazarin (am Hofe Ludwigs) folgte dem Bestreben und Politik seines Vorgängers Kardinal Richelieu des Herausdrängens des Hochadels aus den hohen Gremien und Räten des Königreichs, um die Staatspolitik von den Interessen des des Adels zu befreien. Machtsäulen des absoluten Monarchen: stehende Heeren, Justiz und Polizei, Verwaltung mit dem König an der Spitze, Bindung des Adels an den Hof (den Einfluss des Adels zu kontrollieren und in grossen Teilen zu neutralisieren), die Staatskirche (Klerus) sowie Merkantilismus, eine Wirtschaftspolitik, streng auf das Wohl der Finanzen ausgerichtet.	
Einfluss des Adels war hoch im Spätmittelalter.	

AUTOPHAGY-AUTOIMMUNITY-CURCUMUN	
Rubinsztein et al. (2011) AUTOPHAGY-rubinsztein curcumin at end	
DL ANTIOXIDANT-chiu-schizandrin	
DL AUTOPHAGY-mizushima-protein turnover	
DL AUTOPHAGY-ristow-longevity	
DL AUTOPHAGY-CR-witte	
DL AUTOPHAGY-AUTOIMMUNE-saitoh	
Hartleben et al. (2010) AUTOPHAGY-hartleben-nephrosis	
Anand et al. (2008) CURCUMIN-anand	
Calabrese et al. (2007) CURCUMIN-calabrese	
Eisenbarth & Gottlieb (2004) AUTOIMMUNE –polyendocrine	**Not ref**
Ronco & Debiec (2011) AUTOIMMUNE-nephropathy	**Not ref**
Rubinsztein et al. (2007) AUTOPHAGY-rubinsztein-treatment	**Not ref**
Degenhardt et al. (2006) DL AUTOPHAGY-degenhardt	
DL AUTOPHAGY-gottlieb-NB	
Neumann et al. (2013) DL AUTOIMMUNE-atrophic	
Chen & Blaser (2007) MS AUTOIMMMUNE-chen	
Rook & Brunet (2005) MS IMMUNOREGULATION-rook	
Gershwin & Schoenfeld (2011) DL AUTOIMMUNE-gershwin	**NB-refs**
Banka et al. (2011) DL AUTOIMMUNITY-banka (re genetics)	**Not ref**
Toh et al. (1997) DL AUTOIMMUNITY-toh (familial clustering)	**Not ref**
Vaarala (1999) MS-AUTOIMMUNITY-vaarala	**Not ref**
Sepa et al. (2005) MS MATERNAL-stress-sepa-diabetes	**Not ref**
Mizushima & Komatsu (2011) AUTOPHAGY-mizushima	
Haugen et al. (1999) MS AUTOIMMUNE-haugen-	
	NB
MS AUTOPHAGY-giordani	**Not ref**
MS AUTOPHAGY-haugen-diet therapy	
Ferguson (2001) MS AUTOPHAGY-polyphenols in genomic	**Not ref**
Okin & Medzhitov (2012) MS Evolution of inflammatory diseases	
Hafström et al. (1988). DL AUTOIMMNUE-fasting	**Not ref**
Müller et al. (2001) AUTOIMMUNE-fasting	**Not ref**
(Weindruch & Sohal 1997). CR-weindruch Autoimmune	
DL AUTOIMMUNE-manzel also MS? NB	
DL AUTOIMMUNE-nephropathy-kovacs NB	
MS AUTOIMMUNE-diet-thorburn UCT	
MS AUTOIMMUNE-diet-microbial-thorburn UCT	
DL AUTOIMMUNE-diet-stamp	
DL AUTOIMMUNE-kukroo-fasting	
DL AUTOIMMUNE-mangge-diet-omega	
DL AUTOIMMUNE-hewagama	
EPI-AUTOIMMUNE-costenbader UCT	
INFECTIONS-bach NB	
DL AUTOIMMUNE-versini-obesity	

DL innate immunity-NGUYEN	
DL AUTOIMMUNE-cooper	
MS AUTOIMMUNE-sogawa-fasting	
MS AUTOIMMUNE-selmi	
DL AUTOIMMUNE-OMEGA3-simopoulus	
DL AUTOIMMUNE-cho-genomics	
MS EPI-sarkar-seasonality	
MS AUTOIMMUNE-femal-rubtsov	**To ref**
DL AUTOIMMUNE-richardson	**To ref**
DL AUTOIMMUNE-pendell-sex	
DL AUTOIMMUNE-GENDER -REGIONS	
DL AUTOIMMUNE-pan-gender-longevity	
DL AUTOIMMUNE-borcherts-gender	
DL AUTOIMMUNE-carp-infertility	
DL AUTOIMMUNE-autoimmune review	
DL AUTOIMMUNE-lettre	
DL AUTOIMMUNE-mackay	
XDIET-autoimmune-scott	
MS AUTOIMMUNE-cavallo	
DL AUTOIMMUNE-grains-cordain	
DL AUTOIMMUNE-fish oil-donadio-nephropathy	
MS AUTOIMMUNE-nivaro	
MS AUTOIMMUNE-ierodiakonou	
MS AUTOIMMUNE-boyle	
DL AUTOIMMUNITY-rautava-hygiene-hypothesis	
MS AUTOIMMUNITY-martinez	
MS AUTOIMMUNITY-von hertzen-affluence	**NB**
MS AUTOIMMUNITY-flohr-childhood	
Wendt (1985)	
EPI	
DL EPI-humandisease-portela **MS ADHD nigg-future directions** **DL ADHD nigg-future directions-pdf** **EPI-haynes** **DTB-mcdade-2017 NB NB NB re EPI**	
DL EPI-disease-rodenhiser	
DL EPI-twins-ballestar	
MS EPI-ballestar-rheumatology UCT	
REPI-keller-2002	
MS EPI-wallace UCT	
MS EPI-heijmans-famine	
DL EPI-portela	**To ref**
MS EPI-javierre-SLE	**To ref**
MS EPI-therapeutic targets-feinberg	
DL EPI-walker	

DL EPI-SLE-sawalha	
DL EPI-REVIEW-pacchierotti	
MS Epigenetics of autoimmunity-richardson	
MS EPI-brooks	
AUTOPHAGY	
Wallace (2005) DL ETHNICS-wallace NB	
DL DIET-lifehistory evolution	
DL AUTOPHAGY-pallauf-polyphenols **MS AUTOPHAGY-kroemer-NB**	
DL EVOLUTION-inflammatory diseases	
DL AUTOPHAGY-curcumin-dizanni	
MS AUTOPHAGY-giordano	
MS polyphenols-kim	
DL AUTOPHAGY-polyphenols-hasima	
DL AUTOPHAGY-cancer	
DL EPI-autophagy-fullgrahe	
MS AUTOPHAGY-komatsu	
MS AUTOPHAGY-polyphenols	
MS AUTOPHAGY-cancer	
MS AUTOPHAGY-antitumor-surh	
MS AUTOPHAGY-phenols-surh	
DL AUTOPHAGY-naponelli-NB	
MS AUTOPHAGY-autophagy in the pathogenesis-levine	
DL AUTOPHAGY-immunity-inflammation-levine	
MS AUTOPHAGY-bachetti-protein aggregate diseases	
MS AUTOPHAGY-inflammation-bachetti	
DL AUTOPHAGY-Lleo-NB	
MS AUTOPHAGY-sanjuan	
MS AUTOPHAGY-kroemer-stress response	
MS AUTOPHAGY-levine 2	
MS AUTOPHAGY-mitroulis	
AUTOPHAGY PLUS RELATED Pallauf & Rimbach (2013) MS CR-heydari-heatshock DL CR-steinkraus-2008-heat shock proteins DL CR-yang-autophagy NB MS CR-ran-SIRT1 MS HEATSHOCKPROTEINS-chichester MS Heatshockfactors-akerfelt **DL HEATSHOCK-FACTOR-nishizawa** MS HEAT SHOCK PROTEINS-chen It has been suggested that heat shock proteins may be involved in inflammation-related nociception. HEATSHOCKPROTEINS-mccarty	
HYDRATION **DL CELL HYDRATION-CANCER-mcintyre**	
DL DIET-CANCER-ames	

DL OMEGA3-gogus NB	
DL FRUCTOSE-faeh-omega3	
ADHD-OMEGA-3	
DL OMEGA3-pusceddu NB	
DL OMEGA3-bloch-ADHD	
MS ADHD-pufa-gillies	
MS ADHD-fishoil-kean	
Fcordain simopoulus-omega	
DL GESTATION-omega3	
MS ADHD-fatty acids DL DIET-fishoil-delarue	
DL OMEGA3-GESTATION-harris	
DL OMEGA3-weylandt-mixed evidence	
DL XDIET-autoimmune-scott	
DL AUTOIMMUNE-DIET-stamp	
MS OMEGA-bradbury	
MS OMEGA-BRAIN-lautrizen	
MS OMEGA-yurkomauro-cognition-ageing	
MS OMEGA- yurkomauro-2-alzheimer	
MS OMEGA-DHAversusEPA	
MS OMEGA-low doses-cognition	
MS OMEGA- yurkomauro-2015	
MS OMEGA-EPA-sublette	
MS OMEGA-EPA-martins	
MS IGA-NEPHROPATHYfish oil.donadio 1999	
MS OMEGA3-miles NB	
MS OMEGA3-long-chain	
MS OMEGA3-arteries	
MS OMEGA3-cardiovascular	
MS OMEGA3-diabetes	
MS OMEGA3-cellular mechanisms	
MS OMEGA3-liperoti	
MS PUFA-COGNITION-zhang	
APPLE CIDER VINEGAR	
MS Apple cider vinegar	
MS Apple cider vinegar uses	
DL APPLE CIDER-shahidi NB phenolic, fermentation	
DL APPLE CIDER-iman-diabetes	
DL APPLE CIDER-naziroglu	
MS VITAMIND-lucock	
OXYGEN	
DL OXYGEN-bocci-ozonetherapy	
DL OXYGEN-autohaemotherapy-bocci	
DL oxygen- stroke RELOX procedure	
OBESITY	
MS DIET-mozaffarian-obesity-calories-NB	
MS SLEEP-st-onge-energy balance	

MS SLEEP-bayon-obesity	
MS SLEEP-shlisky-energy balance	
DL DIET-obesity	
DL OBESITY-REGULATION OF BODY WEIGHT-jequier	
IgA NEPHROSIS	
(Weindruch & Sohal 1997). CR-weindruch DL NEPHROPATHYfish oil-appel MS NEPHROSIS-del vecchio MS NEPHROSIS-magistroni MS IGA-NEPHROPATHY-fish oil-donadio MS NEPHROPATHY-Van Es MS NEPHROPATHY-montinaro MS NEPHROPATHY-coppo-gluten MS NEPHROPATHY-grains-cordain-NB DL NEPHROPATHY-donadio-2004-NB MS NEPHROPATHY-miller-n3fattyacids DL IGA-NEPHROPATHY-donadio-1994 DL NEPHROPATHY-kovacs NB	
On the value of marriage/family: **MS MARRIAGE-RELIGION-waite**	
LONGEVITY LONGEVITY-gavrilov-2015-pdf LONGEVITY-caselli SARDINIA GSARDINIA –late-astolfi DO LONGEVITY-gavrilov-2004 LONGEVITY-caselli-2014 NB LONGEVITY-lipsi-2015-SAR DO LONGEVITY-EVOLUTION-baudisch DO LONGEVITY-klusener-germany DO LONGEVITY-winkler-dworak-ACADEMICS DO LONGEVITY-caselli-SARDINIA DO LONGEVITY-salaris-SARDINIA DO SAR-poulain-endogamy LONGEVITY-gavrilov-2010 Gavrilova & Gavrilov (2010) Gheightsurvival DL AGEING-lindner DO Gavrilova et al. (2003) Early life predictors LONGEVITY-gjonka	

LONGEVITY-vaiserman PAPER Gavrilova & Gavrilov (2007a). DL LONGEVITY-gavrilov-symposium-NB Gavrilov & Gavrilova (2007b) Physical characteristics conducive to healthy ageing LONGEVITY-alter-NB DO	
The evolution of cultural traits: **EVOLUTION-CULTURAL-MULDER (Section 3) multiculti**	**NB**
Chronic social stress-Obesity Coccurello et al. (2009): DL Stress-coccurello (FIT INTO TEXT) MS OBESITY-mclaren **DL OBESITY-syed-HPAaxis**	
DL FEVER-elmquist	
DL EMOTION-PARSASYMPATHETIC-porges DL HYPERTENSION-reaven-NB	
DL COGNITION-INSULIN-park	
MS Mitochondrial Medicine-fosslien	
Ballestar (2010) EPI-twins-ballestar	
Sircus (2014b) Sodium bicarbonate Natural Allopathic Medicine focuses *inter alia* on pH management, cell voltage, magnesium and iodine medicine, carbon dioxide medicine, re-mineralization of the body, increasing oxygen transport and oxygenation of tissues, saturation and healing of cells with concentrated nutrition (super foods), emotional transformation processing and detoxification and removal of heavy metals and radioactive particles. Centrally important substances used are magnesium, sodium bicarbonate (baking soda) and iodine.	
DL ACIDOSIS-drocioiu-cachexia	
DL DIET-CANCER-ames **DL DIET-CANCER-key**	
MS DEPRESSION-vancampfort-metaboilicsyndrome **MS VITB12-stanger-B6-folicacid** **MS VITB12-king**	
DIET DIET-MEDITTERANEAN-davis-2017 DIET-CRUCIFEROUS VEGETABLES-mori-2017 DIET-MED-OBESITY-Park-2017 DIET-MED-PALEO-whalen-2017-NB DIET-MED-NORDIC-ratjen-2017 DIET-MED-mattei-2017 DIET-PROTEIN QUALITY-callagham-2017 DIET-DIET-EGGS-dimarco-2017 DIET-PREGNANCY-starling	

LIFE HISTORY-ellis	
Evolutionary aspects DL EVOLUTION-brand ????? DL PURINE-johnson-andrews NB DL PURINES-burnstock- DL URIC ACID-marshall-feedbackfoods MS URIC ACID-bowman-CNS-antioxidant MS URIC ACID-ooki MS DIET-URIC ACID-de oliveira MS METABOLIC SYNDROME-amihaesi Ames et al. (1981) presented evidence that uric acid could function as an antioxidant in various redox reactions. According to the hypothesis of Ames the uricase mutation may have provided an evolutionary advantage by providing key antioxidant functions assisting in the combat of cancer, prevent vascular disease and counteract oxidative stress associated with ageing. MS NEUROPROTECTION-belanger-astroglia Uric acid can also be pro-oxidant under certain conditions. For example, uric acid reacting with peroxynitite generates several radicals as the urate molecule is degraded to triuret (Gersch et al. 2009). Thus, both antioxidant and pro-oxidant effects of uric acid occur, depending on environmental circumstances. Both protective antioxidant activity under stress (starvation) and potentiation of stress and survival responses through increased oxidative activity. Uric acid may have a biological role in the fattening-fasting cycle. Increased uric acid stimulating weight gain to re-establish fat stores. The establishment of insulin resistance could be beneficial by reducing glucose uptake into the skeletal muscle and adipose tissue, thus preserving glucose for utilization by the brain where glucose uptake is insulin independent, as suggested by Reaven (1999). The concept that a rise in uric acid may have a beneficial role in starvation yet when present in excessive amounts may cause obesity and insulin resistance has a parallel with cortisol. Cortisol also increases with uric acid during the proteolytic phase of starvation and is also thought to have a role in the foraging response (Challet et al. 1995). DL CORICOSTERONE-challet Elevated cortisol levels are not generally found in metabolic syndrome subjects; but manifestaions of hypercortisolism include abdominal obesity, dyslepidemia (hypertriglyceridemia), hypertension, insulin resistance anf fatty liver (Friedman et al. 1996). DL HYPERCORTISOLISM-friedman Finally, Johnson et al. (2009) hypothesise that cortisol and uric acid may have similar physiological roles for the survival of the host, but if present in excessive amounts, have deleterious and similar consequences.	

DL GOUT-johnson Johnson & Rideout (2004):
Gout as a disease has been known since antiquity (described by Hippocrates during the Golden Age of Greece). Originally seen as a disease of the affluent as observed in men of the wealthy upper class (Patrician malady) and a disease afflicting kings (e. g. Alexander the Great, Charlemagne, Henry XIII) and statesmen, artists (e.g. Voltaire) and scientists (e. g. Isaac Newton, Charles Darwin, Leonardo da Vinci). It was a disease prevalent among those who could afford and overindulge in the comforts of life. During the Miocene several parallel mutations occurred in our hominoid ancestors, eventually silencing the uricase gene. As a consequence humans and the great apes have higher uric acid levels than other mammals. DL GOUT-choi

DL Nesse-2011-Evolutionary applications Nesse 2011
Understanding the evolutionary origins of disease vulnerability (ultimate causality), together with an understanding of the more proximate causes of disease synergistically promote a fuller understanding of cause-effect relationships of diseases (Nesse 2011). Most diseases are not shaped directly by natural selection or other evolutionary forces and are not in themselves appropriate for evolutionary explanation. Rather, evolutionary explanations require focussing on aspects of the body that make it vulnerable to disease. Predictive adaptive responses are important areas of evolutionary medicine (Gluckman et al. 2005). DL EVOLUTION-gluckman Most vertebrates have the enzyme uricase, whereas the hominid line lost the relevant gene in the Miocene (uricase mutations), resulting in high levels of gout and vulnerability to diverse disease states; most notably gout (Johnson et al. 2010; Choi et al. 2005 +). Uric acid is actively reabsorbed in the kidney suggesting some adaptive function (fitness advantages). Genes which give an advantage in terms of reproductive fitness can become fixed, even when they involve some disease vulnerabilities (Nesse 2011). Competitive competence in males (based on high metabolic turnover underpinned by elevated uric acid levels) increases their fitness more than in females, whereas in females their reproductive body condition promotes fitness (based on lower metabolic turnover favouring storage). Refer to relevant table Men thus, on average would live seven years longer if their metabolism and behaviour were like that of women (Kruger & Nesse 2006). DL GENDER-kruger
EVOLUTION-gluckman
EVOLUTION-gluckman-2
EVOLUTION-gluckman-3

DL EPI-galloukalani-metabolic syndrome

DL URIC ACID-XO-INHIBITORS-pacher

DL STRESS-bjorntorp Björntorp & Rosmond (2000). The HPA axis is stimulated by stress. This results in discrete periodical elevations of cortisol secretion during day-to-day conditions. Prolonged periods of HPA axis stimulation progressively leads to a degradation of regulatory mechanisms. continue **MS STRESS-boonstra** **OBESITY-syed-HPA** Syed & Weaver (2005) **DL FRUCTOSE-faeh-omega3** DL GOUT-CLIFFORD **DL GOUT-ames** **DL GOUT-choi-2005 meat versus dairy ; alcohol** **MS GOUT-GENDER-silbiger** **MS HYPERURICEMIA-GENDER-soutelo** **MS URATE-hughes-NB** **MS URATE-rasheed** **MS URATE-dalbeth**	
DL INTELLIGENCE-sofaer-NB **Sofaer & Emery (1981)** Associations between high IQ and infantile autism, gout and myopia. Pleiotropy occurs when one gene influences two or more seemingly unrelated phenotypic traits. With reference to gout. **MS URATE-mueller-psychosocial** **DL URIC ACID-li-cognitive function** Li et al. (2010) The risk of cognitive impairment was correlated with SUA level in male nonagenarians and centenarians. Higher levels of SUA in men were related to lower risk of cognitive impairment. Unable to determine whether SUA levels were cause or consequence of cognitive impairment. Only in male nonagenarians and centenarians SUA level was correlated with the risk of cognitive impairment (this study). Cognitive impairment was related to the level of education. Men had significantly higher SUA levels and cognitive function scores than women. Woman had a higher prevalence of cognitive impairment and lower education level than men. Despite evidence of its beneficial properties, SUA is elevated in brain function disorders and has an association with increases risk of cognitive dysfunction (op. cit. Li et al. 2010). Despite being an antioxidant, elevated SUA has also been found to accompany hypertension, hyperlipidemia, obesity, renal disease, insulin resistance and metabolic syndrome (op. cit. Li et al. 2010). These conditions increase the risk of cognitive impairment. **DL URIC ACID-lin-metabolic syndrome** Lin et al. (2006)	

Uric acid levels increased as the number of components (of the metabolic syndrome: abnormal triglycerides, waist circumference, high-density lipoprotein cholesterol, blood pressure) increased. Men had significally higher uric acid levels than women. After controlling for BMI, which may be a confounding factor for serum UA levels, and is well correlated with waist circumference, the apparent influence of abnormal metabolic components on uric acid levels decreased.
Elevated serum UA levels are commonly associated with individual cardiovascular risk factors such as hypertriglyceridemia, hypertension, obesity and hyperglycemia, a cluster when found together in the same person, characterises metabolic syndrome (op. cit. Lin et al. 2006).
Insulin resistance is also associated with higher triglycerides, waist circumference and lower HDL-C. ? Lin et al. (2006) proposed that the elevated UA levels in their subjects who had abnormal triglyceride levels, waist circumference and HDL-C values were due to insulin resistance. Subjects with elevated blood pressure had higher UA levels. UA may contribute to endothelial dysfunction, thereby playing a causal role in the pathogenesis of hypertension (Kanellis & Kang 2005). Nakagawa et al. (2006) suggest that uric acid may be a cause of the metabolic syndrome. Studies in humans have found that UA is a good predictor of hyperinsulinemia (op. cit. Lin et al. 2006) and weight gain (Masuo et al. 2003). This is probably due to its ability to inhibit endothelial function by impairing nitric oxide production (Kanellis & Kang 2005; Nakagawa et al. 2006). Whether UA is a bystander, partner or an initiator of the metabolic syndrome cannot be answered from this cross-sectional study.

DL URIC ACID-masuro Masuo et al. (2003)

DL URIC ACID-CNS-tovchiga Tovchiga & Shtrygol' (2014)

Yet today hyperuricemia is considered to be involved in the diseases of civilization. In a study by Bolgova et al. (op.cit. Tovchiga & Shtrygol' 2014), children with hyperuricemia often came from families with high motivation for education and with improved living conditions (Bolgova et al., op.cit. Tovchiga & Shtrygol' 2014) and the authors considered hyperuricemia as a disease of excess associated with such families. Tovchiga & Shtrygol' (2014) only partly agree with this; they concluded that hyperuricemia in children is likely to be also linked to hereditary factors. Tovchiga & Shtrygol' (2014):
Uricemia increases in starvation during the protein-breakdown phase, after exhaustion of lipid reserves, being associated with accelerated body weight loss. Concentrations of uric acid increase simultaneously with cortisol levels; but tend to be negatively correlated with lipid reserves (Tovchiga & Shtrygol' 2014).
According to references cited by Tovchiga & Shtrygol' (2014) uric acid is a marker of catabolic processes but also an activation factor in animals. Like other biologically active metabolites, uric acid has an optimum concentration range in blood. The relationship between

uricemia and intellectual human activity is linear only between certain limits and can be expressed by a curve line in the form of an inverted letter U (Tovchiga & Shtrygol' 2014). AS hypouricemia – uricemia – hyperuricemia.

Burnstock (2007) reviewed the characteristic features of purinergic neurotransmission. (Increase in sympathetic nerve activity in hypertension is well established and there is an associated hyperplasia and hypertrophy of arterial walls)

In the context of uricemia the role of fructose is to elevate the metabolic efficiency for the creation of energy reserves (Johnson et al. 2009 +). However, uric acid levels increased beyond the range of physiological levels (uricemia) represent hyperuricemia and thus health risk factors.

DL URATE-brooks-professors Brooks & Mueller (1966) Regarding 113 professors at the University of Michigan, Brooks & Mueller (1966) found highly significant positive correlations between uricemia and intensity of activity, professional productivity, organizational skills, placing demands on oneself, breadths and mulifacetted nature of activities.

DL hyperuricemia-katz Katz & Weiner (1972) CHECK Considered hyperuricemia a result of, rather than a cause of high social status and material welfare.

MS HEAT SHOCK PROTEINS-chen It has been suggested that heat shock proteins may be involved in inflammation-related nociception.
DL URIC ACID-euser COGNITIVE FUNCTION ANTIOXIDANT Euser et al. (2009).

It was shown that the functions of the CNS (including memory) can be normalized through administration of exogenous precursors of nucleic acids or uric acid (Essman 1967, op. cit. Tovchiga & Shtrygol' 2014), as confirmed by Chen et al. (2000) MS URIC ACID-chen-memory They showed that the memory of senescent mice could be improved with the administration of a mixture of nucleotides and nucleosides. PURINES-rathbone

Purines are involved in the control of the ratio of activities of the sympathetic and parasympathetic systems by modulating the adrenergic and cholinergic transmission.

MS URIC ACID-PURINES-maiuolo

MS URIC ACID-dunn-social class

MS URIC ACID-church-dopamine DL PURINE-church- Church & Rappolt (1999) MS URIC ACID-andreadou-parkinson **DL URIC ACID-so-thorens** **MS URIC ACID—goodman-psychosocial-stress** **MS GENDER-STRESS-kogler** **DL DIET-schwarz-thermogenesis-fructose** **DL HEATSHOCK-FACTOR-nishizawa** **DL URIC ACID-johnso-2003-NB CHECK MORE** **DL PURINE-church CHECK MORE** **MS MATHEMATICS-nyborg-sex differences** **MS URIC ACID-scott-CNS** **MS URIC ACID-becker-physiological function** **MS URIC ACID-hochstein-functions** **MS URIC ACID-squadrito-neuroprotection** **DL URIC ACID-schretlin** **MS URIC ACID-CANCER-taghizadeh** **DL URIC ACID-yoo-metabolic syndrome** UA is a prominent natural antioxidant, accounting for up tp 60% of free radical scavaging in human blood (Ames et al. 1981). It remains unclear whether increased uric acid levels are the cause or consequence of some of the associated disease states. The association of higher uric acid levels in cardiovascular disease may be due to its role as antioxidant (Ames et al. 1981); because an elevated UA may be a defense mechanism against atherosclerosis (consequence not cause). UA concentrations may be increased in an attempt to block lipid peroxidation and other related phenomena (Nietto et al., op. cit. Kutzing & Firestein (2008). However, increased UA levels may instead contribute to the development of cardiovascular disease by having a negative effect on the endothelium. Alterations in UA levels are associated with disease states as UA has important roles in the development and prevention of many diseases.	
DL EPI-galloukalani-metabolic syndrome **MS EPI-zhang** **MS EPI-stearns-Evolutionary** **MS GENETICS-ahuja-tradeoff** **MS Evolution-finch-MEAT** **MS EVOLUTION-MEAT-larson** **MS EVOLUTION-MEAT-milton**	
DL STARVATION-cordain	
DL STARVATION-reaven	

DL STARVATION-cordain-huntergatherers	
CR-KETONES **Kirkwood & Shanley (2005) CR-evolution-kirkwood** **DL KETONES-rho** **DL KETONES-masino revisit** **DL KETONES-thio-NB-metabolism** **DL KETONES-bergquist** **DL KETONES-miranda** **DL KETONES-prins**	
HEAT-SHOCK PLUS **MS HEATSHOCKPROTEINS-chichester** **Heatshock factors-akerfelt**	
MITOCHONDRIAL DYSFUNCTION MS Micronutrients-ames; DIET-ames; MS MITOCHONDRIA-mookerjee MS MITOCHONDRIA-hebert MS MITOCHONDRIA-ames-3 **FTUMERIC-mancuso**	
Demographic transition	
DL DEMOGRAPHIC TRANSITION-newson PRINT DO LIFE HISTORIES-sear- DO-DEM TRANS-mason-fertility DO-bongaarts DL DEM TRANS-hirschman paper copy Gloria-Bottini et al. (2005) DELAYEDCHIDBEARING + DT **DTand LONGEVITY/REPRODUCTION TRADE-OFF** **Jasienska (2009) REPRODUCTION-jasienska** Bolund Burger Beauchamp Hayward 2015 pdf DTB-hayward-disease Hayward-2004 the long arm URBAN-RURAL-hayward LHS-lawson-2011 Gillespie-2008 partly done. In ref list Rickard-2007 pre-industrial DTB-OFFSPRING ch 5	**NB**
DL URBAN-RURAL-hayward-1997	

DO REPRODUCTION COSTS-harshman	
Gavrilova et al. (2003). Data base on European royal and noble families: aristocrats (a family-linked data base) 1800-1854/1855-1880. Mean age at death 1800-1854 of daughters increased from 65.8 to 69.5 years and of sons from 63.8 to 63.7 years (female/male age differential increased from 2.0-5.8). Mean age at death 1855-1880 of daughters increased from 71.3 to 76.0 years and of sons from 64.1 to 65.8 years (female/male age differential increased from 7.2-10.2). Significant increase in lifespan over the studied period, more so in the case of females. Month of birth was an important predictor of women's lifespan. Male lifespan did not depend on season of birth. Month of birth continued to be a predictor for lifespans of women. Defiencies of vitamin B12, folic acid, B6, niacin, C or E apparently may mimic radiation in damaging DNA by causing single- and double-strand breaks, oxidative lesions; thereby contributing to premature ageing (1998). MS Micronutrients-ames; DIET-ames; MS MITOCHONDRIA-mookerjee MS MITOCHONDRIA-hebert MS MITOCHONDRIA-ames-3 Significant differences in birth seasonality between social classes (Bobak & Gjonka 2001). SEASON-bobak-socio. Optimal age to father a daughter is between 35-39 years (particularly negative above age 50); with surprisingly less effects of maternal age. Contrastingly, male lifespan was not related to paternal age at birth. Only daughters inherit paternal X-chromosome and it was accordingly suggested that mutation accumulation in X-chromosome of old sperm cells could be responsible for the shorter lifespan of daughters conceived to older fathers (Gavrilov & Gavrilova 2001). According to Alter et al. (2001) exposure to infections (as tracked by infectious diseases) has a positive effect on late-life survival; this being attributed to either selection of the most fit or early immunization against infectious diseases. DL LONGEVITY-alter-NB-vaccinations also INFLAMMATION-.	
Gavrilova et al. (2009) Early life predictors Gavrilova et al. (2003) Early life predictors ADH_106_0177-gavrilova-2003	
CR MS CR-mair-NB DL CR-yang-autophagy MS CR-ran-SIRT1	

MS CR-koubavo-NB CR-weindruch MS CR-lopez-lluchu-NB MS FREE RADICALS-droge (LEPTIN-OXIDATIVE STRESS-sainz)	
Yamaza et al. 2010 MS CR-antineoplasic-yamaza-2010 DL AUTOPHAGY-SIRT1-hariharan DL CR-SIRT1-cohen **Sirtuins** MS CR-INTERMITTENT-rusli MS AMPK-steinberg MS DIET-FLAVONOIDS-egert DIET-FLAVONOIDS-egert-pdf DL CR-AUTOPHAGY-giller-NB DL CR-MIMETICS-SIDE EFFECTS-nikolai DL CR-AUTOPHAGY-ntsapi-NB DL EPI-CANCER-supic MS OLIVE OIL-menendez-NB MS POYPHENOLS-EPI-joven-NB DL PHENOLS-stefani DL POLYPHENOLS-CANCER-mileo MS CR-SIRT1-feige-ENERGY-NB MS RESVERATROL-MITOCHONDRIAL FUNCTION-lagouge MS CR-DR-resveratrol-pearson MS SIRT1-CRITIQUE-pacholec MS CR-sohal-critique-NB MS CR-robert-primates-critique MS CR-chrysohooi-critique-NB DL CR-spindler-NB MS CR-mitochondrial longevity-raffaello CR-swindell-heat shock protein MS AUTOPHAGYHEALTH SPAN-yen-NB MS AUTOPHAGY-levine-pathogenesis MS CR-MIMICS-lane MS CR-short term-robertson MS CR-mitochondrion-gouspillou MS CR-AUTOPHAGY-xie-green tea MS CR-AUTOPHAGY-wohlgemuth MS AUTOHAGY-KIDNEY-takabatake MS AUTOPHAGY-EXERCISE-kim	

MS CR-AUTOPHAGY-ning-resveratol CR AUTOPHAGY-ahn MS AUTOPHAGY-suzuki-siruin1 MS CR-rizza-diet quality-longevity MS CR-willcox-diets MS HEALTHY AGEING-DIET-santoro-NB MS AUTOHAGY-FRUCTOSE-mellor-- MS ANTON-FASTING MS CR-EPI-chung-NB MS CR-KETONES-xu DIET-liu-NB DIET-liu-2- CR-RESVERATROL-timmers MS Mitochondrial Dysfunction and ageing-mammucari MS EPI-bellet-circadian MS CR-RESVERATROL-timmers-2012 MS AUTOPHAGY-CANCER-min MS EPI-CANCER-ahmad DL SIRTUINS-dali-youcef MS AUTOPHAGY-lee-NB MS AUTOPHAGY-development-hale MS AUTOPHAGY-rubinsztein-2012 DL EPI-rodriguez-metabolism-chromatin MS EPI-LIFE HISTORY-hochberg-child growth MS EPI-NB-hochberg-child health EPI-MATERNAL EFFECTS-INTELLIGENCE-bjorklund	
AUTOPHAGY-AGEING-terman-2007 **AGEING-terman-2010** **MS AUTOPHAGY-petrovski** **MS AUTOPHAGY-cuervo-2012** **IMMUNITY-SYSTEMS-BIOLOGY-afacan** **MS OBESITY-IMMUNITY-kalupahana** **MS AUTOPHAGY-singh-2011** **DL INTERMITTENT FASTING-jacobson-20017-NB** **DL SIRT1-HERBS-jain** **DL AUTOPHAGY-schroeder** **MS AUTOPHAGY-levine** **MS AUTOPHAGY-levine-development** **MS Autophagy-kroemer-integrated stress response** **DL AUTOPHAGY-rubinsztein-functions** **MS AUTOPHAGY-yang-2010-Defective** **MS AUTOPHAGY-OBESITY-INSULIN-RESISTANCE-codogo** **MS AUTOPHAGY-kuma-neonatal**	

MS AUTOPHAGY-HEALTH-DISEASE-shintani **DL STRESS-ALLOSTASIS-berndt-NB** **MS PREGNANCY-STRESS-lim** **MS GLUCOCORTICOID-chrousos-2009** **DL REPRODUCTION-GHRELIN-LEPTIN-tena-sempere** **MS ALLOSTASIS-ganzel** MS EPI-STRESS-zannas-NB	
MS POLYPHENOLS-mennen	
Gluckman	
NATURAL SELECTION-wells	
Sircus (2015)	
Dehydration increases the production of histamine, thereby increasing immune activity and resulting in inflammatory responses. Dehydration is implicated to cause DNA damage, diminished urine output resulting in acid waste accumulates, cell receptor damage (compromising cell communication and hormonal balance) and immune system suppression. Most people are unconscious of their thirst mechanisms. Liquid substitutes drive down hydration levels rather than raising them (e.g. coffee, alcoholic and sodas dehydrate). Required for hydration is pure water; laden with minerals like magnesium and bicarbonate. Homeostatic adaptation responses operate to maintain pH balance, such as using high pH body fluids such as water to neutralize acid residues and pulling bicarbonate from the pancreas and kidneys as an alkanizing agent. Bicarbonate ions are generated from carbon dioxide diffusing into the plasma. Accumulation of acid residues at the cellular level drown out oxygen. Sufficient oxygen in the blood stream does not automatically rule out insufficiency of oxygen within the cell interior. Magnesium deficiency can result in cell membranes over time becoming resistant to the diffusion of oxygen into the cell interior and supplementation is required in order to maintain proper cell oxygenization.	
Unintential chronic dehydration is involved in many degenerative diseases and Batmanghelidj () suspects that inflammation that comes with dehydration is at the causal basis of all disease. DL DEHYDRATION-neurotransmitter-histamine-batmanghelidj; DL DEHYDRATION-batmangelidj-paradigm-change.	
Proper stomach acid production is vital to unlocking perfect digestion. When the food in the stomach reaches a pH of between 2 to 4, the stomach content is slowly released into the duodenum. If the pH is wrong from the beginning, down stream digestive processes are compromised. Chewing your food is the first crucial step to efficient digestion and stomach acid the next. In the resting period (after food has been digested; empty stomach period) sodium bicarbonate dissolves mucus and is absorbed as bicarbonate in the blood stream to directly increase its alkalinity. In the digestive period (full stomach period) it reduces the secretion of gastric acid juice, neutralizes a portion of the hydrochloric acid, liberates the carbinative carbon	

dioxide gas and is absorbed as sodium chloride. Time of administration is accordingly of importance. A dose at bedtime tends to check early morning acidity. Whenever taking a bicarbonate solution internally it should be dissolved in cold water. Some causes of low stomach acid: eating too much too quickly, excess alcohol, stress, zinc deficiency (required for HCl production). Sodium bicarbonate provides more carbon dioxide to the body in the form of bicarbonates. With oral sodium bicarbonate administration it turns into CO_2 in the stomach, driving bicarbonates into the blood, thereby promoting more blood and oxygen reaching the cells. Increased bicarbonate and and CO_2 concentrations supports dilation of blood levels, ensuring more oxygen being delivered to the cells.	
Neumann et al. (2013) DL AUTOIMMUNE-atrophic;	
Wendt (1985):	
ADS GENETICS-wang-ADS GENETICS-ADHD-harpending GENETICS-PERSONALITY-penke-2007 DOPAMINE-ADHD-ding DOPAMINE-chen	
ADAPTOGENS-NB	
Ursächlichkeit als Kernproblem heutiger Medizin (auch Psychosomatik) Ursache von symptommanifesten Krankheitserscheinungen und subklinischen Gesundheitsstörungen sind patho-information-engramm-spezifische Funktionsstörungen	
INTEGRATED PALEO Rest/sleep component important for body condition build-up, especially in TL females with an HMT disbalance (adrenal fatigue). Three meals with protein-CH combination (CH for lowered metabolic functionality favouring anabolic processes). Check Hershlag tricks. Incomplete digestion as HMT booster and heteroprotein influx (re Wendt). Squeeze 3 meals into anabolic phase. • Body condition re fat storage (esp. F) • Protein digestion (Wendt) • Adrenal fatigue • Parasympathetic functionality	
EPIGENETICS **EPI-drake** Champagne & Curley (2009): DL EPI-rearing Cirulli et al. (2009): DL EPI-earlystress Curley et al. (2008): DL EPI-curley-maternal Navarro et al. (2016): MS EPI-prenatal-nutrition Gluckman et al. (2005) EPI-gluckman-fetal Weaver et al. (2004a) DL EPI-weaver-maternal	

Weaver et al. (2004b) DL ADHDweaver- Miller et al. (2009) DL ALLOSTATICLOAD-miller Zambrano et al. (2005b) DL EPI-zambrano-transgenerational Feinberg (2007) EPI-feinberg EPI-agrawal ? Godfrey & Barker (2000) DL EPI-godfrey-fetal Weaver et al. (2004a) EPI-weaver-maternal-programing Egger et al. (2004) EPInature Wallace (2005) ETHNICS-wallace-mitochondria Waterland & Jirtle (2004) EPI-NUTRIGENOMICS NB Pál (1998) PASTICITY-pal Cao-Lei et al. (2015). MS EPI-caolei-prenatalmaternal stress Palma-Gudiel et al. (2015). MS EPI-palmagudiel-maternal Dinan et al. (2010) MS EPI-irritable bowelsyndrome-dinan EPI-environment EPI-thieffry EPI-sreekumar EPI-feinberg monk EPI-issa Epigenetic mechanisms seem to play a crucial role in age-dependent alterations and in pathologies such as cancer. Reik 2x EPI-reik-pdf Major epigenetic modifications apparently occur during early development. Reik-2003 Heydari EPI-heydari-pdf	
EPI-auger-NB DL EPI-holliday EPI-selvi DL EPI-guibert-NB MS EPI-morgan MS EPI-whitelaw MS EPI-whitelaw-2 MS EPI-vickaryous-embrionic environment MS EPI-reik-NB MS EPI-reik-methylation MS EPI-weaver-imprinting MS EPI-gringras MS EPI-leboux-abstact MS EPI-soejima MS EPI-petronis-2 EPI-PREGNANCY-dunford EPI-PREGNANCY-CAROLAN-OLAH	
Demographic colonization	
THIRD DT:	

DTB-coleman-3 NB Lanziera Sobotka (2008b) DT-sobotka-migration **IMMIGRANTS-lesthaeghe-NB** DL DEMOGRAPHIC TRANSITION-ETHNICITY-okun DL DEMOGRAPHIC TRANSITION-coleman-third DL DEMOGRAPHIC TRANSITION-coleman-2010-third-britain DL DEMOGRAPHIC TRANSITION-THIRD-coleman-2009-GLOBALIZATION DL DEMOGRAPHIC TRANSITION-beets-GLOBALIZATION DL DEMOGRAPHIC TRANSITION-ECONOMICS-ivanov MIGRATION-nijkamp FERTILITY TRANSITION-MIGRANTS-sobotka DL MIGRATION-EUROPE-sobotka DL RERTILITY MIGRANTS-schmied FERTILITY-MIGRANTS-espenshade FERTILITY-INTERGENERATIONAL-BRITAIN-booth	

References

Aassve, A., Sironi, M. & Bassi, V. (2013). Explaining attitudes towards demographic behaviour. *European Sociological Review* 29 90: 316-333.

Abdou, A. M., Higashiguchi, S., Horie, K., Kim, M., Hatta, H. & Yokogoshi, H. (2006). Relaxation and immunity enhancement effects of γ-Aminobutyric acid (GABA) administration in humans. *BioFactors* 26 (3): 201-208.

Abumaria, N., Yin, B., Zhang, L., Li, X-Y., Chen, T., Descalzi, G., Zhao, L., An, M., Luo, L., Ran, C., Zhuo, M. & Liu, G. (2011). Effects of elevation of brain magnesium on fear conditioning, fear extinction, and synaptic plasticity in the infralimbic, prefrontal cortex and lateral amygdala. *The Journal of Neuroscience* 31 (42): 14871-14881.

Achen, C. H. & Bartels, L. M. (2016). Democracy for Realists. Why Elections Do Not Produce Responsive Government. Princeton Studies in Political Behavior (edited by Tali Mendelberg). Princeton University Press, Princeton and Oxford.

Achilli, A., Rengo, C., Magri, C., Battaglia, V., Olivieri, A., et al. (2004). The molecular dissection of mtDNA hapolgroup H confirms that the Franco-Cantabrian glacial refuge was a major source for the European gene pool. *American Journal of Human Genetics* 75: 910-918.

Achilli, A., Rengo, C., Battaglia, V., Pala, M., Olivieri, A., Fomarino, S., Magri, C. et al. (2005). Saami and Berbers – An unexpected mitochondrial DNA link. *American Journal of Human Genetics* 76: 883-886.

Adami, H-O., Bergström, R., Möhner, M., Zatoński, W., Storm, H., Ekbom, A., Tretli, S., Teppo, L., Ziegler, H., Rahu, M., Gurevicius, R. & Stengrevics, A. (1994). Testicular cancer in nine Northern European countries. *International Journal of Cancer* 59: 33-38.

Adamia, S., Alania, V., Chabukiani, A., Kutelia, Z. & Sadradze, N. (2011). Great Caucasus (Cavcasioni): A long-lived North-Tethyian Back-arc Basin. *Turkish Journal of Earth Sciences* 20: 611-628.

Adams, J. & White, M. (2004). Biological ageing. A fundamental, biological link between socio-economic status and health? *European Journal of Public Health* 14: 331-334.

Adams, J., White, M. & Forman, D. (2005). Is the rate of biological aging, as measured by age at diagnosis of cancer, socioeconomically patterned? *Journal of Epidemiology and Community Health* 59: 146-151.

Adler, M. I. & Bonduriansky, R. (2014). Why do the well-fed appear to die young? *Bioessays* 36: 439-450.

Agrawal, A. A. (2001). Phenotypic plasticity in the interactions and evolution of species. *Science* 294: 321-326.

Alexander, J. M., Van Kleunen, M., Ghezzi, R. & Edwards, P. J. (2012). Different genetic clines in response to temperature across the native and introduced ranges of a global plant invader. *Journal of Ecology* 100: 771-781.

Alirezaei, M., Kemball, C. C., Flynn, C. T., Wood, M. R., Whitton, J. L. & Kiosses, W. B. (2010). Short-term fasting induces profound neuronal autophagy. *Autophagy* 6 (6): 702-710.

Almoosawi, S., Vingeliene, S., Karagounis, L. G. & Pot, G. K. (2016). Chrono-nutrition: a review of current evidence from observational studies on global tends in time-of-day of energy intake and its association with obesity. *Proceedings of the Nutrition Society* 75: 487-500.

Alonso, F. G. (2009). Can the rising pension fund burden in Europe be mitigated by immigration? Modelling the effects of selected demographic and socioeconomic factors on ageing in the European Union, 2008-2050. *Vienna Yearbook of Population Research* 7: 123-147.

Àlvarez-Lario, B. & Macarrón-Vicente, J. (2010). Uric acid and evolution. *Rheumatology* (Oxford) 49 (11): 2010-2015.

Ames, B. N., Cathcart, R., Schwiers, E. & Hochstein, P. (1981). Uric acid provides an antioxidant defense in humans against oxidant- and radical-caused aging and cancer: A hypothesis. *Proceedings of the National Academy of Sciences of the United States of America* 78 (11): 6858-6862.

American Academy of Pediatrics (2012). Breastfeeding and the use of human milk. Policy statement. *Pediatrics* 129 (3): 827-841.

Anand, P., Sundaram, C., Jhurani, S., Kunnumakkara, A. B. & Aggarwal, B.B. (2008). Curcumin and cancer: An "old age" disease with an "old age" solution. *Cancer Letters* 267: 133-164.

Anderson, J. W., Smith, B.M. & Gustafson, N. J. (1994). *American Journal of Clinical Nutrition* 59 (suppl): 1242S-1247S.

Anderson, D. C. (2008). Assessment and nutraceutical management of stress-induced adrenal dysfunction. *Integrative Medicine* 7 (5): 18-25.

Angelone, M., Vaselli, O., Bini, C., Coradossi, N. & Pancani, M. G. (1991). Total and EDTA extractable element content of ophiolitic soils from Tuscani (Italy). *Zeitschrift für Pflanzenernährung und Bodenkunde* 154: 217-223.

Anson, R. M., Guo, Z., De Cabo, F., Iyun, T., Rios, M., Hagepanus, A., Ingram, D. K., Lane, M. A. & Mattson, M. P. (2003). Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistence to injury from calorie intake. *Proceedings of the National Academy of Sciences* 100 (10): 6216-6220.

Aragón, C. & López-Corcuera, B. (2003). Structure, function and regulation of glycine neurotransporters. *European Journal of Pharmacology* 479 (1-3): 249-262.

Arden, R., Luciano, M., Deary, I. J., Reynolds, C. A., Pedersen, N. L., Plassman, B. L. McGue, M. Christensen, K. & Visscher, P. M. (2016). The association between intelligence and lifespan is mostly genetic. *International Journal of Epidemiology* 45 (1): 178-185.

Arnold, J. L. (1999). Church History. The Height and Decline of the Papacy (1073-1517). Medieval Church History, part 3. IIIM Magazine Online 1 (33), October 11 to October 17, 1999. Third Millenium Ministry.

Artis, D. (2008). Epithelial cell recognition of commensal bacteria and maintenance of immune homeostasis in the gut. *Nature Reviews Immunology* 8: 411-420.

Asher, G. & Sassone-Corsi, P. (2015). Time for food: The intimate interplay between nutrition, metabolism, and the circadian clock. *Cell* 161: 84-92.

Astolfi, P., Caselli, G., Fiorani, O., Lipsi, R. M., Lisa, A. & Tentoni, S. (2009). Late reproductive behaviour in Sardinia: spatial analysis suggests local aptitude towards reproductive longevity. *Evolution and Human Behavior* 30: 93-102.

Atkinson, D. & Sibly, R. M. (1997). Why are organisms usually bigger in colder environments? Making sense of a life history puzzle. *Trends in Ecology and Evolution* 12 (6): 235-239.

Atkuri, K. R., Mantovani, J. J., Herzenberg, L. A. & Herzenberg, L. A. (2007). N-acetylcysteine – a safe antidote for cysteine/glutathione deficiency. *Current Opinion in Pharmacology* 7 (4): 355-359.

Augustin, L. S., Franceschi, S., Jenkins, D. J. A., Kendall, C. W. C. & La Vecchia, C. (2002). Glycemic index in chronic disease: a review. *European Journal of Clinical Nutrition* 56: 1049-1071.

Ayub, Q., Mezzavilla, M., Pagani, L., Haber, M., Mohyuddin, A., Khaliq, S., Mehdi, S. Q. & Tyler-Smith, C. (2015). The Kalash genetic isolate: ancient divergence, drift, and selection. *The American Journal of Human Genetics* 96: 775-783.

Bach, J-F. (2002). The effect of infections on susceptibility to autoimmune and allergic diseases. *New England Journal of Medicine* 347 (12): 911-920.

Badyaev, A. V. & Uller, T. (2009). Parental effects in ecology and evolution: mechanisms, processes and implications. *Philosophical Transactions of the Royal Society B*, 364: 1169-1177.

Balan, C. B. & Jaba, E. (2016): Birth seasonality patterns in Central and Eastern Europe during 1996-2012. *Romanian Statistical Review* 1: 9-20.

Balbo, N., Billari, F. C. & Mills, M. (2013). Fertility in advanced societies: A review of research. *European Journal of Population* 29: 1-38.

Ballestar, E. (2010). Epigenetics lessons from twins: prospects for autoimmune disease. *Clinical Reviews in Allergy & Immunology* 39 (1): 30-41.

Ballmer, P. E., McNurlan, M. A., Hulter, H. N., Anderson, S. E., Garlick, P. J. & Krapf, R. (1995). Chronic metabolic acidosis decreases albumin synthesis and induces negative nitrogen balance in humans. *Journal of Clinical Investigation* 95: 39-45.

Bano, A., Rehman, A. & Winiger, M. (2009). Altitudinal variation in the content of protein, proline, sugar, and abscisic acid (ABA) in the alpine herbs from Hunza valley, Pakistan. *Pakistan Journal of Botany* 41 (4): 1593-1602.

Barbiroli, B., Iotti, S., Cortelli, P., Martinelli, P., Lodi, R., Carelli, V. & Montagna, P. (1999). Low brain intracellular free magnesium in mitochondrial cytopathies. *Journal of Cerebral Blood Flow and Metabolism* 19: 528-532.

Barbujani, G. & Bertorelle, G. (2001). Genetics and the population history of Europe. *Proceedings of the National Acaemy of Sciences* 98 (1): 22-25.

Bardgett, M. E., Schultheis, P. J., McGill, D. L., Richmond, R. E. & Wagge, J. R. (2005). Magnesium deficiency impairs fear conditioning in mice. *Brain Research* 1038: 100-106.

Barker, D. J. P. (2001a). Preface. Type 2 diabetes: the thrifty phenotype. *British Medical Bulletin* 60 (1): 1-3.

Barker, D. J. P. (2001b). The malnourished baby and infant; Relationship with type 2 diabetes. *British Medical Bulletin* 60 (1): 69-88.

Bateson, P., Barker, D., Clutton-Brock, T., Deb, D., D'Udine, B., Foley, R. A., Gluckman, P., Godfrey, K., Kirkwood, T., Lahr, M. M., McNamara, J., Metcalfe, N. B., Monaghan, P., Spencer, H.G. & Sultan, S. E. (2004). Developmenta plasticity and human health. *Nature* 430: 419-421.

Baumard, N., Hyafil, A., Morris, I. & Boyer, P. (2015). Increased affluence explains the emergence of ascetic wisdoms and moralizing religions. *Current Biology* 25: 10-15

Baur, G. (1982). Kybernetische Denkmodelle in der Homöopathie. Steuerung und Informatik. Karl F. Haug Verlag, Heidelberg, Deutschland.

Baur, J. A., Chen, D., Chini, E.N., Chua, K., Cohen, H.Y., De Cabo, R., Deng, C., Dimmeler, S., et al. (2010). Dietary restriction: Standing up for sirtuins. *Science* 329 (5995): 1012-1014.

Becker, B. F. (1993). Towards the physiological function of uric acid. *Free Radical Biology & Medicine* 14 (6): 615-631.

Becker, S. O., Cinnirella, F. & Woessmann, L. (2010). The trade-off between fertility and education: evidence from before the demographic transition. *Journal of Economic Growth* 15: 177-204.

Beishuizen, A. & Thijs, L. G. (2003). Endotoxin and the hypothalamo-pituitary-adrenal (HPA) axis. *Journal of Endotoxin Research* 9 (1): 1-24.

Bellwood, P. (2018). The search for ancient DNA heads list. *Science* 361 (6397): 31-32.

Belsky, J., Steinberg, L. & Draper, P. (1991). Childhood experience, interpersonal development, and reproductive strategy: an evolutionary theory of socialization. *Child Development* 62 (4): 647-670.

Belsky, J. & Pluess, M. (2009). Beyond diathesis stress: differential susceptibility to environmental influences. *Psychological Bulletin* 135 (6): 885-908.

Ben-Dor, M., Gopher, A., Hershkovitz, I. & Barkai, R. (2011). Man the fat hunter: the demise of Homo erectus and the emergence of a new hominin lineage in the Middle Pleistocene (ca 400 kyr) Levant. *PLoS One* 6 (12): e28689.

Bere, E. & Brug, J. (2008). Towards health-promoting and environmentally friendly regional diets – a Nordic example. *Public Health Nutrition* 12 (1): 91-96.

Bergamini, E., Cavallini, G., Donati, A. & Gori, Z. (2007). The role of autophagy in aging. Its essential part in the anti-aging mechanism of caloric restriction. *Annals of the New York Academy of Sciences* 1114: 69-78.

Bertram, C., Trowern, A. R., Copin, N., Jackson, A. A. & Whorwood, C. B. (2001). The maternal diet during pregnancy programs altered expression of the glucocorticoid receptor and type 2 11ß-hydroxysteroid dehydrogenase: potential molecular mechanism underlying the programming of hypertension *in utero*. *Endocrinology* 142 (7): 2841-2853.

Betz, H., Gomeza, J., Armsen, W., Scholze, P. & Eulenburg, V. (2006). Glycine transporters: essential regulators of synaptic transmission. *Biochemical Society Transactions* 34 (Part 1): 55-58.

Bhattacharya, S. K. & Muruganandam, A. V. (2003). Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress. *Pharmacology, Biochemistry and Behavior* 75 (3): 547-555.

Biddulph, J. (1880). The Tribes of the Hindoo-Koosh. Calcutta, India.

Billari, F. C. & Kohler, H. P. (2004). Patterns of low and lowest-low fertility in Europe. *Population Studies* (Camb): 58 (2): 161-176.

Billingsley, S. (2010). The post-communist fertility puzzle. *Population Research and Policy Review* 29: 193-231.

Bingley, P. J., Douek, I. F., Rogers, C. A. & Gale, E. A. M. (2000). Influence of maternal age at delivery and birth order on risk of type 1 diabetes in childhood: prospective population based family study. *British Medical Journal* 321: 420-424.

Björntorp, P. & Rosmond, R. (2000). Neuroendocrine abnormalities in visceral obesity. *International Jounal of Obesity* 24 (Suppl 2): S80-S85.

Bloch, M. H. & Qawasmi, A. (2011). Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder symptomatology: systematic review and meta-analysis. *Journal of American Academy of Child and Adolescent Psychiatry* 50 (10): 991-1000.

Blom, W. A. M., Lluch, A., Staffleu, A., Vinoy, S., Holst, J. J., Schafsma, G. & Hendriks, H. F. J. (2006). Effect of a high-protein breakfast on the postprandial ghrelin response. *American Journal of Clinical Nutrition* 83: 211-220.

Bobak, M. & Gjonka, A. (2001). The seasonality of live birth is strongly influenced by socio-demographic factors. *Human Reproduction* 16 (7): 1512-1517.

Bonduriansky, R. & Day, T. (2009). Nongenetic inheritance and its evolutionary implications. *Annual Review of Ecology, Evolution and Systematics* 40: 103-125.

Boothroyd, L. G. & Cross, C. P. (2017). Father absence and and gendered traits in sons and daughters. *PLoS One* 12 (7): e0179954.

Borgerhoff Mulder, M. (1998). The demographic transition: are we closer to an evolutionary explanation? *Trends in Ecology & Evolution* 17 (3): 266-270.

Boschmann, M. & Michalsen, A. (2013). Fasting therapy – old and new perspectives. *Forschende Komplementärmedizin* 20: 410-411.

Botev, N. (1990). Nuptiality in the course of the demographic transition: the experience of the Balkan countries. *Population Studies* 44 (1): 107-126.

Bottini, E., Meloni, G. F., MacMurray, J., Ammendola, M., Meloni, T. & Gloria-Bottini, F. (2001). Maternal age and traits of offspring in humans. *Placenta* 22: 787-789.

Boyce, W. T. & Ellis, B. J. (2005). Biological sensitivity to context: I. An evolutionary-developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology* 17: 271-301.

Bracht, P. (2018). Intervallfasten. Für ein langes Leben - Schlank und Gesund. Gräfe und Unzer Verlag, Germany.

Bradley R. H. & Corwyn, R. F. (2002). Socioeconomic status and child development. *Annual Review of Psychology* 53: 371-399.

Braverman, E. R., Pfeiffer, C. C., Blum, K. & Smayda, R. (2003). The Healing Nutrients Within. Facts, Findings, and New Research on Amino Acids. Basic Health Publications, Inc., Laguna Beach, California 92651, USA.

Bravo, L. (1998). Polyphenols: Chemistry, dietary sourcres, metabolism, and nutritional significance. *Nutrition Reviews* 56 (11): 317-333.

Brawley, L., Torrens, C., Anthony, F. W., Itoh, S., Wheeler, T., Jackson, A. A., Clough, G. F., Poston, L. & Hanson, M. A. (2004). Glycine rectifies vascular dysfunction induced by dietary protein imbalance during pregnancy. *Journal of Physiology* 554 (2): 497-504.

Breschi, M., Mazzoni, S., Esposito, M. & Pozzi, L. (2014). Fertility transition and social stratification in the town of Alghero, Sardinia (1866-1935). *Demographic Research* 30: 823-852.

Brestoff, J. R. & Artis, D. (2013). Commensal bacteria at the interface of host metabolism and the immune system. *Nature Immunology* 14 (7): 676-684.

Brewster, K. L. & Rindfuss, R. R. (2000). Fertility and women's employment in industrialized nations. *Annual Review of Sociology* 26: 271-296.

Brizendine, L. (2006). The Female Brain. Bantam Press, London, Toronto, Johnnesburg.

Brizendine, L. (2010). The Male Brain. Bantam Press, London, Toronto, Johnnesburg.

Brooks, G. W. & Mueller, E. (1966). Serum urate concentrations among university professors. Relation to drive, achievement, and leadership. *Journal of the American Medical Association* 195 (6): 415-418.

Brosig, V. (2011). Die Originale Schrothkur. Das altbewährte Naturheilverfahren nach Johann Schroth. 4. Auflage. Schlütersche Verlagsgesellschaft, Hannover, Germany.

Brown, E. M. (2000). Why Wagner-Jauregg won the Nobel Prize for discovering malaria therapy for general paresis of the insane. *History of Psychiatry* 11 (44): 371-382.

Brown, J. C. & Guinnane, T. W. (2002). Fertility transition in a rural, Catholic population: Bavaria, 1880-1910. *Population Studies* 56 (1): 35-49.

Brumbach, B. H., Figueredo, A.J & Ellis, B. J. (2009). Effects of harsh and unpredictable environments in adolescence on development of life history strategies: a longitudinal test of an evolutionary model. *Human Nature* 20 (1): 25-51.

Brunet, A., Sweeney, L. B., Sturgill, J. F., et al. (2004). Stress-dependent regulation of FOXO transcription factors by the SIRT1 deacetylase. *Science* 303: 2011-2015.

Bruni, O., Ferri, R., Miano, S. & Verrillo, S. (2004). L-5-Hydroxytryptophan treatment of sleep terrors in children. *European Journal of Pediatrics* 163: 402-407.

Brzezinski, A. (1997). Melatonin in humans. *New England Journal of Medicine* 336: 186-195.

Buchinger, O. [Senior] (1987). Das Heilfasten. 21. Auflage, Hippokrates Verlag, Stuttgart, Deutschland.

Buckland, G., Travier, N., Barricarte, A., Ardanaz, E., Moreno-Iribas, C., Sánchez, M-J., Molina-Montes, E., et al. (2012). Olive oil intake and CHD in the European Prospective Iinvestigation into cancer and Nutrition Spanish cohort. *British Journal of Nutrition* 108: 2075-2082.

Buettner, D. (2012). The Blue Zones. 9 Lessons for Living Longer from the people who've lived the longest. Zweite Auflage. National Geographic Society, Washington D. C., USA.

Bushinsky, D. A. (2001). Acid-base imbalance and the skeleton. *European Journal of Nutrition* 40: 238-244.

Cagnacci, A., Pansini, F. S., Bacchi-Modena, A., Giulini, N., Mollica, G., De Aloysio, D., Vadora, E. & Volpe, A. (2005). Season of birth influences the timing of menopause. *Human Reproduction* 20 (8): 2190-2193.

Calabrese, V., Guagliano, E., Sapienza, M., Panebianco, M., Calafato, S., Puleo, E., Pennisi, G., Mancuso, C., Butterfield, D. A. & Stella, A. G. (2007). Redox regulation of cellular stress response in aging and neurodegenerative disorders: Role of vitagenes. *Neurochemical Research* 32: 757-773.

Cámara-Martos, F. & Amaro-López, M. A. (2002). Influence of dietary factors on calcium bioavailablity. A brief review. *Biological Trace Element Research* 89: 43-52.

Cantó, C. & Auwerx, J. (2009). Caloric restriction, SIRT1 and longevity. Trends in *Endocrinology and Metabolism* 20 (7): 325-331.

Cantó, C. & Auwerx, J. (2012). Targeting Sirtuin 1 to improve metabolism: all you need is NAD^+? *Pharmacological Reviews* 64 (1): 166-187.

Cao-Lei, L., Veru, F., Elgbeili, G., Szyf, M., Laplante, D. P., King, S. (2016). DNA methylation mediates the effect of exposure to prenatal maternal stress on cytokinin production in children at age $13^1/_2$ years: Project Ice Storm. *Clinical Epigenetics* 8: 54.

Caramelli, D., Vernesi, C., Sanna, S., Samprieto, L., Lari, M., Castri, L., Vona, G., Floris, L., Francalacci, P., Tykot, R., Casoli, A., Bertranpetit, J., Lalueza-Fox, C., Bertorelle, G. & Barbujani, G. (2007). Genetic variation in prehistoric Sardinia. *Human Genetics* 122: 327-336.

Cardona, F., Andrés-Lacueva, C., Tulipani, S., Tinahones, F. J. & Queipo-Ortuño, M. I. (2013). Benefits of polyphenols on gut microbiota and implications in human health. *Journal of Nutritional Biochemistry* 24: 1415-1422.

Carrera-Bastos, P., Fontes-Villalba, M., O'Keefe, J., Lindeberg, S. & Cordain, L. (2011). The western diet and life style and diseases of civilization. *Research Reports in Clinical Cardiology* 2: 15-35.

Castro Martin, T. (1992). Delayed childbearing in contemporary Spain: trends and differentials. *European Journal of Population* 8: 217-246.

Castrogiovanni, P., Iapichino, S., Pacchierotti, C., & Pieraccini, F. (1998). Season of birth in Psychiatry. *Neuropsychobiology* 37: 175-181.

Cavallo, M. G., Fava, D., Monetini, L., Barone, F. & Pozzilli, P. (1996). Cell-mediated immune response to ß casein in recent-onset insulin-dependant diabetes: implications for disease pathogenesis. *Lancet* 348 (9032): 926-928.

Caviccia, P. P., Steck, S. E., Hurley, T. G., Hussey, J. R., Ma, Y., Ockene, I. S. & Hebert, J. R. (2009). A new dietary inflammatory index predicts interval changes in serum high-sensitivity C-reactive protein. *The Journal of Nutrition* 139 (12): 2365-2372.

Celotti, F. & Bignamini, A. (1999). Dietary calcium and mineral/vitamin supplementation: a controversial problem. *The Journal of International Medical Research* 27: 1-14.

Chakravarthy, M. V. & Booth, F. W. (2004). Eating, exercise, and ‘‘thrifty’’ genotypes: connecting the dots toward an evolutionary understanding of modern chronic diseases. *Journal of Applied Physiology* 96: 3-10.

Champagne, F. A. & Curley, J. P. (2009). Epigenetic mechanisms mediating the long-term effects of maternal care on development. *Neuroscience & Biobehavioral Reviews* 33: 593-600.

Champagne, F. A. (2010). Epigenetic influence of social experiences across the lifespan. *Developmental Psychobiology* 52 (4): 299-311.

Chan, S. & Debono, M. (2010). Replication of cortisol circadian rhythm: new advances in hydrocortisone replacement therapy. *Therapeutic Advances in Endocrinology and Metabolism* 1 (3): 129-138.

Chang, H-C. & Guarente, L. (2013). SIRT1 mediates central circadian control in the SCN by a mechanism that decays with aging. *Cell* 153: 1448-1460.

Chapman, T., Liddle, L. F., Kalb, J. M., Wolfner, M. F. & Partridge, L. (1995). Cost of mating in Drosophila melanogaster females is mediated by male accessory gland products. *Nature* 373: 241-244.

Charlton, B. G. (1996). What is the ultimate cause of socio-economic inequalities in health? An explantion in terms of evolutionary psychology. *Journal of the Royal Society of Medicine* 89: 3-8.

Chen, Y. & Blaser, M.J. (2007). Inverse associations of *Helicobacter pylori* with asthma and allergy. *Archives of Internal Medicine* 167: 821-827.

Cherkas, L. F., Aviv, A., Valdes A. M., Hunkin, J. L., Gardner, JP., Surdulescu, G. L., Kimura, M. & Spencer, T. D. (2006). The effect of social status on biological aging as measured by white-blood-cell telemore length. *Aging Cell* 5 (5): 361-365.

Chmielewski, P. & Boryslawski, K. (2016). Understanding the links between month of birth, body height, and longevity: why some studies reveal that shorter people live longer – further evidence of seasonal programming from the Polish population. *Anthropological Review 79* (4): 375-395.

Chiarpotto, E., Bergamini, E. & Poli, G. (2006). Molecular mechanisms of calorie restrictions protection against age-related sclerosis. *IUBMB Life* 58 (12): 695-702.

Chisholm, J. S., Quinlivan, J. A., Petersen, RW. & Coall, D. A. (2005). Early stress predicts age at menarche and first birth, adult attachment, and expected lifespan. *Human Nature* 16 (3): 233-265.

Chodick, G., Flash, S., Deoitch, Y. & Shalev, V. (2009). Seasonality in birth weight: Review of global patterns and potential causes. *Human Biology* 81 (4): 463-477.

Choi, H.K., Mount, D. B. & Reginato, A. M. (2005a). Pathogenesis of gout. *Annals of Internal Medicine* 143: 499-516.

Choi, H.K., Atkinson, K. Karlson, E. W. & Curhan, G. (2005b). Obesity, weight changes, hypertension, diuretic use, and risk of gout in men. *Archives of Internal Medicine* 165: 742-748.

Choi, H. K., Liu, S. & Curhan, G. (2005c). Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid: the Third National Health and Nutrition Examination Survey. *Arthritis and Rheumatology* 52 (1): 283-289.

Cirulli, F., Francia, N., Berry, A., Aloe, L., Alleva, N. & Suomi, S. J. (2009). Early life stress as risk factor for mental health: Role of neutrophins from rodents to non-human primates. *Neuroscience & Biobehavioral Reviews* 33: 573-585.

Citro, M. (2011). The Basic Code of the Universe. The Scienc of the Invisible in Physics, Medicine, and Spirituality. Park Street Press, Toronto. Canada.

Clark, G. & Cummins, N. (2009). Urbanization, mortality, and fertility in Malthusian England. *American Economic Review: Papers and Proceedings* 99 (2): 242-247.

Clement, B. R. (2010). Supplements Exposed. The Truth They Don't Want You to Know About Vitamins, Minerals, and Their Effects on Your Health. New Page Books, The Career Press, Inc., Franklin Lakes, New Jersey.

Clutton-Brock, T. H. & Harvey, P. H. (1983). The functional significance of variation in body size among mammals. In: Eisenberg J.F., Kleiman, D.G. (eds) Advances in the Study of Mammalian Behavior. Special Publication No. 7. The American Society of Mammalogists, Shippensburg. Pp. 632-663. USA.

Coccurello, R., D'Amato, F.R. & Moles, A. (2009). Chronic social stress, hedonism and vulnerability to obesity: Lessons from rodents. *Neuroscience & Biobehavioral Reviews* 33: 537-550.

Cockburn, P. (2015). The Rise of the Islamic State. ISIS and the New Sunni Revolution. Verso, London, New York.

Codron, J., Codron, D., Lee-Thorp, J. A., Sponheimer, M., Bond, W. J., De Ruiter, D., Grant, R. (2005). Taxonomic, anatomical and spatio-temporal variations in the stable carbon and nitrogen isotopic compositions of plants from an African savanna. *Journal of Archaeological Science* 32: 1757-1772.

Coleman, D. (2004). Why we don't have to believe without doubting in the "Second Demographic Transition" – some agnostic comments. *Vienna Yearbook of Population Research* 2: 11-24.

Coleman, D. (2006). Immigration and ethnic change in low-fertility countries: a Third Demographic Transition. *Population & Development Review* 32 (3): 401-446.

Coleman, D. (2009). Migration and its consequences in 21st century Europe. *Vienna Yearbook of Population Research* 7: 1-18.

Coleman, D. & Rowthorn, R. (2011). Who's afraid of population decline? A critical examination of its consequences. In *Demograhic Transitions and Its Consequences*. Lee, R.D. and Reher D.S. (editors). *Population & Development Review* 37 (Supplement): 217-248.

Comings, D. E. & MacMurray, J.P. (2006). Maternal age at the birth of the first child as an epistatic factor in polygenic disorders. *American Journal of Medical Genetics Part B (Neuropspychiatric Genetics)* 141B: 1-6.

Contu, D., Morelli, L., Santoni, F., Foster, J. W., Francallaci, P., & Cucca, F. (2008). Y-chromosome based evidence for pre-Neolithic origin of the genetically homogeneous but diverse Sardinian population: Inference for association scans. *PLoS ONE* 3 (1): e1430.

Cordain, L. (1999). Cereal grains: humanity's double-edged sword. *World Review of Nutrition and Dietetics* 84: 19-73.

Cordain, L., Miller, J. & Mann, N. (1999). Scant evidence of periodic starvation among hunter-gatherers. *Diabetologia* 42 (3): 383-384.

Cordain, L., Brand-Miller, J., Eaton, S. B., Mann, N., Holt, S. H. A. & Speth, J. D. (2000). Plant-animal subsistence ratios and macronutrient energy estimations in worldwide hunter-gatherer diets. *American Journal of Clinical Nutrition* 71 (3): 682-692.

Cordain, L., Toohey, L., Smith, M. J. & Hickey, M. S. (2000). Modulation of immune function by dietary lectins in rheumatoid arthritis. *British Journal of Nutrition*, 83: 207-217.

Cordain, L., Eaton, S. B., Miller, G. B., Mann, N. & Hill, K. (2002a). The paradoxical nature of hunter-gatherer diets: meat-based, yet non-atherogenic. *European Journal of Clinical Nutrition*, 56 Suppl. 1, S42-S52.

Cordain, L., Eaton, S. B., Brand Miller, J., Lindebrg, S. & Jensen, C. (2002b). An evolutionary analysis of the aetiology and pathogenesis of juvenile-onset myopia. *Acta Ophthalmologica Scandinavica* 80 (2): 125-135.

Cordain, L., Eaton, S. B., Sebastian, A., Mann, N., Lindeberg, S., Watkins, B. A., O'Keefe, J. H. & Brand- Miller, J. (2005). Origins and evolution of the Western diet: health implications for the 21st century. *American Journal of Clinical Nutrition* 81: 341-354.

Cordain, L. (2007). Implications of Plio-Pleistocene Hominin Diets for Modern Humans. In: Ungar, P. S. (ed). Evolution of the Human Diet: The Known, the Unknown, and the Unknowable. Chapter 19: 363-383. Oxford University Press, Oxford, United Kingdom.

Cordain, L. (2011). The Paleo Diet. Revised edition. John Wiley & Sons, Inc., Hoboken, New Jersey.

Coudray, C., Demignè, C. & Rayssiguier, Y. (2003). Effects of dietary fibers on magnesium absorption in animals and humans. *Journal of Nutrition* 133 (1): 1-4.

Craine, J.M., Elmore, A.J., Aidar, M.P.M., Bustamante, M., Dawson, T.E., Hobbie, E.A., Kahmen, A., Mack, M.C., McLauchlan, K.K., Michelsen, A., Nardoto, G.B., Pardo, L.H., Peñuelas, J., Reich, P.B., Schuur, E.A.G., Stock, W.D., Templer, P.H., Virginia, R.A., Welker, J.M., Wright, I.J. (2009). Global patterns of foliar nitrogen isotopes and their relationships with climate, mycorrhizal fungi, foliar nutrient concentrations, and nitrogen availability. *New Phytologist* 183: 980-992.

Crooke, A. (2014). You can't understand ISIS if you don't know the history of Wahhabism in Saudi Arabia. *The World Post*, October 27, 2014.

Crozier, A., Jaganath, I. B. & Clifford, M.N. (2009). Dietary phenolics: chemistry, bioavailability and effects on health. *Natural Product Reports* 26: 1001-1043.

Crujeiras, A. B., Parra, D., Goyenechia, E. & Martínez, J. A. (2008). Sirtuin gene expression inhuman mononuclear cells is modulated by caloric restriction. *European Journal of Clinical Investigation* 38: 672-678.

Cuervo, A. M., Bergamini, E., Brunk, U. T., Dröge, W., Ffrench, M. & Terman, A. (2005). Autophagy and aging. The importance of maintaining 'clean' cells. *Autophagy* 1 (3): 131-140.

Cuervo, A. M. (2008). Autophagy and aging. *Trends in Genetics* 24 (12): 604-612.

Cummins, N. (2013). Marital fertility and wealth during the fertility transition: rural France, 1750-1850. *Economic History Review* 66 (2): 449-476.

Cummins, N. (2014). Longevity and the rise of the West: Lifespans of the European elite, 800-1800. Economic History Working Papers No 209/2014, The London School of Economics and Political Science, London, United Kingdom.

Cunnane, S. C. & Crawford, M. A. (2003). Survival of the fattest: fat babies were the key to evolution of the large human brain. *Comparative Biochemistry and Physiology* Part A 136: 17-26.

Curley, J. P., Champagne, F. A., Bateson, P. & Keverne, E. B. (2008). Transgenerational effects of impaired maternal care on behaviour of offspring and grandoffspring. *Animal Behaviour* 175: 1551-1561.

Currat, M. & Excoffier, L. (2005). The effect of the Neolithic expansion on European molecular diversity. *Proceedings of the Royal Society B* 272: 679-688.

Curtis, L. T. & Patel, K. (2008). Nutritional and environmental approaches to preventing and treating autism and attention deficit hyperactivity disorder (ADHD): a review. *The Journal of Alternative and Complementary Medicine* 14 (1): 79-85.

D'Addio, A. C. & d'Ercole, M. M. (2005). Trends and determinants of fertility rates: the role of policies. *OECD Social, Employment and Migration Working Papers* No. 27. OECD Publishing.

Dagfinn Aune, M. S., Saugstad, O.D., Henriksen, T. & Tonstad, S. (2014). Maternal body mass index and the risk of fetal death, stillbirth, and infant death. *Journal of the American Medical Association* 311 (15): 1536-1546.

Dahlberg, J. & Andersson, G. (2018). Changing seasonal variation in births by sociodemographic factors: a population-based register study. *Human Reproduction Open* 1-8.

Dahlitz, M., Alvarez, B., Parkes, J. D., English, J., Arendt, J. & Vignau, J. (1991). Delayed sleep phase syndrome response to melatonin. *The Lancet* 337 (8750): 1121-1124.

Dahlke, R. (1990). Bewusst Fasten. Ein Wegweiser zu neuen Erfahrungen. 5. Auflage. Urania Verlag, CH-8212, Neuhausen. ISBN 3-908644-68-2.

Dahlke, R. (1994). Der Mensch und die Welt sind Eins. 4. Auflage. Wilhelm Heyne Verlag, München. Deutschland.

Dahlke, R. (2018). Kurzzeitfasten. Mit Esspausen gesünder, länger und schlanker leben. Südwest Verlag, Germany.

Daly, H. E. (2008). Growth and development: critique of a credo. *Population & Development Review* 34 (3): 511-518.

Daniel, K. (2003). Why broth is beautiful: Essential roles for proline, glycine and gelatine. *Wise Traditions in Food, Farming and the Healing Arts* 4 (1). Spring 2003. Weston A. Price Foundation; USA.

Darlington, C. D. (1959). Die Gesetze des Lebens. (Englische Originalausgabe: The Facts of Life). F. A. Brockhaus, Wiesbaden, Deutschland.

Davis, A. (1972). Let's Get Well. Signet, New American Library Inc., New York. USA.

Davydov, M. & Krikorian, A. A. (2000). *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look. *Journal of Ethnopharmacology* 72: 345-393.

De Benedictis, Rose, G., Carrieri, M., Falcone, E., Passarino, G., Bonafé, M., Monti, D., Baggio, G., Bertolini, S., Mari, D., Matacce, R. & Franceschi, C. (1999). Mitochondrial DNA inherited variants are associated with successful aging and longevity in humans. *FASEB Journal* 13: 1532-1536.

De Castro, J. M. (2007). The time of day and the proportions of macronutrients eaten are related to total daily food intake. *British Journal of Nutrition* 98: 1077-1083.

De Giorgi, A., Fabbian, F., Pala, M., Tiseo, R., Prisi, C., Misurati, E. & Manfredini, R. (2015). Uric acid: friend or foe? Uric acid and cognitive function 'Gout kills more wise men than simple'. *European Review for Medical and Pharmacological Sciences* 19: 640-646.

De Oliveira, E. P. & Burini, R. C. (2012). High uric acid plasma concentration: causes and consequences. *Diabetology and Metabolic Syndrome* 4: 12.

De Rose, A., Racioppi, F. & Zanatta, A. L. (2008). Italy: Delayed adaptations of social institutions to changes in family behaviour. *Demographic Research* 19: 665-704.

Dean, C. (2014). The Magnesium Miracle. Revised and updated. Ballantine Books, New York. USA.

Degenhardt, K., Mathew, R., Beaudoin, B., Bray, K., Anderson, D., Chen, G., Mukherjee, C., Shi, Y., Gélinas, C., Fan, Y., Nelson, D. A., Jin, S. & White, E. (2006). Autophagy promotes tumor cell survival and restricts necrosis, inflammation, and tumorigenesis. *Cancer Cell* 10: 51-64.

Del Campo, N., Chamberlain, S. R., Sahakian, B. J. & Robbins, T. W. (2011). The roles of dopamine and noradrenaline in the pathophysiology and treatment of attention-deficit/hyperactivity disorder. *Biological Psychiatry* 69: e145-e157.

Delarue, J., Matzinger, O., Binnert, C., Schneiter, P., Chioléro, R. & Tappy, L. (2003). Fish oil prevents the adrenal activation elicited by mental stress in healthy men. *Diabetes and Metabolism* 29 (3): 289-295.

Demeny, P. (2005). Policy challenges of Europe's demographic changes: from past perspecives to future prospects. In: *The New Demographic Regime. Population Challenges and Policy Responses*. Macura, M., MacDonald, A. L. and Haug, W. (eds). pp 1-9. United Nations Economic Commission for Europe/United Nations Population Fund, United Nations, New York and Geneva.

Demeny, P. (2011). Population policy and demographic transition: performance, prospects, and options. In *Demograhic Transitions and Its Consequences*. Lee, R.D. and Reher D.S. (editors). *Population & Development Review* 37 (Supplement): 249-274.

Demeny, P. (2016). Europe's two demographic crises: the visible and the unrecognized. *Population and Development Review* 42 (1): 111-120.

Dessein, P. H., Shipton, E. A., Stanwix, A. E., Joffe, B. I. & Ramokgadi, J. (2000). Beneficial effects of weight loss associated with moderate calory/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study. *Annals of the Rheumatic Diseases* 59:539-543.

Dethlefsen, L., McFall-Ngai, M. & Relman, D. A. (2007). An ecological and evolutionary perspective on human-microbe mutualism and disease. *Nature* 449: 811-818.

DeWitt, T. J., Sih, A. & Wilson, D. S. (1998). Costs and limits of phenotypic plasticity. *Trends in Ecology & Evolution* 13 (2): 77-81.

Dilek, Y. (2003). Ophiolites pulses, mantle plumes and orogeny. In: Ophiolites in Earth History. Dilek, Y. & Robinson, P. T. (eds), Geological Society, London, Special Publication 218: 9-19.

Dinan, T. G., Cryan, J., Shanahan, F., Keeling, N. P. W. & Quigley, E. M. M. (2010). IBS: an epigenetic perspective. *Nature Reviews Gastroenterology & Hepatology* 7: 465-571.

Dirks, A. J. & Leeuwenburgh, C. (2006). Caloric restriction in humans: potential pitfalls and health concerns. *Mechanisms of Aging and Development* 127: 1-7.

Doblhammer, G. (2000). Reproductive history and mortality later in life. A comparative study of England and Wales and Austria. *Population Studies (Cambridge)* 54: 169-176.

Doblhammer, G. & Vaupel, J. W. (2001). Life span depends on month of birth. *Proceedings of the National Academy of Sciences of the United States of America* 98 (5): 2934-2940.

Doblhammer, G. & Oeppen, J. (2003). Reproduction and longevity among the British peerage: the effect of frailty and health election. *Proceedings of the Royal Society of London B* 270: 1541-1547.

Dockerty, J. D., Draper, G., Vincent, T., Rowan, S. D. & Bunch, K. J. (2001). Case-control study of parental age, parity and socioeconomic level in relation to childhood cancers. *International Journal of Epidemiology* 30 1428-1437.

Dolukhanov, P. M., Shukurov, A., Davison, K., Sarson, G., et al. (2009). The spread of the Neolithic in the south east European Plain: Radiocarbon chronology, subsistence, and environment. *Radiocarbon* 51 (2): 783-793.

Dorbritz, J. (2008). Germany: Family diversity with low actual and desired fertility. *Demographic Research* 19: 557-598.

Dorbritz, J., Palova, R. & Passet-Wittig, J. (2015). Gewollt oder ungewollt? Der Forschungsstand zur Kinderlosigkeit. Bundesinstitut für Bevölkerungsforschung, Wiesbaden, Germany.

Dorius, S. E. (2008). Global demographic convergence? A reconsideration of changing intercountry inequality in fertility. *Population & Development Review* 34 (3): 519-537.

Dowling, D. K. & Simmons, L. W. (2009). Reactive oxygen species as universal constraints in life history evolution. Proceedings of the Royal *Scociety B: Biological Sciences* 276: 1737-1745.

Drake, A. J. & Walker, B. R. (2004). The intergenerational effects of fetal programming: non-genomic mechanisms for the inheritance of low birth weight and cardiovascular risk. *Journal of Endocrinology* 180: 1-16.

Draper, P. & Harpending, H. (1982). Father absence and reproductive strategy: an evolutionary perspective. *Journal of Anthropological Research* 38: 255-279.

Dribe, M., Oris, M. & Pozzi, L. (2014). Socioeconomic status and fertility before, during and after the demographic transition: An introduction. *Demographic Research* 31: 161-182.

Dribe, M., Breschi, M., Gagnon, A., Gauvreau, D., Hanson, H. A., Maloney, T. N., Mazzoni, S., Molitoris, J., Pozzi, L., Smith, K. R. & Vézina, H. (2017). Socio-economic status and fertility decline: Insights from fertility transitions in Europe and North America. *Population Studies* 71 (1): 3-21.

Durlach, J., Bac, P., Bara, M., & Guiet-Bara, A. (2000). Physiopathology of symptomatic and latent forms of central nervous hyperexcitability due to magnesium deficiency: a current general scheme. *Magnesium Research* 13 (4): 293-302.

Durlach, J., Pagès, N., Bac, P., Bara, M. & Guiet-Bara, A. (2002). Biorythms and possible central regulation of magnesium status, phototherapy, darkness therapy and chronopathological forms of magnesium depletion. *Magnesium Research* 15: 49-66.

Dyson, T. (2011). The role of the demographic transition in the process of urbanization. In *Demograhic Transitions and Its Consequences*. Lee, R.D. and Reher D.S. (editors). *Population & Development Review* 37 (Supplement): 34-54.

Eastwood, M. A. (1999). Interaction of dietary antioxidants *in vivo*: how fruit and vegetables prevent disease? *Quarterly Journal of Medicine* 92: 527-530.

Eaton, S. B. & Konner, M (1985). Paleolithic Nutrition. *The New England Journal of Medicine,* 312 (5): 283-289.

Eaton, S. B. & Cordain, L. (1997). Evolutionary Aspects of Diet: Old Genes, New Fuels. *World Review of Nutrition and Diet*, 81: 26-37.

Eaton, S. Boyd. & Eaton, Stanley, B. (2003). An evolutionary perspective on human physical activity: implications for health. *Comparative Biochemistry and P0hysiology*, Part A 136: 153-159.

Eaton, S. B., Strassman, B. I., Nesse, R. M., Neel, J. V., Ewald, P. W., Williams, G. C., Weder, A. B., Eaton, S. B. III, Lindeberg, S., Konner, M.J., Misterud, I. & Cordain, L. (2002). Evolutionary health promotion. *Preventive Medicine*, 34: 109-118.

Eaton, S. B., Cordain, L. & Sparling, P. B. (2009). Evolution, body composition, insulin receptor competition, and insulin resistance. *Preventive Medicine*, 49: 283-285.

Eaton, S. B., Konner, M. J. & Cordain, L. (2010). Diet-dependant acid load, paleolithic nutrition, and evolutionary health promotion. *American Journal of Clinical Nutrition* 91: 295-297.

Edwards, C. A. & Parrett, A. M. (2002). Intestinal flora during the first months of life: new perspectives. *British Journal of Nutrition* 88 (Suppl. 1): S11-S18.

Egert, S. & Rimbach, G. (2011). Which sources of flavonoids: complex diets or dietary supplements? *Advances in Nutrition* 2: 8-14.

Eguez, A., Alvarado, A., Yepes, A., Machete, M. N., Costa, C. & Dart, R. L. (2003). Database and Map of Quarternary faults and folds of Ecuador and its offshore regions. Open-file Report 03/289. International Lithosphere Program, USGS.

Eisenberg, J.F. (1983). The Mammalian Radiations. An Analysis of Trends in Evolution, Adaptation and Behaviour. Paperback edition. The University of Chicago Press, Chicago, USA.

Elliot, S. S., Keim, N. L., Stern, J. S., Teff, K. & Havel, P. J. (2002). Fructose, weight gain, and the insulin resistance syndrome. *The American Journal of Clinical Nutrition* 76 (5): 911-922.

Ellis, B. J., Bates, J. E., Dodge, K. A., Fergusson, D. M., Horwood, L. J., Pettit, G. S. & Woodward, L. (2003). Does father absence place daughters at special risk for early sexual activity and teenage pregnancy? *Child Development* 74 (3): 801-821.

Ellis, B. J., Figueredo, A. J., Brumbach, B. H. & Schlomer, G. L. (2009). Fundamental Dimensions of Environmental Risk. The impact of harsh versus unpredictable environments on the evolution and development of life history strategies. *Human Nature* 20: 204-268.

Ellis, B. J., Boyce, W. T., Belsky, J., Bakermans-Kranenburg, M. J., & Van Ijzendorn, M. H. (2011a). Differential susceptibility to the environment: an evolutionary-neurodevelopmental theory. *Development and Psychopathology* 23: 7-28.

Ellis, B. J., Shirtcliff, E. A., Boyce, W. T., Deardorff, J. & Essex, M. J. (2011b). Quality of early family relationships and the timing and tempo of puberty: Effects depend on biological sensitivity to context. *Development and Psychopathology* 23: 85-99.

Ellison, P. T. (2003). Energetics and reproductive effort. *American Journal of Human Biology* 15: 342-351.

Ellison, P. T., Vallegia, C. R. & Sherry, D. S. (2005). Human birth seasonality. In *Seasonality in Primates: Studies of Living and Extinct Human and Non-Human Primates*. D. K. Brockman and C. P. van Schaik (eds), Cambridge University Press. Pp. 379-399.

Ellison, P. T. (2008). Energetics, reproductive ecology, and human evolution. *PaleoAnthropology* 2008: 172-200.

Espeseto, K. & Giugliano, D. (2006). Whole-grain intake cools down inflammation. *American Journal of Clinical Nutrition* 83 (6): 1440-1441.

Eurostat (2009). Data in focus. Population Statistics in Europe in 2008: first results. Author: Marcu, M., Publications Office of the European Union, Luxembourg, European Commisson.

Eurostat (2013). Fertility statistics in relation to economy, parity, education and migration. Statistics in Focus 13 (2013). Author: G. Lanzieri. ISSN 2314-9647. European Commisson.

Eurostat (2015). Demography Report. Employment, Social Affars and Inclusion. Publications Office of the European Union, Luxembourg, European Commisson.

Euser, S. M., Hofman, A., Westendorp, R. G. J. & Breteler, M. M. B. (2009). Serum uric acid and cognitive function and dementia. *Brain*. A Journal of Neurology. 132: 377-382.

Fahrner, H. (1985). Fasten als Therapie. Buchinger-Heilfasten-Pathophysiologie-Indikationen und Verläufe-Methode-Fastenpsychologie. Hippokrates Verlag, Stuttgart, Deutschland.

Fardet, A. (2010). New hypotheses for the health-protective mechanisms of whole-grain cereals: what is beyond fibre? *Nutrition Research Reviews* 23: 65-134.

Feinberg, A. P. (2007). Phenotypic plasticity and the epigenetics of human disease. *Nature* 447 (7143): 433-440.

Fernstrom, J. D. (1986). Acute and chronic effects of protein and carbohydrate ingestion on brain tryptophan levels and serotonin synthesis. *Nutrition Reviews* Supplement (May 1986): 25-36.

Fialová, L. & Kučera, M. (1997). The main features of population development in the Czech Republic during the transformation of society. *Czech Sociological Review* 5 (1): 93-111.

Figueredo, A. J., Vásquez, G., Brumbach, B. H. & Schneider, S. M.R. (2004). The heritability of life history strategy: The K-factor, covitality, and personality. *Social Biology* 51 (3/4): 121-143.

Figueredo, A. J., Vásquez, G., Brumbach, B. H., Schneider, S. M. R. (2006a). The K-factor, covitality, and personality: A psychosomatic test of life history theory. *Human Nature* 18: 47-73.

Figueredo, A. J., Vásquez, G., Brumbach, B. H., Schneider, S. M. R., Sefcec, J. A., Tal, I. R., Hill, D., Wenner, C. J. & Jacobs, W. J. (2006b). Consilience and life history theory: from genes to brain to reproductive strategy. *Developmental Review* 26: 243-275.

Finkelstein, J. D., Martin, J. J., Harris, B. J. & Kyle, W.E. (1983). Regulation of hepatic betaine-homocysteine methyltransferase by dietary betaine. *Journal of Nutrition* 113: 519-521.

Finkelstein, J. D. (1998). The metabolism of homocysteine: pathways and regulation. *European Journal of Pediatrics* 157 (Suppl 2): S40-S44.

Finkelstein, J. D. & Martin, J. J. (2000). Homocysteine. *International Journal of Biochemistry and Cell Biology* 32 (4): 385-389.

Fish, E. W., Shahrokh, D., Bagot, R., Caldji, C., Bredy, T., Szyf, M., Meaney, M. J. (2004). Epigenetic programming of stress responses through variations in maternal care. *Annals of the New York Academy of Sciences*, 1036: 167-180.

Fisher, R. A. (1930). The Genetical Theory of Natural Selection. Oxford University Press, Oxford, United Kingdom.

Flouris, A. D., Spiropoulos, Y., Sakellariou, G. J. & Koutedakis, Y. (2009). Effect of seasonal programming on fetal development and longevity: links with environmental temperature. *American Journal of Human Biology* 21: 214-216.

Fogel, R. W. (2004). The Escape from Hunger and Premature Death, 1700-2100. Cambridge University Press, Cambridge, United Kingdom.

Fontana, L., Partridge, L. & Longo, V. D. (2010). Dietary restriction, growth factors and aging: from yeast to humans. *Science* 328 (5976): 321-326.

Fontana, L. & Partridge, L. (2015). Promoting health and longevity through diet: from model organisms to humans. *Cell* 161: 106-118.

Fox, I. H., Palella, T. D. & Kelley, W. N. (1987). Hyperuricemia: a marker for cell energy crisis. *New England Journal of Medicine* 317: 111-112.

Frame, L. T., Hart, R. W. & Leakey, J. E. A. (1998). Caloric restriction as a mechanism mediating resistence to environmental disease. *Environmental Health Perspectives* 106 (S uppl 1): 313-324.

Frankenhuis, W. E., Panchanathan, K. & Nettle, D. (2016). Cognition in harsh and unpredictable environments. *Current Opinion in Psychology* 7: 76-80.

Frassetto, L. A., Schloetter, M., Mietus-Synder, M., Morris, R. C. jr. & Sebastian, A. (2009). Metabolic and physiologic improvements from consuming a paleolothic, hunter-gatherer type diet. *European Journal of Clinical Nutrition* 63: 947-955.

Frejka, T., Sobotka, T., Hoem, J. M. & Toulemon, L. (2008). Summary and general conclusions: childbearing trends and policies in Europe. *Demographic Research* 19: 5-13.

Fung, T. T., Van Dam, R. M., Hankinson, S. E., Stampfer, M., Willett, W. C. & Hu, F. B. (2010). Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. *Annals of Internal Medicine* 153 (5): 289-298.

Fuse, Y., Hirao, A., Kuroda, H., Otsuga, M., Tahara, Y. & Shibata, S. (2012). Differential roles of breakfast only (one meal per day) and a bigger breakfast with a small dinner (two meals per day) in mice fed a high fat diet with regard to induced obesity and lipid metabolism. *Journal of Circadian Rhythms* 10: 4.

Gaggero, L., Oggiano, G., Bucci, L., Slejko, F., & Cortesogno, L. (2007). Post-Variscan mafic dykes from the late orogenic collapse to the Tethyan Rift: evidence from Sardinia. *Ofilioti* (An International Journal on Ophiolites and Modern Oceanic Lithospere) 32 (1): 15-37.

Gallagher, M. (2002). What is marriage for? The public purposes of marriage law. *Louisiana Law Review* 62 (3): 773-791.

Galland, L. (1985). Nutrition and candidiasis. *Journal of Orthomolecular Psychiatry* 14 (1): 50-60.

Galli, M., Van Gool, F. & Leo, O. (2011). Sirtuins and inflammation: Friends or foes? *Biochemical Pharmacology* 81: 569-576.

Garn, S. M. & Leonard, W. R. (1989). What did our ancesters eat? *Nutrition Reviews* 47: 337-345.

Gamkrelidze, I.P. (1991). Tectonic nappes and horizontal layering of the Earth's crust in the Meditteranian belt (Carpathians, Balkanides and Caucasus). *Tectonophysics* 196: 385-396.

Gangestad, S.W., Merriman, L. A., & Emery Thomson, M. (2010). Men's oxidative stress, fluctuating asymmetry and physical attractiveness. *Animal Behaviour* 80: 1005-1013.

Gansser, A. (1980). The Division between Himalaya and Karakorum. *Geological Bulletin of the University of Peshawar* 13: 9-22.

Gavrilov, L. A., Gavrilova, N. S., Olshansky, S. J. & Carnes, B. A. (2002). Genealogical data and the biodemography of human longevity. *Social Biology* 49 (3-4): 160-173.

Gavrilov, L. A. & Gavrilova, N. S. (2004). Early-life programing of aging and longevity. The idea of high initial damage load (the HIDL hypothesis). *Annals of the New York Academy of Sciences* 1019 (1): 496-501.

Gavrilov, L. A. & Gavrilova, N. S. (2007). New findings on human longevity predictors. Gerontological Society of America Symposium on Quantitative Approaches to Aging and Exceptional Longevity, November 2007. San Francisco, USA.

Gavrilov, L. A. & Gavrilova, N. S. (2011). Season of birth and exceptional longevity: comparative study of American centenarians, their siblings, and spouses. *Journal of Aging Research* Volume 2011, Article ID 104616. 11 pages.

Gavrilov, L. A. & Gavrilova, N. S. (2012). Biodemography of exceptional longevity: Early-life and mid-life predictors of human longevity. *Biodemography & Social Biology* 58 (1): 14-39.

Gavrilov, L. A. & Gavrilova, N. S. (2013). Determinants of exceptional human longevity: new ideas and findings. *Vienna Yearbook of Population Research* 11: 295-323.

Gavrilov, L. A. & Gavrilova, N. S. (2015). Predictors of exceptional longevity: effects of early-life and midlife conditions, and familial longevity. *North American Actuarial Journal* 19 (3): 174-186.

Gavrilova, N. S., Gavrilov, L.A., Evdokushkina, G. N. & Semyonova, V. G. (2003). Early life predictors of human longevity: Analysis of the XIXth century birth cohorts. *Annales de Démographie Historique* 2003/2 (106): 177-198.

Gavrilova, N. S. & Gavrilov, L. A. (2007). Search for predictors of exceptional human longevity: Using computerized genealogies and internet resources for human longevity studies. *North American Actuarial Journal* 11 (1): 49-67.

Gavrilova, N. S. & Gavrilov, L. A. (2009). Rapidly aging populations: Russia/Eastern Europe. In: P. Uhlenberg (ed.). International Handbook of Population Aging. Springer Science and Business Media B. V.

GBD (2019). Global Burden Disease Study. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 393: 1958-1972.

Gedgaudas, N. T. (2011). Primal Body, Primal Mind. Beyond the Paleo Diet for Total Health and a Longer Life. Healing Arts Press; Rochester, Vermont; Toronto, Canada.

Geesing, H. (1987). Heilfasten. Der Weg zur neuen Jugend. F.A. Herbig Verlagsbuchhandlung, München, Berlin. Deutschland.

Gersch, M. S., Mu, W., Cirillo, P., Reungjui, S., Zhang, L., Roncal, C., Sautin, Y. Y., Johnson, R. J. & Nakagawa, T. (2007). Fructose, but not dextrose, accelerates the progression of chronic kidney disease. *American Journal of Physiology. Renal Physiology* 293 (4): F1256-F1261.

Gersch, C., Palii, S. P., Imaran, W., Kim, K. M., Karumanchi, S. A., Angerhofer, A., Johnson, R. J. & Henderson, G. N. (2009). Reactions of peroxynitrite with uric acid: formation of rective intermediates, alkylated products and triuret, and in vivo production of triuret under conditions of oxidative stress. *Nucleosides, Nucleotides and Nucleic Acids* 28 (2): 118-149.

Gershwin, M. E. & Schoenfeld, Y. (2011). Cutting-edge issues in organ-specific autoimmunity. *Clinical Reviews in Allergy and Immunology* 41: 123-125.

Geuter, U. (2003). Keine Erfahrung wird vergessen. *Psychologie Heute (Compact)*, 12:14-17.

Ghadirian, P., Shatenstein, B., Verdy, M. & Hamet, P. (1995). The influence of dairy products on plasma uric acid in women. *European Journal of Epidemiology* 11: 275-281.

Gilchrist, G. W. (1995). Specialists and generalists. I. Fitness landscapes of thermal sensitivity. *American Naturalist* 146 (2): 252-270.

Gillespie, D. O. S., Russell, AF. & Lummaa, V. (2008). When fecundity does not equal fitness: evidence of an offspring quantity versus quality trade-off in pre-industrial humans. *Proceedings of the Royal Society B* 275: 713-722.

Giugliano, D., Ceriello, A. & Esposito, K. (2006). The effects of diet on inflammation. Emphasis on the metabolic syndrome. *Journal of the American College of Cardiology* 48 (4): 677-685.

Gloria-Bottini, F., Cosmi, E., Nicotra, M., Cosmi, E. V. & Bottini, E. (2005). Is delayed childbearing changing gene frequencies in Western populations? *Human Biology* 77 (4): 433-441.

Gluckman, P.D., Cutfield, W., Hofman, P. & Hanson, M. A. (2005). The fetal, neonatal, and infant environments - long-term consequences for disease risk. *Early Human Development* 81: 51-59.

Gluckman, P.D., Hanson, M. A. & Beedle, A. S. (2007). Early life events and their consequences for later disease: A life history and evolutionary perspective. *American Journal of Human Biology* 19: 1-19.

Godfrey, K., Robinson, S., Barker, D. J. P., Osmond, C. & Cox, V. (1996). Maternal nutrition in early and late pregnancy in relation to placental and fetal growth. *British Medical Journal* 312: 410-414.

Godfrey, K. M. & Barker, D. J. P (2000). Fetal nutrition and adult disease. *American Journal of Clinical Nutrition* 71 (Suppl): 1344S-1352S.

Godfrey, K. M., Lillycrop, K. A., Burdge, G. C., Gluckman, P. D. & Hanson, M. A. (2007). Epigenetic mechanisms and the mismatch concept of the developmental origins of health and disease. *Pediatric Research* 61 (5): 5R-10R.

Göhring, E. (1986). Die aktive Fiebertherapie – ein immunologisches Instrument bei onkologischen und chronischen Erkrankungen. *Ärztezeitschrift für Naturheilverfahren* 27: 390-394.

Goraya, N. & Wesson, D. E. (2013). Does correction of metabolic acidosis slow chronic kidney disease progression? *Current Opinion in Nephrology and Hypertension* 22 (2): 193-197.

Goswami, A. (2004). The Quantum Doctor. A Quantum Physicist Explains the Healing Power of Integral Medicine. Hampton Roads Publishing Company, Inc., Charlottesville, VA 22906, USA.

Gottesmann, C. (2002). GABA mechanisms and sleep. *Neuroscience* 111 (2): 231-239.

Grant, J., Hoorens, S., Sivadasan, S., Van Het Loo, M., Davanzo, J., Hale, L. & Butz, W. (2006). Trends in European fertility: should Europe try to increase its fertility rate…or just manage the consequences? *International Journal of Andrology* 29: 17-24.

Greger, J. L. (1999). Non-digestible carbohydrates and mineral bioavailabilty. *Journal of Nutrition* 129: 1434S-1435S.

Griskevicius, V., Ackerman, J. M., Cantú, S. M., Delton, A. W., Robertson, T. E., Simpson, J. A., Thompson, M. E. & Tybur, J. M. (2013). When the economy falters, do people spend or save? Responses to resource scarcity depend on childhood environments. *Psychological Science* 24 (2): 197-205.

Grundy, E. & Read, S. (2015). Pathways from fertility history to later life health: Results from analyses of the English Longitudinal Study of Ageing. *Demographic Research* 32: 107-146.

Guarner, F. & Malagelada, J. R. (2003). Gut flora in health and disease. *Lancet* 361: 512-519.

Guarente. L. (2011). Sirtuins, aging and medicine. *New England Journal of Medicine* 364: 2235-2244.

Guarente. L. (2013). Calorie restriction and sirtuins revisited. *Genes and Development* 27: 2072-2085.

Haaga, J. G. (2001). Comment: The pace of fertility decline and the utility of evolutionary approaches. *Population & Development Review* 27 (Supplement): 53-59.

Haandrikman, K. & Van Wissen, L. J. G. (2008). Effects of the fertility transition on birth seasonality in the Netherlands. *Journal of Biosocial Science* 40 (5): 655-672.

Haigis, M. C. & Sinclair, D. A. (2010). Mammalian sirtuins: Biological insights and disease relevance. *Annual Review of Pathology* 5: 253-295.

Hajnal, J. (1965). European marriage pattern in historical perspective. In: D.V. Glass and D. E. C. Eversley (eds.). Population in History. Arnold, London.

Hajnal, J. (1982). Two kinds of preindustrial household formation system. *Population and Development Review* 8 (3): 449-494.

Halberg, N., Henriksen, M., Söderhamn, N., Stallknecht, B., Ploug, T., Schjerling, P. & Dela, F. (2005). Effect of intermittent fasting and refeeding on insulin action in healthy men. *Journal of Applied Physiology* 99: 2128-2136.

Hales, C. N. & Barker, D. J. P. (2001). The thrifty phenotype hypothesis: Type 2 diabetes. *British Medical Bulletin* 60 (1): 5-20.

Halfon, N., Larson, K., Lu, M., Tullis, E. & Russ, S. (2014). Life course health development: past, present and future. *Maternal and Child Health Journal* 18 (2): 344-365.

Halliwell, B. (2001). Free radicals and other reactive species in disease. Encyclopedia of Life Sciences 2001, Nature Publishing Group.

Halliwell, B. (2012). The antioxidant paradox: less paradoxical now? *British Journal of Clinical Pharmacology* 75 (3): 637-644.

Halton, T. L. & Hu, F. B. (2004). The effects of high protein diets on thermogenesis, satiety and weight loss: a critical review. *Journal of the American College of Nutrition* 23 (5): 373-385.

Hanhineva, K., Törrönen, R., Bondia-Pons, I., Pekkinen, J., Kolehmainen, M., Mykkänen, H. & Poutanen, K. (2010). Impact of dietary polyphenols on carbohydrate metabolism. *International Journal of Molecular Sciences* 11: 1365-1402.

Hank, K. (2001). Regional fertility differences in western Germany: an overview of the literature and recent descriptive findings. *Population, Space and Place* 7 (4): 243-257.

Hank, K. (2002). Regional social contexts and individual fertility decisions: A multilevel analysis of first and second births in Western Germany. German Institute for Economic Research (DIW) Discussion Papers, No. 270.

Hanson, H.A. (2013). Understanding the determinants of aging and longevity: The influence of the social environment, biology, and heritability throughout the life course. PhD dissertation, Department of Sociology, The University of Utah. USA.

Harpending, & Rogers (1990). Fitness in stratified societies. *Ethology and Sociobiogy* 11: 497-509.

Hartleben, B., Gödel, M., Meyer-Schesinger, C., Liu, L., Ulrich, T., Köbler, S., Wiech, T., Grahammer, F., Arnold, S. J., Lindenmeyer, M. T., Cohen, C. D., Pavenstädt, H., Kerjaschki, D., Mizushima, N., Shaw, A. S. Walz, G. & Huber, T. B. (2010). Autophagy influences glomerular disease susceptibility and maintains podocyte homeostasis in aging mice. *Journal of Clinical Investigation* 120 (4): 1084-1096.

Hasina, N. & Ozpolat, B. (2014). Regulation of autophagy by polyphenolic compounds as a potential therapeutic strategy for cancer. *Cell Death and Disease* 5, e1509; doi: 10.1038/cdds.2014.467

Hatori, M., Vollmers, C., Zarrinpar, A., DiTacchio, L., Bushong, E. A., Gill, S., Leblanc, M., Chaix, A., Joens, M., Fitzpatrick, J. A. J., Ellisman, M. H. & Panda, S. (2012). Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. *Cell Metabolism* 15 (6): 848-860.

Haugen, M., Fraser, D. & Førre, Ø. (1999). Diet therapy for the patient with rheumatoid arthritis? *Rheumatology (Oxford)* 38 (11): 1039-1044.

Hauner, H., Schmid, P. & Pfeiffer, E. F. (1987). Glucocorticoids and insulin promote the differentiation of human adipocyte precursor cells into fat cells. *Journal of Clinical Endocrinology and Metabolism* 64 (4): 832-835.

He, C., Sumpter, R. & Levine, B. (2012). Exercise induces autophagy in peripheral tissues and in the brain. *Autophagy* 8 (10): 1548-1551.

Head, K H. & Kelly, G. S. (2009). Nutrients and botanicals for treatment of stress: adrenal fatigue, neurotransmitter imbalance, anxiety, and restless sleep. *Alternative Medicine Review* 14 (2): 114-140.

Heckel, M. (1990). Ganzkörper-Hyperthermie und Fiebertherapie. Grundlagen und Praxis. Hippokrates Verlag, Stuttgart, Deutschland.

Heijmans, B. T., Tobi, E. W., Stein, A. D., Putter, H., Blauw, G. J., Susser, E. S., Slagboom, P. E. & Lumey, L. H. (2008). Persistent epigenetic differences associated with prenatal exposure of famine in humans. *Procedings of the National Academy of Sciences of the United States of America* 105 (44): 17046-17049.

Heiland, F., Prskawetz, A. & Sanderson, W. C. (2008). Are individuals' desired family sizes stable? Evidence from West German panel data. *European Journal of Population* 24 (2): 129-156.

Heinrichs, M., Neumann, I. & Ehlert, U. (2002). Lactation and stress: protective effects of breast-feeding in humans. *Stress: The International Journal on the Biology of Stress* 5 (3): 195-203.

Hekimi, S., Lapointe, J. & Wen, Y. (2011). Taking a 'good' look at free radicals in the aging process. *Trends in Cell Biology* 10: 569-576.

Henrotte, J. G., Franck, G., Santarromana, M., Francès, H., Mouton, D. & Motta, R. (1997). Mice selected for low and high blood magnesium levels: a new model for stress studies. *Physiology & Behavior* 61 (5): 653-658.

Hensel, H. (1980). Die Funktion des Fiebers im Krankheitsgeschehen. Vortrag XXVIV, Deutscher Kongress für Arztliche Fortbildung, Unveröffentliches Manuskript.

Hermisson, J. & Wagner, G. P. (2004). Evolution of phenotypic robustness. In *Robust Design: a Repertoire from Biology, Ecology, and Engineering*. E. Jen (ed); pp 47-70. Oxford University Press, Oxford, United Kingdom.

Herschlag, Y. (2015). Maimonides and Metabolism. Physiology of Fat-Loss. CreateSpace Independent Publishing Platform, North Charleston, South Carolina, USA.

Hill, K. & Kaplan, H. (1999). Life history traits on humans: Theory and empirical studies. *Annual Review of Anthropology* 28: 397-430.

Hillebrand, H. (2004). On the generality of the latitudinal diversity gradient. *American Naturalist* 163 (2): 192-211.

Hirschman, C. (2001). Comment: Globalization and theories of fertility decline. *Population and Development Review* 27 (Supplement): 116-125.

Hirvikoski, T., Lindholm, T., Nordenström, H., Nordström, A-L. & Lajic, S. (2009). High self-perceived stress and many stressors, but normal diurnal cortisol rhythm, in adults with ADHD (attention-deficit/hyperactivity disorder). *Hormones & Behavior* 55 (3): 418-424.

Hoem, B. & Hoem, J. M. (1996). Sweden's family policies and roller-coaster fertility. *Journal of Population Problems* 52 (3/4): 1-22.

Holt, E. M., Steffen, L.M., Moran, A., Basu, S., Steinberger, J., Ross, J. A., Hong, C-P. & Sinaiko, A. R. (2009). Fruit and vegetable consumption and its relation to markers of inflammation and oxidative stress in adolescence. *Journal of American Diet Association* 109 (3): 414-421.

Hormann, W. (1985). Biologie und Politik. Der Staat am Steuer der Evolution. Hohenrain-Verlag, Tübingen, Zürich, Paris.

Hotamisligil, G. S. & Erbay, E. (2008). Nutrient sensing and inflammation in metabolic diseases. *Nature Reviews Immunology* 8: 923-934.

Hotamisligil, G. S. (2010). Endoplasm reticulum stress and the inflammatory basis of metabolic disease. *Cell* 140 (6): 900-917.

Howes, R. M. (2006). The free radical fantasy. A panoply of paradoxes. *Annals of the New York Academy of Sciences* 1067: 22-26.

Howes, R. M. (2011). Mythology of antioxidant vitamins? *Journal of Evidence-Based Complementary & Alternative Medicine* 16 (2): 149-159.

Huber, S., Fieder, M., Wallner, B., Iber, K. & Moser, G. (2004a). Effects of season of birth of reproduction in contempory humans: Brief communication. *Human Reproduction* 19 (2): 445-447.

Huber, S., Fieder, M., Wallner, B., Iber, K. Moser, G. & Arnold, W. (2004b). Brief communication: Birth month influences reproductive performance in contempory women. *Human Reproduction* 19 (5): 1081-1082.

Huber, S., Bookstein, F. L. & Fieder, M. (2010). Socioeconomic status, education, and reproduction in modern women: An evolutionary perspective. *American Journal of Human Biology* 22: 578-587.

Huizink, A. C., Mulder, E. J. H. & Buitelaar, J. K. (2004). Prenatal stress and risk of psychopathology: specific effects or induction of general susceptibility? *Psychological Bulletin* 130 (1): 115-142.

Hyman, M. (2008). The UltraMind Solution. Fix Your Broken Brain by Healing Your Body First. Scribner, New York, London, Toronto, Sydney.

Inouye, E., Park, K. S. & Asaka, A. (1984). Blood uric acid and IQ: a study in twin families. *Acta Geneticae Medicae et Gemellologiae: Twin Research* 33 (2): 237-242.

Irwin, M. R., Wang, M., Ribeiro, D., Cho, H. J., Olmstead, R., Breen, E. C., Martinez-Maza, O. & Cole, S. (2008). Sleep loss activates cellular inflammatory signalling. *Biological Psychiatry* 64 (6): 538-540.

Irwin, M. R. (2015). Why sleep is important for health: a psychoneuroimmunology perspective. *Annual Review of Psychology* 66: 143-172.

Ising, H. & Braun, C. (2000). Acute and chronic endocrine effects of noise: Review of the research conducted at the Institute for water, soil and air hygiene. *Noise & Health* 2: 7-24.

Iwashita, Y., Kuwabara, T., Hayata, M., Kakizoe, Y., Izumi, Y., Lyama, J., Kitamura, K. & Mukoyama, M. (2016). Mild systemic thermal therapy ameliorates renal dysfunction in a rodent model of chronic renal disease. *American Journal of Physiology. Renal Physiology* 310 (11): F1206-F1215.

Jablonka, E. & Lamb, M.J. (1995). Epigenetic Inheritance and Evolution. Oxford University Press, UK.

Jablonka, E., Oborny, B., Molnar, I., Kisdi, E., Hofbauer, J. & Czaran, T. (1995). The adaptive advantage of phenotypic memory in changing environments. *Philosophical Transactions of the Royal Society: Biological Sciences*, 350 (1332): 133-141.

Jablonka, E. & Raz, G. (2009). Transgenerational epigenetic inheritance: Prevalence, mechanisms, and implications for the study of heredity and evolution. *The Quarterly Review of Biology*, 84 (2): 131-176.

Jablonka, E. & Lamb, M. J. (2014). Evolution in Four Dimensions. Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life. Revised edition. The MIT Press, Cambridge, Massachusetts.

Jackson, A. A. (1989). Optimizing amino acid and protein supply and utilization in the newborn. *Proceedings of the Nutrition Society* 48: 293-301.

Jackson, J. A., Riordan, H. D., Hunninghake, R. & Revard, C. (1999). Candida albicans: the hidden infection. *Journal of Orthomolecular Medicine* 14 (4): 198-200.

Jakubowicz, D., Barnea, M., Wainstain, J. & Froy, O. (2013). High caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. *Obesity* 21 (12): 2504-2512.

Jasienska, G. (2003). Energy metabolism and the evolution of reproductive suppression in the human female. *Acta Biotheoretica* 51: 1-18.

Jasienska, G., Thune, I. & Ellison, P.T. (2006). Fatness at birth predicts adult susceptibility to ovarian suppression: An empirical test of the Predictive Adaptive Response hypothesis. *Proceedings of the National Academy of Sciences* 103 (34): 12759-12762.

Jasienska, G. (2009). Reproduction and lifespan: trade-offs, overall energy budgets, intergenerational costs, and costs neglected by research. *American Journal of Human Biology* 21: 524-532.

Javierre, B. M., Hernando, H. & Ballestar, E. (2011). Environmental triggers and epigenetic deregulation in autoimmune disease. *Discovery Medicine* 12 (67): 535-545.

Jenkins, D. J., Kendall, C. W., Augustin, L. S., Franceschi, S., Hamidi, M., Marchi, A., Jenkins, A. L. & Axelsen, M. (2002). Glycenic index: overview of implications in health and disease. *American Journal of Clinical Nutrition* 76 (1): 266S-273S.

Jentschura, P. & Lohkämper, J. (2014). Gesundheit durch Entschlackung. 20. Auflage, Taschenbuch. Verlag Peter Jentschura, Münster, Deutschland. Dieses Buch ist in den folgenden Sprachen erhältlich: Englisch, Russisch, Französisch, Spanisch, Niederländisch, Italienisch, Polnisch, Ungarisch, Lettisch, Slowenisch, Tschechisch und Polnisch.

Jia, K. & Levine, B. (2007). Autophagy is required for dietary restriction-mediated life span extension in *C. elegans*. *Autophagy* 3 (6): 597-599.

Jirtle, R. L. & Skinner, M, K. (2007). Environmental epigenomics and disease susceptibility. *Nature Reviews Genetics* 8 (4): 253-262.

Johnson, R. H. & Rideout, B. A. (2004). Uric acid and diet – Insights into the epidemic of cardiovascular disease. *New England Journal of Medicine* 350 (11): 1071-1073.

Johnson, R. J., Segal, M. S., Sautin, Y., Nakagawa, T., Feig, D. I., Kang, D., Gersch, M. S., Benner, S. & Sánchez-Lozada, L. G. (2007). Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. *American Journal of Clinical Nutrition* 86: 899-906.

Johnson, R. H., Gaucher, E. A., Sautin, Y. Y., Henderson, G. N., Angerhofer, A. J. & Benner, S. A. (2008). The planetary biology of ascorbate and uric acid and their relationship with the epidemic of obesity and cardiovascular disease. *Medical Hypotheses* 71: 22-31.

Johnson, R. H., Sautin, Y. Y., Oliver, W.J., Roncal, C., Mu, W., Sanchez-Lozada, L. G., Rodriguez-Iturbe, B., Nakagawa, T. & Benner, S. A. (2009). Lessons from

comparative physiology: could uric acid represent a physiological alarm signal gone awry in western society? *Journal of Comparative Physiology B* 179 (1): 67-76.

Johnson, R. J. & Andrews, P. (2010). Fructose, uricase, and the back-to-Africa hypothesis. *Evolutionary Anthropology* 19: 250-257.

Johnson, R. J., Lanaspa, M. A. & Gaucher, E. A. (2011). Uric acid: a danger signal from the RNA world that may have a role in the epidemic of obesity, metabolic syndrome and cardiorenal disease: evolutionary considerations. *Seminars in Nephrology* 31 (5): 394-399.

Johnstone, J. D. (2014). Physiological responses to food intake throughout the day. *Nutrition Research Reviews* 27: 107-118.

Jones, G., Riley, M. D. & Dwyer, T. (2000). Maternal diet during pregnancy is associated with bone mineral density in children: a longitudinal study. *Journal of Clinical Nutrition*, 54: 749-756.

Jørgensen, N., Andersen, A-G., Eustache, F., Irvine, D. S., Suominen, J., Petersen, J. H., Andersen, A. N., Andersson, A. M., Auger, Cawood, E. H. H., J., Horte, A., Jensen, T. K., Jouannette, P., Keiding, N., Vierula, M., Toppari, J. & Skakkebæk, N. E. (2001). Regional differences in semen quality in Europe. *Human Reproduction* 16 (5): 1012-1019.

Jørgensen, N., Carlsen, E., Nermoen, I., Punab, M., Suominen, J., Andersen, A-G., Andersson, A. M., Haugen, T. B., Horte, A., Jensen, T. K., Magnus, Ø., Petersen, J. H., Vierula, M., Toppari, J. & Skakkebæk, N. E. (2002). East-west gradient in semen quality in the Nordic-Baltic area: a study of men in the general population in Denmark, Norway, Estonia and Finland. *Human Reproduction* 17 (8): 2199-2208.

Joseph, K. S. & Kramer, M.S. (1996). Review of the evidence on fetal and early childhood antecedence of adult chronic disease. *Epidemiologic Reviews*, 18 (2): 158-174.

Joss-Moore, L.A., Metcalfe, D.B., Albertine, K.H., McKnight, R.A. & Lane, R.H. (2010). Epigenetics and fetal adaptation to perinatal events: Diversity through fidelity. *Journal of Animal Science*, 88 (E. Suppl.): E216- E222.

Kahleova, H., Lloren, J. I., Mashchak, A., Hill, M. & Fraser, G. E. (2017). Meal frequency and timing are associated with changes in body mass index in Adventist Health Study 2. *The Journal of Nutrition.* 147 (9): 1722-1728.

Kalmijn, M. (2007). Explaing cross-national differences in marriage, cohabitation, and divorce in Europe, 1990-2000. *Population Studies* 61 (3): 243-263.

Kaplan, H. S., Lancaster, J., Bock, J. & Johnson, S. (1995). Does observed fertility maximize fitness among New Mexican men? A test of an optimality model and a new theory of parental investment in the embodied capital of offspring. *Human Nature* 6: 325-360.

Kaplan, H. S. (1996). A theory of fertility and parental investment in traditional and modern human societies. *Yearbook of Physical Anthropology* 39: 91-135.

Kaplan, H. S., Hill, K., Lancaster, J. B. & Hurtado, A. M. (2000). A theory of human life evolution: diet, intelligence, and longevity. *Evolutionary Anthropology* 9: 156-185.

Kaplan, H. S., Lancaster, J. B., Tucker, W. T. & Anderson, K. G. (2002). An evolutionary approach to below replacement fertility. *American Journal of Human Biology* 14: 233-256.

Kaplan, H. S & Lancaster, J. B. (2003). An evolutionary and ecological analysis of human fertility, mating patterns, and parental investment. In: Wachter, K. W. & Bulatao, R. A. (Eds.) *Offspring: Human Fertility Behavior in Biodemograhic Perspective*. Pp. 170-223. Washington DC: National Academia, USA.

Kapoor, A., Dunn, E., Kostaki, A., Andrews, M. H. & Matthews, G. (2006). Fetal programming of the hypothalamo-pituitary-adrenal function: prenatal stress and glucocorticoids. *Journal of Physiology* 572 (1): 31-44.

Karamanou, M., Liappas, I., Antoniou, Ch., Androutsos, G. & Lykouros, E. (2013). Julius Wagner-Jauregg (1857-1940): Introducing fever therapy in the treatment of neurosyphilis. *Psychiatriki* 24 (3): 208-212.

Kasl, S. V., Brooks, G. W. & Rodgers, W.L. (1970). Serum uric acid and cholesterol in achievement behaviour and motivation. II. Relationship to College attendance, extracurricular and social activities, and vocational aspirations. *Journal of the American Medical Association* 213 (8): 1291-1299.

Katari, S., Turan, N., Bibikova, M., Erinle, O., Chalian, R., Foster, M., Gaughan, J. P., Coutifaris, C. & Sapienza, C. (2009). DNA methylation and gene expression differences in children conceived *in vitro* or *in vivo*. *Human Molecular Genetics* 18 (20): 3769-3778.

Keefe, D. L., Franco, S., Liu, L., Trimarchi, J., Cao, B., Weitzen, S., Agarwal, S. & Blasco, M. A. (2005). Telomere length predicts embryo fragmentation after in vitro fertilization in women – toward a telomere theory of reproductive aging in women. *American Journal of Obstetrics & Gynecology* 192 (4): 1256-1260.

Kegel, B. (2015). Epigenetk. Wie unsere Erfahrungen vererbt werden. DuMont Buchverlag, Köln, Deutschland.

Keller, E. F. (2002). Developmental robustness. *Annals of the New York Academy of Sciences*, 981: 189-201.

Kellner, G. (1984a). Der Herd in experimentell-histologischer Sicht. In *Grundsystem und Regulationsstörungen*. Hrsg. O. Bergsmann, R. Bergsmann & Kellner, M.; 132-139. Karl F. Haug Verlag, Heidelberg. Deutschland.

Kellner, G. (1984b). Die Neuraltherapie im Spiegel der humoralen Regulationspathologie. *Grundsystem und Regulationsstörungen*. Hrsg. O. Bergsmann, R. Bergsmann & Kellner, M.; 427-440. Karl F. Haug Verlag, Heidelberg. Deutschland.

Kemkes-Grottenthaler, A. (2004). Parental effects on offspring longevity – evidence from 17th to 19th centuries reproductive histories. *Annals of Human Biology* 31 (2): 139-158.

Kertzer, D. I. & Barbagli, M. (eds., 2001). Family Life in Early Modern Times 1500-1789. The History of the Early European Family. Vol. 1. Yale University Press, New Haven and London.

Kertzer, D. I., White, M. J., Bernardi, L. & Gabrielli, G. (2009). Italy's path to very low fertility: The adequacy of economic and second demographic transition theories. *European Journal of Population* 25 (1): 89-115.

Kiffin, R., Bandyopadhyay, U. & Cuervo, M. (2005). Oxidative stress and autophagy. *Antioxidants and Redox Signaling* 8 (1/2): 152-162.

Kim, W., Shin, D. J., Harihara, S., & Kim, Y.J. (2000). Y chromosomal DNAvariation in East Asian populations and its potential for inferring the peopling of Korea. *Journal of Human Genetics* 45: 76-83.

Kim, D. J., Xun, P., Liu, K., Loria, C., Yokota, K., Jacobs Jr, D. R. & He, K. (2010). Magnesium intake in relation to systematic inflammation, insulin resistance, and the incidence of diabetes. *Diabetes Care* 33 (12): 2604-2610.

Kim, Y. S., Young, M. R., Bobe, G., Colburn, N. H. & Milner, J. A. (2009). Bioactive food components, inflammatory targets, and cancer prevention. *Cancer Prevention Research* 2 (3): 200-208.

Kim, H-S., Quon, M.J. & Kim, J. (2014). New insights into the mechanisms of polyphenols beyond antioxidant properties; lessens from the green tea polyphenol, epigallocatechin 3-gallate. *Redox Biology* 2: 187-195.

Kimura, K., Ozeki, M., Junea, R. L. & Ohira, H. (2007). L-Theanine reduces psychological and physiological stress responses. *Biological Psychology* 74: 39-45.

Kirkwood, T. B. L., Kapahi, P. & Shanley, D. P. (2000). Evolution, stress, and longevity. *Journal of Anatomy* 197: 587-590.

Kirkwood, T. B. L. (2002). Molecular gerontology. *Journal of Inherited Metabolic Disease* 25 (3): 189-196.

Kirkwood, T. B. L. & Shanley, D. P. (2005). Food restriction, evolution and ageing. *Mechanisms of Ageing and Development* 126: 1011-1016.

Kluger, M.J. (1979). Fever. Its Biology, Evolution and Function. Princeton University Press, Princeton, USA.

Knaul, E. (1985). Das biologische Massenwirkungsgesetz. Ursache von Aufstieg und Untergang der Kulturen. Türmer-Verlag, Berg/Starnberger See, Deutschland.

Knodel, J. & Wilson, C. (1981). The secular increase in fecundity in German village populations: An analysis of reproductive histories of couples married 1750-1899. *Population Studies* 35 (1): 53-84.

Köhnlechner, M. (1980). Handbuch der Naturheilkunde I. Wilhelm Heyne Verlag, München, Deutschland.

Kohler, H-P., Billari, F. C. & Ortega, J. A. (2002). The emergence of lowest-low fertility in Europe during the 1990s. *Population and Development Review* 28: 641-680.

Kohler, H-P. & Rodgers, J. L. (2003). Education, fertility, and heritability: Explaining a paradox. In K. W. Wachter & RA Bulatao (Eds.), *Offspring: Fertility behaviour in biodemographic perspective*. Washington DC: National Academic Press. pp. 46-90.

Kohler, H-P., Billari, F. C. & Ortega, J. A. (2006). Low fertility in Europe: Causes, implications and policy options. In F. R. Harris (Ed), *The Baby Bust: Who will do the Work? Who Will Pay the Taxes?* Lanham, MD: Rowman & Littlefield Publishers. Pp. 48-109.

Korpelainen, H. (2000). Fitness, reproduction and longevity among European aristocratic and rural Finnish families in the 1700s and 1800s. *Proceedings of the Royal Society of London* B 267: 1765-1770.

Korpelainen, H. (2003). Human life histories and the demographic transition: a case study from Finland, 1870-1949. *American Journal of Physical Anthropology* 120: 384-390.

Kollath, W. (1978). Regulatoren des Lebens – vom Wesen der Redox-Systeme. Zweite Auflage. Karl F. Haug Verlag, Heidelberg, Deutschland.

Korte, S. M., Koolhaas, J. M., Wingfield, J. C. & McEwen, B. S. (2005). The Darwinian concept of stress: benefits of allostasis and costs of allostaic load and the trade-offs in health and disease. *Neuroscience and Biobehavioral Reviews* 29: 3-38.

Krastev, I. (2008). The strange death of the liberal consensus. In: Swoboda, H., Wiersma, J. M. (eds) *Democracy, Populism and Minority Rights*. Pp 67-76. Printed in Belgium by Antelope.

Kraut, J. A. & Madias, N. E. (2016). Metabolic acidosis of CKD: an update. *American Journal of Kidney Diseases* 67 (2): 307-317.

Kruger, D. J. & Nesse, R. M. (2006). An evolutionary life history framework for understanding sex differences in human mortality rates. *Human Nature* 17 (1): 74-97.

Kudielka, B. M., Hellhammer, D. H. & Wüst, S. (2009). Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. *Psychoneuroendocrinology* 34: 2-18.

Kuijpers, E. P. (1980). The geologic history of the Nicoya Ophiolite Complex, Costa Rica, and its geotectonic significance. *Tectonophysics*, 68 (3-4): 233-255.

Külken, T. (1985). Fieberkonzepte in der Geschichte der Medizin. Verlag für Medizin Dr Ewald Fischer, Deutschland.

Kutzing, M. K. & Firestein, B. L. (2008). Altered uric acid and disease states. *Journal of Pharmacology and Experimental Therapeutics* 324 (1): 1-7.

Kuzawa, C. W. (2005). Fetal origins of developmental plasticity: Are fetal cues reliable predictors of future nutritional environmemts? *American Journal of Human Biology* 17: 5-21.

Kuzawa C. W. & Quinn, E. A. (2009). Developmental origins of adult function and health: Evolutionary hypotheses. *Annual Reviw of Anthropology* 38: 131-147.

Lackschewitz, H., Hüther, G. & Kröner-Herwig, B. (2008). Physiological and psychological stress responses in adults with attention-deficit/hyperactivity disorder (ADHD). *Psychoneuroendocrinology* 33 (5): 612-624.

Laires, M. J., Monteiro, C. P. & Bicho, M. (2004). Role of cellular magnesium in health and human disease. *Frontiers in Bioscience* 9: 262-276.

Laires, M. J. & Monteiro, C. (2008). Exercise, magnesium and immune function. *Magnesium Research* 21 (2): 92-96.

Lamming, D. W., Wood, J.G. & Sinclair, D. A. (2004). Small molecules that regulate lifespan: evidence for xenohormesis. *Molecular Microbiology* 53 (4): 1003-1009.

Lane, M. A., Ingram, D. K., Ball, S. S. & Roth, G. S. (1997). Dehydroepiandrosterone sulfate: a biomarker for primate aging slowed by calorie restriction. *Journal of Clinical Endocrinology and Metabolism* 82 (7): 2093-2096.

Langreder, W. (1991). Von der biologischen zur biophysikalischen Medizin. 2. Auflage. Karl F. Haug Verlag, Heidelberg, Deutschland.

Lanzieri, G. (EUROSTAT 2011). Fewer, older and multicultural? Projections of the EU populations by foreign/national background. EUROSTAT Methodologies and Working papers. European Commission.

Lao, O., Lu, T. T., Nothnagel, M., Junge, O., Freitag-Wolf, S., Caliebe, A., Balascakova, M. et al. (2008). Correlation between genetic and geographic structure in Europe. *Current Biology* 18: 1241-1248.

Laszlo, E. (2008). The Quantum Shift in the Global Brain. Inner Traditions, Rochester, Vermont, Toronto. Canada.

Laszlo, E. (2014a). The Self-Actualizing Cosmos. The Akasha Revolution in Science and Human Consciousness. Inner Traditions, Rochester, Vermont, Toronto. Canada.

Laszlo, E. (2014b). The Immortal Mind. Science and the Continuity of Consciousness beyond the Brain. Inner Traditions, Rochester, Vermont, Toronto. Canada.

Latner, J. D. & Schwartz, M. (1999). The effects of a high-carbohydrate, high-protein or balanced lunch upon later food intake and hunger ratings. *Appetite* 33: 119-128.

Laughlin, G. A., Barrett-Connor, E. & Bergstrom, J. (2008). Low serum testosterone and mortality in older men. *Journal of Clinical Endocrinology and Metabolism* 93: 68-75.

Lazaridis, I., Patterson, N., Mittnik, A., Renaud, G., Mallick, S., Kirsanow, K., Sudmant, P. H., et al., (2014). Ancient human genomes suggest three ancestral populationsfor present-day Europeans. *Nature* 18: 513 (7518): 409-413.

Le Bourg, E., Thon, B., Légaré, J., Desjardins, B. & Charbonneau, U. (1993). Reproductive life of french-canadians in the 17th-18th centuries: A search for a trade-off between early fecundity and longevity. *Experimental Gerontology* 8 (3): 217-232.

Leenders, M., Sluijs, I., Ros, M. M., et al. (2013). Fruit and vegetable consumption and mortality. European prospective investigation into cancer and nutrition. *American Journal of Epidemiology* 2013. doi: 10.1093/aje/kwt006.

Leonard, W. R., Sorenson, M. V., Galloway, V. A. Spencer, G. J., Mosher, M. J., Osipova, L. & Spitsyn, V. A. (2002). Climatic influences on basal metabolic rates among circumpolar populations. *American Journal of Human Biology* 14: 609-620.

Leonard, W. R., Robertson, M. L., Snodgrass, J. J., & Kuzawa, C. W. (2003). Metabolic correlates of hominid brain evolution. *Comparative Biochemistry and Physiology* Part A 136: 5-15.

Lerchl, A., Simoni, M. & Nieschlag, E. (1993). Changes in seasonality of birth rates in Germany from 1951-1990. *Naturwissenschaften* 80: 516-518.

Lesthaeghe, R. & Moors, G. (2000). Recent trends in fertility and household formation in the industrialized world. *Review of Population and Social Policy* 9: 121-170.

Lesthaeghe, R. & Neels, K. (2002). From the first to the second demographic transition – An interpretation of the spatial continuity of demographic innovation in France, Belgium and Switzerland. *European Journal of Population* 18: 325-360.

Lesthaeghe, R. & Surkyn, J. (2008). When history moves on. The foundations and diffusion of a second demographic transition. *International Family Change: Ideational Perspectives* 2008: 81-117.

Lesthaeghe, R. & Neidert, L. (2009). US presidential elections and the spatial pattern of the American demographic transition. *Population & Development Review* 35 (2): 391-400.

Lesthaeghe, K. (2010). The unfolding story of the second demographic transition. *Population and Development Review* 36 (2): 211-251.

Lewontin, R. C. (1988). On measures of gametic disequilibrium. *Genetics* 120: 849-852.

Li, J., Dong, B., Lin, P., Zhang, J. & Liu, G. (2010). Association of cognitive function with serum uric acid level among Chinese nonagenarians and centenarians. *Experimental Gerontology* 45: 331-335.

Li, C., Ning, C., Hagelberg, E., Li, H., Zhao, Y., Li, W., Abuduresule, I., Zhu, H. & Zhu, H. (2015). Analysis of ancient mitochondrial DNA from the Xiaohe cemetery: Insights into prehistoric population movements into the Tarim Basin, China. *BMC Genetics* 16: 78.

Lichtenstein, A. H. & Russell, R. M. (2005). Essential nutrients: food or supplements? Where should the emphasis be? *Journal of the American Medical Association* 294 (3): 351-358.

Lindeberg, S., Cordan, L. & Eaton, S. B. (2003). Biological and clinical potential of a Paleolithic diet. *Journal of Nutritional & Environmental Medicine* 13 (3): 149-160.

Lindstedt, S. L. & Boyce, M. S. (1985). Seasonality, fasting endurance, and body size in mammals. *American Naturalist* 125 (6): 873-878.

Lisa, A., Astolfi, P., Zei, G. & Tentoni, S. (2014). Consanguinity and late fertility: Spatial analysis reveals positive association patterns. *Annals of Human Genetics* 79: 34-45.

Lodi, R., Montagna, P., Soriani, S., Iotti, S., Arnaldi, C., Cortelli, P., Pierangeli, G., Patuelli, A., Zaniol, P. & Barbiroli, B. (1997). Deficit of brain and skeletal muscle bioenergetics and low brain magnesium in juvenile migraine: an *in vivo*

^{31}P magnetic resonance spectroscopy interictal study. *Pediatric Research* 42: 866-871.

Lodi, R., Iotti, S., Cortelli, P., Pierangeli, G., Cevoli, S., Clementi, V., Soriani, S., Montagna, P. & Barbiroli, B. (2001). Deficient energy metabolism is associated with low free magnesium in the brains of patients with migraine and cluster headache. *Brain Research Bulletin* 54 (4): 437-441.

Lohbeck, R. (1966). Selbsvernichtung durch Zivilisation. Marienburg-Verlag, Würzburg, Deutschland.

Lorenz, K. (1978). Die acht Todsünden der zivilisierten Menschheit. R. Piper & Co. Verlag, München, Germany.

Lorenz, K. (1986). Der Abbau des Menschlichen. R. Piper & Co. Verlag, München, Germany.

Lorenzi, T. M., Borba, D. L., Dutra, G. & Lara, D. R. (2010). Association of serum uric acid levels with emotional and affective disorders. *Journal of Affective Disorders* 121 (1-2): 161-164.

Low, B. S. (1991). Reproductive life in nineteenth century Sweden: An evolutionary perspective on demographic phenomena. Ethology and Sociobiology 12: 411-448.

Low, B. S. & Clarke, A. L. (1991). Family patterns in nineteenth-century Sweden: Impact of occupational status and landownership. *Journal of Family History* 16 (2): 117-138.

Low, B. S. & Clarke, A. L. (1992). Resources and life course: Patterns through the demographic transition. *Ethology and Sociobiology* 13: 463-494.

Low, B. S. (1994). Men in the demographic transition. *Human Nature* 5 (3): 223-253.

Lubec, G., Wolf, C. & Bartosch, B. (1989). Aminoacid isomerisation and microwave exposure. *The Lancet* 334 (8676): 1392-1393.

Lummaa, V. & Temblay, M. (2003). Month of birth predicted reproductive success and fitness in pre-modern Canadian women. *Proceedings of the Royal Society London B* 270: 2355-2361.

Lünzer, I. (1985). Grundzüge des ökologischen/biologischen Landbaus. In: Ökologischer Landbau. Landwirtschaft mit Zukunft. Herausgeber H. Vogtmann. Seiten 142-145. Pro Natur Verlag, Stuttgart und Eden-Stiftung, Bad Soden. Deutschland.

Lustig, R. H. (2010). Fructose: Metabolic, hedonic, and societal parallels with ethanol. *Journal of the Academy of Nutrition and Dietetics* 110 (9): 1307-1321.

Lutz, W. (1996). The Future Population of the World. What Can We Assume Today? Revised 1996 Edition. W. Lutz (ed), International Institute for Applied Systems Analysis, Laxenburg, Austria. Earthscan Publications Ltd, London, United Kingdom.

Lutz, W. & Qiang, R. (2002). Determinants of human population growth. *Philosophical Transactions of the Royal Society B* 377: 1197-1210.

Lutz, W. (2006). Fertility rates and future population trends: Will Europe's birth rate recover or continue to decline? *International Journal of Andrology* 29: 25-33.

Lutz, W., Skirbekk, V. & Testa, M. R. (2006). The low fertility trap hypothesis: Forces that may lead to further postponement and fewer births in Europe. *Vienna Yearbook of Population Research* 2006: 167-192.

Lycett, J. E., Dunbar, R. I. M. & Voland, E. (2000). Longevity and the cost of reproduction in a historical human population. *Proccedings of the Royal Society of London B* 267: 31-35.

Ma, D., Li, S., Molusky, M. M. & Lin, J.D. (2012). Circadian autophagy rhythm: a link between clock and metabolism? *Trends in Endocrinology and Metabolism* 23 (7): 319-325.

Mabovula, N. N. (2011). The erosion of African communal values: a reappraisal of the African Ubuntu philosophy. *Inkanyiso: Journal of Humanities and Social Sciences* 3 (1): 38-47.

Maciocia, G. (1989). The Foundations of Chinese Medicine. Churchill Livingstone, London, Melbourne, New York.

MacLean, P.D. (1990). The Triune Brain. Role in Paleocerebral Functions. Plenum Press, New York.

Manach, C., Scalbert, A., Morand, C., Rémésy, C. & Jiménez, L. (2004). Polyphenols: food sources and bioavailability. *American Journal of Clinical Nutrition* 79: 727-747.

Manafi, M., Arian, M., Raeesi, S. H. T. & Solgi, A. (2013). Tethys subduction history in the Caucasus region. *Open Journal of Geology* 3: 222-232.

Mancuso, C., Scapagnini, G., Currò, D., Stella, A. M. G., De Marco, C., Butterfield, D. A. & Calabrese, V. (2007). Mitochondrial dysfunction, free radical generation and cellular stress response in neurodegenerative disorders. *Frontiers in Bioscience* 12: 1107-1123.

Markus, C. R., Jonkman, L. M., Lammers, J. H. C. M., Deutz, N. E. P., Messer, M. H. & Rigtering, N. (2005). Evening intake of α-lactalbumin increases plasma tryptophan availability and improves morning alertness and brain measures of attention. *American Journal of Clinical Nutrition* 81 (5): 1026-1033.

Martin, W. F., Armstrong. L. E. & Rodriguez, N. R. (2005). Dietary protein intake and renal function. *Nutrition and Metabolism* 2: 25-34.

Martin, F. P., Rezzi, S., Peré-Trepat, E., Kamlagr, B., Collino, S., Leibold, E., Kastler, J. et al. (2009). Metabolic effects of dark chocolate consumption on energy, gut microbiota, and stress-related metabolism in free-living subjects. *Journal of Proteome Research* 8 (12): 5568-5579.

Masel, J. & Siegal, M. L. (2009). Robustness: mechanisms and consequences. *Trends in Genetics* 25 (9): 395-403.

Masiero, E., Agatea, L., Mammucari, C., Blaauw, B., Loro, E., Komatsu, M., Metzger, D., Reggiani, C., Schiaffino, S. & Sandri, M. (2009). Autophagy is required to maintain muscle mass. *Cell Metabolism* 10: 507-515.

Mason, R. (1985). Ophiolites. *Geology Today*, 1 (5): 136-140.

Mason, K. O. (1997). Explaining fertility transitions. *Demography* 34 (4): 443-454.

Masoro, E. J. (2009). Caloric restriction-induced life extension of rats and mice: A critique of proposed mechanisms. *Biochimica et Biophysica Acta* 1790: 1040-1048.

Matsumura, H. & Hudson, M. J. (2005). Dental pespectives on the population history of Southeast Asia. *American Journal of Physical Anthropology* 127: 182-209.

Mattson, M. P. (2003). Gene-diet interactions in brain aging and neurodegenerative disorders. *Annals of Internal Medicine* 139 (5): 441-444.

Mattson, M. P. & Cheng, A. (2006). Neurohormetic phytochemicals: low-dose toxins that induce adaptive neuronal stress responses. *Trends in Neurocience*s 29 (11): 632-639.

Mattson, M. P., Allison, D. B., Fontana, L., Harvie, M., Longo, V. D., Malaisse, W. J., Mosley, M., et al. (2014). Meal frequency and timing in health and disease. *Proceedings of the National Academy of Sciences of the USA* 111 (47): 16647-16653.

Mauskop, A. & Varughese, J. (2012). Why all migraine patients should be treated with magnesium. *Journal of Neural Transmission* 119: 575-579.

Maxwell, J. C. (2007). The 21 Irrefutable Laws of Leadership. Revised an updated. 10th Anniversary Edition. Thomas Nelson, Nashville, Dallas. USA.

Mayer, J. (1967). Nutrition and Civilization. *Transcations of the NewYork Academy of Sciences*, 29: 1014-1032.

McCarty, M. F., DiNicolantonio, J. J. & O'Keefy, J. H. (2015). Ketosis may promote macroautophagy by activating Sirt1 and hypoxia-inducable factor-1. *Medical Hypotheses* 85: 631-639.

McDade, T. W. (2003). Life history theory and the immune system: steps toward a human ecological immunology. *Yearbook of Physical Anthropology* 46: 100-125.

McDade, T.W., Rutherford, J., Adair, L. & Kuzawa, W. (2010). Early origins of inflammation: microbial exposures in infancy predict lower levels of C-reactive protein in adulthood. *Proceedings of the Royal Society B* 277: 1129-1137.

McDade, T.W. (2012). Early environments and the ecology of inflammation. *Proceedings of the National Academy of Sciences of the United States of America* 109 (Suppl. 2): 17281-17288.

McDade, T.W., Metzger M. W., Chyu, L., Duncan, G. J., Garfield, C. & Adam, E. K. (2014). Long-term effects of birth weight and breastfeeding duration on inflammation in early adulthood. *Proceedings of the Royal Society B* 281: 1-9.

McDade, T. W., Georgiev, A.V. & Kuzawa, C. W. (2016). Trade-offs between acquired and innate immune defences in humans. *Evolution, Medicine and Public Health* (2016): 1-16.

McDade, T.W., Ryan, C., Jones, M. J., MacIsaac, J. L., Morin, A.M., et al. (2017). Social and physical environments early in development predict DNA methylation of inflammatory genes in young adulthood. *Proceedings of the National Academy of Sciences of the United States of America* 114 (29): 7611-7616.

McEwen, B. S. (1998a). Protective and damaging effects of stress mediators. *New England Journal of Medicine* 338 (3): 171-179.

McEwen, B. S. (1998b). Stress, adaptation, and disease. *Annals of the NewYork Academy of Sciences* 840 (1): 33-44.

McEwen, B., Bullock, K. & Stewart, J. (1999). Parasympathetic function. Summary. Research: Allostatic Load Notebook, MacArthur Research Network on Socioeconomic Status & Health, University of California, San Francisco, USA.

McEwen, B. S. & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and Behavior* 43: 2-15.

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews* 87: 873-904.

McEwen, B. S. & Gianaros, P. J. (2010). Central role of the brain in stress and adaptation: Links to socioeconomic status, health and disease. *Annals of the New York Academy of Sciences* 1186: 190-222.

McEwen, B. S. (2016). In pursuit of resilience: stress, epigenetics, and brain plasticity. *Annals of the NewYork Academy of Sciences* 1373: 56-64.

McGraw, J. B. & Caswell, H. (1996). Estimation of individual fitness from life-history data. *American Naturalist* 147: 47-64.

Mcmillen, C. & Robinson, J. S. (2005). Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. *Physiological Reviews* 85 (2): 571-633.

McNab, B.N. (1980). Food habits, energetics and the population biology of mammals. American Naturalist 166(1): 106-124.

McNab, B.K. (1983). Ecological and behavioral consequences of adaptation to various food resources. In: Eisenberg J.F., Kleiman, D.G. (eds) Advances in the Study of Mammalian Behavior. Special Publication No. 7. The American Society of Mammalogists, Shippensburg. Pp. 664-697. USA.

McNab, B. K. (1986). The influence of food habits on the energetics of eutherian mammals. *Ecological Monographs* 56 (1): 1-19.

Meany, M. J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience* 24: 1161-1192.

Mennerich, O. (1979). Zeitwende. Durch eine Neue Biologie, Metaphysik und Medizin. Edited for publication by Gerda Torkler. Martin-Verlag/Walter Berger, Buxheim, Deutschland.

Meves, C. (1981). Der Weg zum sinnerfüllten Leben. Verlag Herder, Freiburg im Breisgau, Basel, Wien.

Meves, C. (1984). Wohin gehen wir? Orientierungspunkte. Herderbücherei Band 1149, Herder-Verlag; Freiburg im Breisgau, Basel, Wien.

Mielnik-Sikorska, M., Daca, P., Malyarchuk, B., Derenko, M., Skonieczna, K., Perkova, M., Dobosz, T. & Grzybowski, T. (2013). The history of Slavs inferred from complete mitochondrial genome sequences. *PLoS ONE* 8 (1): e54360.

Miettinen, A., Rotkirch, A., Szalma, I., Donna, A. & Tanturri, M. (2014). Increasing childnessless in Europe: Time trends and country differences. Väestöliitto Working Paper No 5.

Mill, J. & Petronis, A. (2008). Peri- and pre-natal environmental risks for attention-deficit hyperactivity disorder (ADHD): the potential role of epigenetic processes in mediating susceptibility. *Journal of Child Psychology & Psychiatry* 49: 1020-1030.

Miller, L. J., McIntosh, D. N., McGrath, J., Shyu, V., Lampe, M., Taylor, A. K., Tassone, F., Neitzel, K., Stackhouse, T. & Hagerman, R. J. (1999). Electodermal responses to sensory stimuli in individuals with fragile X syndrome. A preliminary report. *American Journal of Medical Genetics* 83: 268-279.

Miller, G. E., Chen, E., Fok, A. K., Walker, H., Lim, A., Nicholls, E. F., Cole, S. & Kobor M. S. (2009). Low early-life social class leaves a biological residue manifested by decrease glucocorticoid and increased proinflammatory signaling. *Proceedings of the National Academy of Sciences of the United States of America* 106 (34): 14716-14721.

Milton, K. (1999). A hypothesis to explain the role of meat-eating in human evolution. *Evolutionary Anthropology* 8: 11-21.

Milton, K. (2000). Hunter-gatherer diets - a different perspective. *American Journal of Clinical Nutrition* 71: 665-667.

Mirescu, C., Peters, J. D., & Gould, E. (2004). Early life experience alters of adult neurogenesis to stress. *Nature Neuroscience*, 7 (8): 841-846.

Mizushima, N., Levine, B., Cuervo, A. M. & Klionsky, D. J. (2008). Autophagy fights disease through cellular self-digestion. *Nature* 451 (7182): 1069-1075.

Mizushima, N. & Komatsu, M. (2011). Autophagy: Renovation of cells and tissues. *Cell* 147: 728-741.

Moatt, J. P., Nakagawa, S., Lagisz, M. & Walling, C. A. (2016). The effect of dietary restriction on reproduction: a meta-analytical perspective. *BMC Evolutionary Biology* 16: 199.

Molet, J., Heins, K., Zhuo, X., Mei, Y.T., Regev, L., Baram, T. Z. & Stern, H. (2016). Fragmentation and high entropy of neonatal experience predict adolescent emotional outcome. *Translational Psychiatry* 6 (e702): 1-7.

Montesanto, A., Passarino, G., Senatore, A., Carotenuto, L. & De Benedictis, G. (2008). Spatial analysis and surname analysis: complementary tools for shedding light on human longevity patterns. *Annals of Human Genetics* 72: 253-260.

Montesanto, A., Dato, S., Belizzi, D., Rose, G. & Passarino, G. (2012). Epidemiological, genetic and epigenetic aspects of the research on healthy ageing and longevity. *Immunity and Ageing* 9: 6.

Morselli, E., Maiuri, M. C., Markaki, M., Megalou, E., Pasparaki, A., Palikaras, K., Criollo, A., et al. (2010). Caloric restriction and resveratrol promote longevity through the Sirtuin-1-dependent induction of autophagy. *Cell Death and Disease* 1, e10; doi: 10.1038/cddis.2009.8

Moskowitz, R. W. (2000). Role of collagen hydrolysate in bone and joint disease. *Seminars in Arthritis & Rheumatism* 30: 87-99.

Mousain-Bosc, M., Roche, M., D., Rapin, J. & Bali, J. (2004). Magnesium VitB6 intake reduces central nervous system hyperexcitability in children. *Journal of the American College of Nutrition* 23 (5): 545S-548S.

Mousain-Bosc, M., Roche, M., Polge, A., Pradal-Prat, D., Rapin, J. & Bali, J. (2006a). Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. I. Attention deficit hyperactivity disorders. *Magnesium Research* 19 (1): 46-52.

Mousain-Bosc, M., Roche, M., Polge, A., Pradal-Prat, D., Rapin, J. & Bali, J. (2006b). Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. II. Pervasive developmental disorder-autism. *Magnesium Research* 19 (1): 53-62.

Mousain-Bosc, M., Siatka, C. & Bali, J. (2011). Magnesium, hyperactivity and autism in children. In: Vink, R. & Nechifor, M. (eds) Magnesium in the Central Nervous System. University of Adelaide Press, Adelaide, Australia. Chapter 21: 283-302.

Mueller, U. (2001). Is there a stabilizing selection around average fertility in modern human populations? *Population and Development Review* 27 (3): 469-498.

Müller, H-G., Chiou, J-M. Carey, J. R. & Wang, J-L. (2002). Fertility and life span: Late children enhance female longevity. *Journal of Gerontology* 57 (5): B202-B206.

Mullington, J. M., Simpson, N. S., Meier-Ewert, H. K. & Haack, M. (2010). Sleep loss and inflammation. *Best Practice Research in Clinical Endocrinology and Metabolism* 24 (5): 775-784.

Myres, N. M., Rootsi, S., Lin, A. A., Järve, M., King, R. J., Kutuev, I., Cabrera, M., et al., (2011). A major Y-chromosome haplogroup R1b Holocene era founder effect in Central and Western Europe. *European Journal of Human Genetics* 19: 95-101.

Myrskylä, M., Kohler, H-P. & Billari, F. C. (2011). High development and fertility: Fertility at older reproductive ages and gender equality explain the positive link. Population Studies Center, University of Pennsylvania. *PSC Working Paper Series* 30.

Myrskylä, M., Goldstein, J. R. & Cheng, Y. A. (2013). New cohort fertility forecasts for the developed world: rises, falls, and reversals. *Population and Development Review* 39 (1): 31-56.

Nakagawa, S., Lagisz, M., Hector, K. L. & Spencer, H. G. (2012). Comparative and meta-analytic insights into life extension via dietary restriction. *Aging Cell* 11: 401-409.

Nasri, H. (2016). Uric acid as an index of chronic diseases or as an index of antioxidant? A mini-review to the recent trends. *Journal of Renal Endocrinology* 2016; e04: 1-4.

Navarro, E., Funtikova, A. N., Fíto, M. & Schröder, H. (2016). Prenatal nutrition and the risk of adult obesity: Long-term effects of nutrition on epigenetic

mechanisms regulating Gene expression. *Journal of Nutritional Biochemistry* 39: 1-14.

Nemeroff, C. B. (2003). The role of GABA in the pathophysiology and treatment of anxiety disorders. *Psychopharmacology Bulletin* 37 (4): 133-146.

Nemeroff, C. B. (2004). Early-life adversity, CRF dysregulation, and vulnerability to mood and anxiety disorders. *Psychopharmacology Bulletin* 38 (1): 14-20.

Nepomnaschy, P. A., Welch, K. B., McConnell, D. S., Low, B. S., Strassmann, B. I. & England, B. G. (2006). Cortisol levels and very early pregnancy loss in humans. *Proceedings of the National Academy of Sciences of the United States of America* 103 (10): 3938-3942.

Nes, R. B. & Røysamb, E. (2015). The heritability of subjective well-being: review and meta-analysis. Chapter 5. In *Genetics of Psychological Well-Being: The Role of Heritability and Genetics in Positive Psychology*. M. Pluess (ed). Pp 75-96. Oxford University Press, Oxford. United Kingdom.

Nesse, R. M. (2011). Ten questions for evolutionary studies of disease vulnerability. *Evolutionary Applications* 4: 264-277.

Nettle, D. (2010). Dying young and living fast: variation in life history across English neighbourhoods. *Behavioral Ecology* 21: 387-395.

Neumann, W. L., Coss, E., Rugge, M. & Genta, R. M. (2013). Autoimmune atrophic gastritis – pathogenesis, pathology and management. *Nature Reviews. Gastroenterology & Hepatology* 10: 529-541.

Newson, L. (2009). Cultural versus reproductive success: why does economic development bring new trade-offs? *American Journal of Human Biology* 21: 464-471.

Niederhofer, H. & Pittschieler, K. (2006). A preliminary investigation of ADHD symptoms in persons with celiac disease. *Journal of Attention Disorders* 20 (10): 1-5.

Niemi, A-K., Hervonen, A., Hurme, M., Karhunen, P. J., Jylhä, M. & Majamaa, K. (2003). Mitochondrial DNA polymorphisms associated with longevity in a Finnish population. *Human Genetics* 112: 29-33.

Noakes, T., Creed, S., Proudfoot, J. & Grier, D. (2014). The Real Meal Revolution. Eleventh edition. Quivertree Publications, Cape Town, South Africa.

Nobre, A. C., Rao, H. & Owen, G. N. (2008). L-theanine, a natural constituent of tea, and its effect on mental state. *Asia Pacific Journal of Clinical Nutrition* 17 (S1): 167-168.

Norum, J., Heyd, A. & Svee, T. E. (2014). Most Scandinavians are born during summer time and less Norwegians are born the first quarter of the year: A study comparing Scandinavian birth patterns 2000-2012. *Global Journal of Health Science* 6 (4): 163-168.

Oberlander, T. F., Weinberg, J., Papsdorf, M., Grunau, R., Misri, S., & Devlin, A. M. (2008). Prenatal exposure to maternal depression, neonatal methylation of human glucorticoid receptor gene (*NR3C1*) and infant cortisol stress responses. *Epigenetics* 3 (2): 97-106.

Okin, D. & Medzhitov, R. (2012). Evolution of inflammatory diseases. *Current Biology* 22: R733-R740.

Olsen, A., Egeberg, R., Halkjær, J., Christensen, J., Overvad, K. & Tjønneland, A. (2011). Healthy aspects of the Nordic diet are related to lower total mortality. *Journal of Nutrition* 141: 639-644.

Omran, A. R. (2005). The epidemiologic transition: A theory of the epidemiology of population change. *The Milbank Quarterly* 83 (4): 731-757.

Pacher, P., Beckman, J.S. & Liaudet, L. (2007). Nitric oxide and peroxynitrite in health and disease. *Physiology Reviews* 87: 315-424.

Pál, C. (1998). Plasticity, memory and the adaptive landscape of the genotype. *Proceedings of the Royal Society of London B*, 265: 1319-1323.

Pala, M., Olivieri, A., Achilli, A., Accetturo, M., Metspalu, E., Reidla, M., Tamm, E., et al. (2012). Mitochondrial DNA signals of Late Glacial recolonization of Europe from Near Eastern refugia. *American Journal of Human Genetics* 90: 915-924.

Palacios, J. A., Herranz, D., De Bonis, M. L., Velasco, S., Serrano, M. & Blasco, M. A. (2010). SIRT1contributes to telomere maintenance and augments global homologous recombination. *Journal of Cell Biology* 191 (7): 1299-1313.

Pallauf, K. & Rimbach, G. (2013). Autophagy, polyphenols and healthy ageing. *Ageing Research Reviews* 12: 237-252.

Pallauf, K., Giller, K., Huebbe, P. & Rimbach, G. (2013). Nutrition and healthy ageing: Calorie restriction or polyphenol-rich "MediterrAsian" diet? *Oxidative Medicine and Cellular Longevity* 2013, Article ID 707421, 14 pages.

Palma-Gudiel, H., Córdova-Palomera, A., Eixarch, E., Deuschle, M. & Fañanás, L. (2015). Maternal psychosocial stress during pregnancy alters the epigenetic signature of the glucocorticoid receptor gene promotor in their offspring: a meta-analysis. *Epigenetics* 10 (10): 893-902.

Panagiotakos, D.B., Chrisohoou, C., Siasos, G., Zisimos, K., Skoumas, J., Pitsavos, C. & Stefanidis, C. (2011). Sociodemographic and life-style statistics of old people (> 80 years) living in Ikaria Island: The Ikaria Study. *Cardiology Research and Practice*, Volume 2011, Article ID 679187, 7 pages.

Paoli, A., Rubini, A., Volek, J. S. & Grimaldi, K. A. (2013a). Beyond weight loss: a review of of the therapeutic uses of very-low-carbohydrate (ketogenic) diets. *European Journal of Clinical Nutrition* 67: 789-796.

Paoli, A., Bianco, A., Grimaldi, K. A., Lodi, A. & Bosco, G. (2013b). Long term successful weight loss with a combination of biphasic ketogenic Mediterranian diet and Mediterranian maintenance protocol. *Nutrients* 5 (12): 5205-5217.

Paolisso, G. & Barbagallo, M. (1997). Hypertension, diabetes mellitus, and insulin resistance: the role of intracellular magnesium. *American Journal of Hypertension* 10: 346-355.

Parsons, T. J., Power, C. & Manor, O. (2001). Fetal and early life growth and body mass index from birth to early adulthood in 1950 British cohort: longitudinal study. *British Medical Journal* 323: 1331- 1335.

Patel, S. A., Velingkaar, N., Makwana, K., Chaudhari, A. & Kondratov. R. (2016). Caloric restriction regulates circadian clock gene expression through BMAL1 dependent and independent mechanisms. *Scientific Reports* 6:25970, DOI: 10.1038/srep25970.

Patterson, E., Vall, R., Fitzgerald, G. F., Ross, R. P. & Stanton, C. (2012). Health implications of high dietary omega-6 polyunsaturated fatty acids. *Journal of Nutrition and Metabolism* 2012, Article ID 539426, 16 pages.

Pendell, E. (1977). Why Civilizations Self-Destruct. Elmer Pendell, Tuscaloosa, USA.

Pe-Piper, G. & Photiades, A. (2006). Geochemical characteristics of the Cretaceous ophiolitic rocks of Ikara island, Greece. *Geological Magazine*, 143 (4): 417-429.

Pérez-Guisado, J. & Muñoz-Serrano, A. (2011). A pilot study of the Spanish Ketonic Mediterranian Diet: an effective therapy for the metabolic syndrome. *Journal of Medicinal Food* 14 (7/8): 681-687.

Perls, T. T., Alpert, L. & Fretts, R. C. (1997). Middle-aged mothers live longer. *Nature* 389: 133.

Perls, T. T., Kunkel, L. M. & Puca, A. A. (2002). The genetics of exceptional human longevity. *Journal of the American Geriatric Society* 50: 359-368.

Pesaud, C., McDermott, J., De Benoist, B. & Jackson, A. A. (1989). The excretion of 5-oxoproline in urine, as an index of glycine status, during normal pregnancy. *British Journal of Obstetrics & Gynaecology* 96 (4): 440-444.

Petterson, M. G. (2010). A review of the geology and tectonics of the Kohistan island arc, northern Pakistan. In: The Evolving Continents: Understanding Processes of Continental Growth. T. M. Kusky, M. Zhai & W. Xiao (eds.). Geological Society, London. Special Publications, 338: 287-327. United Kingdom.

Philipov, D. (2003). Possible explanations of demographic changes in central and eastern Europe. Chapter 3. In Philipov, D. & Dorbritz, J. (eds). Demographic consequences of economic transition in countries of central and eastern Europe. Population Studies No. 39; Council of Europe Publishing, Strasbourg, Cedex.

Philipov, D. & Dorbritz, J. (2003). Demographic consequences of economic transition in countries of central and eastern Europe. Population Studies No. 39: 151-164; Council of Europe Publishing, Strasbourg, Cedex.

Philipov, D., Spéder, Z. & Billari, F.C. (2006). Soon, later, or ever? The impact of anomie and social capital on fertility intentions in Bulgaria (2002) and Hungary (2001). *Population Studies* 60 (3): 289-308.

Phillipson, C. (1997). Paleonutrition and modern nutrition. *World Review of Nutrition and Dietetics* 81: 38-48.

Phillips, D. I. W., Walker, B. R., Reynolds, R. M., Flanagan, D. E. H., Wood, P. J., Osmond, C., Barker, D. J. P. & Whorwood, C. B. (2000). Low birth weight predicts elevated plasma cortisol concentrations in adults from 3 populations. *Hypertension* 35: 1301-1306.

Phillips, S. M., Chevalier, S. & Leidy, H. J. (2016). Protein "requirements" beyond the RDA: implications for optimizing health. *Applied Physiology, Nutrition and Metabolism* 41: 565-572.

Piatti, P. M., Monti, L. D., Magni, F., Fermo, I., Baruffaldi, L., Nasser, R., Santambrogio, G., Librenti, M. C., Galli-Kienle, M., Pontiroli, A. E. & Pozza, G. (1994). Hypocaloric high-protein diet improves glucose oxidation and spares lean body mass: comparison to hypocaloric high carbohydrate diet. *Metabolism* 43 (12): 1481-1487.

Pigliucci, M. (2007). Do we need an extended evolutionary synthesis? *Evolution: International Journal of Organic Evolution* 61: 2743-2749.

Pischinger, A. (1989). Das System der Grundregulation: Grundlagen für eine ganzheitsbiologische Theorie der Medizin. 7. Auflage. Neubearbeitet von H. Heine unter Mitarbeit von O. Bergsmann und F. Perger. Karl F. Haug Verlag, Heidelberg, Deutschland.

Pitskhelauri, G. Z. (1982). The Longliving of Soviet Georgia. Human Sciences Press Inc., New York. USA.

Plaskett, L. G. (2003). On the essentiality of dietary carbohydrate. *Journal of Nutritional and Environmental Medicine* 13 (3): 161-168.

Pluess, M. & Belsky, J. (2009). Differential susceptibility to rearing experience: The case of childcare. *Journal of Child Psychology and Psychiatry and Allied Disciplines* 50: 396-404.

Pluess, M. & Belsky, J. (2011). Prenatal programming of postnatal plasticity? *Development and Psychopathology* 23: 29-38.

Pluess, M. & Belsky, J. (2013). Vantage sensitivity: Individual differences in response to positive experiences. *Psychological Bulletin* 139 (4): 901-916.

Popp, F. (1987). Neue Horizonte in der Medizin. Zweite, erweiterte Auflage. Karl F. Haug Verlag, Heidelberg. Deutschland.

Poulain, M., Pes, G. & Salaris, L. (2011). A population where men live as long as women: Villagrande Strisaili, Sardinia. *Journal of Aging Research*, Volume 2011, Article ID 153756, 10 pages.

Poulain, M., Herm, A. & Pes, G. (2013). The Blue Zones: areas of exceptional longevity around the world. *Vienna Yearbook of Population Research*, 11: 87-108.

Preusser, W. (1987). Regulationstherapie über palpable Kolloidveränderungen im Bindegewebe (Gelosenbehandlung). Karl F. Haug Verlag, Heidelberg. Deutschland.

Price, W. A. (1939). Nutrition and Physical Degeneration. A Comparison of Primitive and Modern Diets and Their Effects. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, London.

Prins, M. L. (2008). Cerebral metabolic adaptation and ketone metabolism after brain injury. *Journal of Cerebral Blood Flow Metabolism*, 28 (1): 1-16.

Pritchett, L. & Viarengo, M. (2012). Why demographic suicide? The puzzles of European fertility. *Population and Development Review* 38 (Supplement): 55-71.

Psaltopoulou, T., Sergentanis, T. N., Panagiotakos, D. B., Sergentanis, I. N., Kosti, R. & Scarmeas, N. (2013). Mediterranean diet, stroke, cognitive impairment, and depression: a meta-analysis. *Annals of Neurology* 74: 580-591.

Quinlan, R. J. (2003). Father absence, parental care, and female reproductive development. *Evolution and Human Behavior* 24: 376-390.

Rabinovitz, H, R., Boaz, M., Ganz, T., Jakubowicz, D., Matas, Z., Madar, Z. & Wainstein, J. (2014). Big breakfast rich in protein and fat improves glycemic control in type 2 diabetics. *Obesity* 22 (5): E46-E54.

Raphael, K. L. (2016). Apptoach to the treatment of chronic metabolic acidosis in CKD. *American Journal of Kidney Diseases* 67 (4): 696-702.

Ratjen, I., Schafmayer, C., Di Giuseppe, R., Waniek, S., Plachta-Danielzik, S., Koch, M., et al. (2017). Postdiagnostic Mediterraneanand health Nordic dietary patterns are inversely associated with all-cause mortality in log-term colorectal cancer survivors. *Journal of Nutrition* 147: 636-644.

Rauch, E. (1967). Heilung der Erkältungs- und Infektionskrankheiten durch natürliche Behandlung. Karl F. Haug Verlag, Heidelberg. Deutschland.

Rauch, E. (1986). Die Darmreinigung. 36. Ausgabe. Karl F. Haug Verlag, Heidelberg. Deutschland.

Ravikumar, B., Sarkar, S., Davis, J. E., Futter, M., Garcia-Arencibia, M., Green-Thomson, Z. W. et al. (2010). Regulation of mammalian autophagy in physiology and pathophysiology. *Physiological Review* 90: 1383- 1435.

Reaven, G. M. (1995). Pathophysiology of insulin resistance in human disease. *Physiological Reviews* 75 (3): 473-486.

Reaven, G. M. (2005). The insulin resistance syndrome: definition and dietary approaches to treatment. *Annual Review of Nutrition* 25: 391-406.

Reckeweg, H-H. (1986). Homotoxikologie – Ganzheitsschau einer Synthese der Medizin. Aurelia Verlag, Baden-Baden, Deutschland.

Redfern, G. (2009). Ancient Wisdoms: Exploring the Mysteries and Connections. Authors House, Bloomington, Indiana, USA.

Reher, D. S. (1998). Family ties in Western Europe: persistent contrasts. *Population and Development Review* 24 (2): 203-234.

Reich, P. B & Oleksyn, J. (2004). Global patterns of plant leaf N and P in relation to temperature and latitude. *Proceedings of the National Academy of Sciences of the United States of America* 101 (30): 11001-11006.

Remy, W., Hammerschmid, K., Zänker, K.S., Ulm, K., Theisinger, W., Lange. J., Trappe, A., Maubach, P.A. & Rastetter, J (1983). Tumorträger haben selten Infekte in der Vorgeschichte. Medizinische Klinik 78: 95-98.

Rhode, J. (2012). Johann Schroth (1798-1856) – Gründer der Schroth-Kur. *Schweizerische Zeitschrift für Ganzheitsmedizin* 24: 109-116.

Richards, C. L., Bossdorf, O. & Pigliucci, M. (2010). What role does heritable epigenetic variation play in phenotypic evolution. *BioScience*, 60 (3): 232-237.

Richardson, C. T., Walsh, J. H., Hicks, M. I. & Fordtran, J. S. (1976). Studies on the mechanisms of food-stimulated gastric acid secretion in normal human subjects. *The Jounal of Clinical Investigation* 58: 623-631.

Rickard, I. J., Holopainen, J., Helama, S., Helle, S., Russel, A. F. & Lummaa, V. (2010). Food availability at birth limited reproductive success in historical humans. *Ecology* 91 (12): 3515-3525.

Riggs, A.D. & Xiong, Z. (2004). Methylation and epigenetic fidelity. *Proceedings of the National Academy of Sciences*, 101 (1): 4-5.

Riley, J. C. (2005). Estimates of regional and global life expectancy, 1800-2001. *Population Development Review* 31 (3): 537-543.

Rimm, E. B. (2002). Fruit and vegetables – building a solid foundation. *American Journal of Clinical Nutrition* 76: 1-2.

Rindfuss, R. R., Bumpass, L. & St. John, C. (1980). Education and fertility: Implications for the roles women occupy. *American Sociological Review* 1980: 431-447.

Rizza, W., Veronese, N. & Fontana, L. (2014). What are the roles of calorie restriction and diet quality in promoting healthy longevity? *Ageing Research Reviews* 13: 38-45.

Robinson, D., Handley, L. L., Scrimgeour, C. M., Gordon, D. C., Forster, B. P. & Ellis, R.P. (2000). Using stable natural abundances ($\delta^{15}N$ and $\delta^{13}C$) to integrate the sress responses of wild barley (*Hordeum spontaneum* C. Koch) genotypes. Jornal of Experimental Botany 51 (342): 41-50.

Robinson, P.P. (2012). An Operations Manual for Humankind. The Complete Compendium of Natural Health. Third Edition. ISBN-978-0-615-46747-4.

Rochlitz, S. (1989). Die fehlende Dimension: Energiebalance. (Aus dem Englischen übersetzt). Droemersche Verlagsanstalt Th Knaur Nachf., München, Germany.

Rodale, J.I. (1949). The Healthy Hunza. Rodale Press, Emmaus, PA, United States of America.

Rogovin, K. A., Bushuev, A. V., Khruscheva, A. M. & Vasilieva, N. Y. (2014). Resting metabolic rate, stress, testosterone, and induced immune response in spring- and fall-born males of Campbell's dwarf hamster: maintenance in long-day conditions. *Biological Bulletin Reviews* 4 (3): 181-191.

Rook, G. A. W. & Brunet, L. R. (2005). Microbes, immunoregulation, and the gut. *Gut* 54 (3): 317-320.

Rootsi, S., Magri, C., Kivisild, T., Benuzzi, G., et al., (2004). Phylogeography of Y-chromosome haplogroup I reveals distinct domains of prehistoric gene flow in Europe. *American Journal of Human Genetics* 75: 128-137.

Rose, G., Passarino, G., Carrieri, G., Altomare, K., Greco, V., Bertolini, S., Bonafé, M., Franceschi, C. & De Benedictis, B. (2001). *European Journal of Human Genetics* 9: 701-707.

Rosenberg, N. A., Pritchard, J. K., Weber, J. L., Cann, H. M., Kidd, K. K., Zhivotovsky, L. A. & Feldman, M.W. (2002). Genetic structure of human populations. *Science* 298: 2381-2385.

Rosero-Bixby, L., Dow, W. H. & Rehkopf, D.H. (2013). The Nicoya region of Costa Rica: a high longevity island for elderly males. *Vienna Yearbook of Population Research* 11: 109-136.

Rotariu, T. (2006). Romania and the second demographic transition: the traditional value system and low fertility rates. *International Journal of Sociology* 36 (1): 10-27.

Rubinsztein, D. C., Mariño, G. & Kroemer, G. (2011). Autophagy and aging. *Cell* 146: 682-695.

Ruiz-Núñez, B., Pruimboom, L., Dijk-Brouwer, D. A. J. & Muskiet, F. A. J. (2013). Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context. *Journal of Nutritional Biochemistry* 24: 1183-1201.

Rusch, H. P. (1979). Es geht um die Substanz des Menschen! *Mikroökologie und Therapie* 9: 33-37. Institut für Mikroökologie, Herborn-Dill, Deutschland.

(Rusch, H. P. (1979). About the essence of Man. *Microecology and Therapy* 9: 33-37. Institut für Mikroökologie, Herborn-Dill, Germany).

Rusch, H. P. (1985). Bodenfruchtbarkeit. Eine Studie biologischen Denkens. 5. Auflage. Karl F. Haug Verlag, Heidelberg. Deutschland.

Rusch, V., Rusch, H. P., Fischer, A., Hantel, F-H., Kolb, H., Maass, C., Männle, T., Mommsen, H. & Zimmermann, K. (1985). Empfehlungen zur Mikrobiologischen Therapie und Ernährungstherapie für Jung und Alt. 3. Überarbeitete Auflage. Verlag: Institut für Mikroökologie, D 6348, Herborn-Dill, Deutschland.

Russell, W. R., Gratz, S. W., Duncan, S. H., Holtrop, G., Ince, J., Scobbie, L., Duncan, G., Johnstone, A. M., Lobley, G. E., Wallace, R. J., Duthie, G. G. & Flint, H.J. (2011). High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health. *American Journal of Clinical Nutrition* 93 (5): 1062-1072.

Ryff, C. D. & Singer, B. (1998). The contours of positive human health. *Psychological Inquiry* 9 (1): 1-28.

Saczuk, K. (2003). A development and critique of the concept of replacement migration. Central European Forum for Migration Research (CEFMR) Working Paper 4/2003, Warsaw, Poland.

Salaris, L., Poulain, M. & Samaras, T. T. (2012). Height and survival at older ages among men born in an inland village in Sardinia (Italy), 1866-2006. *Biodemography and Social Biology* 58: 1-13.

Samaras, T.T. & Elrick, H. (1999). Height, body size and longevity. *Acta Medicae Okayama* 53 (4): 149-169.

Samaras, T. T., Storms, L. H. & Elrick, H. (2002). Longevity, mortality and body weight. *Ageing Research Reviews* 1: 673-691.

Samaras, T. T., Elrick, H. & Storms, L. H. (2003). Is height related to longevity? *Life Sciences* 72 (16): 1781-1802.

Sanden, H. L. (1971). Was muss geschehen? Weisse Welt am Wendepunkt. Druffel-Verlag, Leoni am Starnberger See, Deutschland.

Sanfilippo, D. (2012). Practical Paleo: A customized approach to health and a whole foods lifestyle. Victory Belt Publishing Incorporation, Las Vegas, USA.

Sanz, A., Caro, P. & Barja, G. (2004). Protein restriction without strong caloric restriction decreases mitochondrial oxygen radical production and oxidative DNA damage in rat liver. *Journal of Bioenergetics and Biomembranes* 36 (6): 545-552.

Sapolsky, R. M. (2004). Mothering style and methylation. Nature Neuroscience, 7 (8): 791-792.

Sarris, J., Murphy, J., Mischoulon, D., Papakostas, G. I., Fava, M., Berk, M. & Ng, C. H. (2016). Adjunctive nutraceuticals for depression: a systematic review and meta-analyses. *American Journal of Psychiatry* 173 (6): 575-587.

Sautin, Y. Y. & Johnson, R. J. (2008). Uric acid: the oxidant-antioxidant paradox. *Nucleosides Nucleotides Nucleic Acids* 27 (6): 608-619.

Savini, I., Catani, M. V., Evangelista, D., Gasperi, V. & Avigliano, L. (2013). Obesity-associated oxidative stress: Strategies finalized to improve redox state. *International Journal of Molecular Sciences* 14: 10497-10538.

Schade, H. (1974). Völkerflut und Völkerschwund. Kurt Vowinckel Verlag, Neckargemünd, Deutschland.

Schaefer, H. (1979). Hunza. Ein Volk ohne Krankheit. Eugen Diederichs Verlag, Düsseldorf, Köln, Deutschland.

Scheer, F. A. J. L., Morris, C. J. & Shea, S. A. (2013). The internal circadian clock increases hunger and appetite in the evening independent of food intake and other behaviors. *Obesity* 21 (3): 421-423.

Scheuerlen, P.G. (1959). Beitrag zur Therapie des Nephrotischen Syndroms mit künstlichen Entzündungen. *Verh. Dtsch. Ges. Inn. Med*. 65: 671-675.

Schleicher, P. (1991). Krankheiten verhindern. Stärken Sie die Abwehrkräfte Ihres Körpers. 2. Auflage, ECON Taschenbuch Verlag, Düsseldorf.

Schmidt, K. L. (1987). Hyperthermie und Fieber. Wirkungen bei Mensch und Tier. 2., überarbeitete Auflage, Hippokrates Verlag Stuttgart, Deutschland.

Schmidt, A. & Thews, G. (1989). Autonomic nervous system. In: Janig, W. Human Physiology (Second edition). Springer Verlag, New York. Pp. 333-370.

Scott, G. S. & Hooper, D. C. (2001). The role of uric acid in protection against peroxynitrite-mediated pathology. *Medical Hypotheses* 56 (1): 95-100.

Scott, T. (2011). The Anti-Anxiety Food Solution. How the Foods You Eat Can Help You Calm Your Anxious Mind, Improve Your Mood & End Cravings. New Harbinger Publications, Inc., Oakland, California, USA.

Sebastian, A., Harris, S. T., Ottaway, J. H., Todd, K. M., Morris, R. C. (1994). Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *New England Journal of Medicine* 330: 1776-1781.

Sebastian, A., Frassetto, L. A., Sellmeyer, D. E., Merriam, R. L. & Morris Jr, R. E. (2002). Estimation of the net acid load of the diet of ancestral preagricultural

Homo sapiens and their hominid ancestors. *American Journal of Clinical Nutrition* 76: 1308-1316.

Seccombe, W. (1992). A Millenium of Family Change: Feudalism to Capitalism in Northwestern Europe. Verso, London.

Seckl, J. R. (2004). Prenatal glucocorticoids and long-term programming. *European Journal of Endocrinology* 151: U49-U62.

Seelig, M. S., Berger, A. R. & Spielholz, N. (1975). Latent tetany and anxiety, marginal magnesium deficit, and normocalcemia. *Diseases of the Nervous System* 36 (8): 461-465.

Seelig, M. S. (1980). Magnesium Deficiency in the Pathogenesis of Disease. Early Roots of Cardiovascular, Skeletal, and Renal Abnormalities. Plenum Medical Book Company, New York, London.

Seeman, T. E., Singer, B. H., Rowe, J. W., Horwitz, R. I. & Mc Ewen , B. S. (1997). Price of adaptation – allostatic load and its health consequences. *Archives of Internal Medicine* 157: 2259-2268.

Seldin, M. F., Shigeta, R., Villoslada, P., Selmi, C., Tuomilehto, J., Silva, G., Belmont, J. W., Klareskog, L. & Gregersen, P.K. (2006). European population substructure: Clustering of Northern and Southern populations. *PLoS Genetics* 2 (9): e143.

Sellen, D. W. (2007). Evolution of infant and young child feeding: implications for contempory public health. *Annual Review of Nutrition* 27: 123-148.

Selye, H. (1953). Einführung in die Lehre vom Adaptionssyndrom. Thieme, Stuttgart, Deutschland.

Selye, H. (1978). The Stress of Life. Revised edition. McGraw-Hill Co., New York, USA.

Shah, S. H. A. (1984). The ophiolite belts and suture traces in Pakistan. Geological Bulletin of the University of Peshawar 17: 113-117.

Shanley, D. P. & Kirkwood, T. B. L. (2000). Calorie restriction and aging: a life-history analysis. *Evolution* 54 (3): 740-750.

Sheldrake, R. (2009). Morphic Resonance. The Nature of Formative Causation. Vermont. USA. Park Street Press, Rochester, Toronto, Canada.

Sho, H. (2001). History and characteristics of Okinawan longevity food. *Asia Pacific Journal of Clinical Nutrition* 10 (2): 159-164.

Sichelschmidt, G. (1973). Wie im alten Rom. Dekadenzerscheinungen damals und heute. Blick und Bild Verlag für politische Bildung, S. Kappe KG Velbert, Germany.

Silber, & Schmitt, (2010). Effects of tryptophan loading on human cognition, mood, and sleep. *Neuroscience and Biobehavioral Review*s 34: 387-407.

Sinding, S. W. (2009). Population, poverty and economic development. *Philosophical Transactions of the Royal Society B* 364: 3023-3030.

Simmons, R. A. (2009). Developmental origins of adult disease. Pediatric *Clinics of North America* 56: 449-466.

Simopoulos, A.P. (2006). Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases. *Biomedicine and Pharmacotherapy*, 60: 502-507.

Simpson, N. & Dinges, D. F. (2007). Sleep and inflammation. *Nutrition Reviews* 65 (12): S244-252.

Simpson, S. J. & Raubenheimer, D. (2009). Macronutrient balance and lifespan. *Aging* 1 (10): 875-880.

Sinclair, D. A. (2005). Toward a unified theory of caloric restriction and longevity regulation. *Mechanisms of Ageing and Development* 126: 987-1002.

Sircus, M. (2014a). Treatment Essentials. Practising Natural Allopathic Medicine. International Medical Veritas Association. eBook.

Sircus, M. (2014b). Sodium Bicarbonate. Rich Man's Poor Man's Cancer Treatment. Second edition. Full Medical Review. International Medical Veritas Association. eBook.

Sircus, M. (2015). Anti-Inflammatory Oxygen Therapy. Your Complete Guide to Understanding and Using Natural Oxygen Therapy. Square One Publishers, New York. USA.

Skilton, M. R., Ayer, J. G., Harmer, J. A., Webb, K., Leeder, S. R., Marks, G. B. & Celermajer, D. S. (2012). Impaired fetal growth and arterial wall thickening: a randomized trial of omega-3 supplementation. *Pediatrics* 129 (3): e698-e703.

Skinner, M. K. (2008). What is an epigenetic transgenerational phenotype? F3 or F2. *Reproductive Toxicology* 25 (1): 2-6.

Skinner, M. K., Manikkam, M. & Guerrero-Bosagna, C. (2010). Epigenetic transgenerational actions of environmental factors in disease etiology. *Trends in Endocrinology and Metabolism* 21 (4): 214-222.

Skakkebæk, N. E., Rajpert-De Meyts, E. & Main, K. M., (2001). Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. *Human Reproduction* 16 (5): 972-978.

Skakkebæk, N. E., Jørgensen, N., Main, K. M., Rajpert-De Meyts, E., Leffers, H., Andersson, A-M., Juul, A., Carlsen, E., Mortensen, G. K., Jensen, T. K. & Toppari, J. (2006). Is human fecundity declining? *International Journal of Andrology* 29: 2-11.

Skirbekk, V. (2008). Fertility trends by social status. *Demographic Research* 18: 145-180.

Slutsky, I., Abumaria, N., Wu, L-J., Huang, C., Zhang, L., Li, B., Zhao, X., Govindarajan, A., Zhao, M-G., Zhuo, M., Tonegawa, S. & Liu, G. (2010). Enhancement of learning and memory by elevating brain magnesium. *Neuron* 65: 165-177.

Smits, L., Zielhuis, G., Jongbloet, P. & Bouchard, G. (1999). The association of birth interval, maternal age and season of birth with the fertility of daughters: a retrospective cohort study based on family reconstitutions from nineteenth and early twentieth century Quebec. *Paediatric and Perinatal Epidemiology* 13: 408-420.

Smits, L., Zielhuis, G., Jongbloet, P. & Van Poppel, F. W. A. (2002). Mother's age and daughter's fecundity. An epidemiological analysis of late 19th to early 20th century family reconstitutions. *International Journal of Epidemiology* 31 (2): 349-358.

Smuts, B. (1995). The evolutionary origins of patriarchy. *Human Nature* 6 (1): 1-32.

So, A. & Thorens, B. (2010). Uric acid transport and disease. *Journal of Clinical Investigation* 120 (6): 1791-1799.

Sobotka, T. (2008). Overview Chapter 6: The diverse faces of the second demographic transition in Europe. *Demographic Research* 19: 171-224.

Sobotka, T. (2009). Migration continent Europe. *Vienna Yearbook of Population Research* 7: 217-233.

Sofaer J. A. & Emery, A. E. (1981). Genes for super-intelligence? *Journal of Medical Genetics* 18: 410-413.

Sofi, F., Abbate, R., Gensini, G. F. & Casini, A. (2010). Accruing benefits on adherence of the Mediterranean diet on health: an updated systematic review and meta-analysis. *American Journal of Clinical Nutrition* 92 (5): 1189-1196.

Sohal, R. S. & Forster, M. J. (2014). Caloric restriction and the aging process: a critique. *Free Radical Biology and Medicine* 73: 366-382.

Solon-Biet, S. M., Mitchell, S. J., De Cabo, R., Raubenheimer, D., Le Couteur, D. G. & Simpson, S. J. (2015). Macronutrients and caloric intake in health and lomgevity. *Journal of Endocrinology* 226 (1): R17-R28.

Song, Y., Li, T. Y., Van Dam, R. M., Manson, J. E. & Hu, F. B. (2007). Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. *American Journal of Clinical Nutrition* 85: 1068-1074.

Speakman, J. R., Talbot, D. A., Selman, C., Snart, S., McLaren, J. S., Redman, P., Krol, E., Jackson, D. M., Johnson, M. S. & Brand, M. D. (2004). Uncoupled and surviving: individual mice with high metabolism have greater mitochondrial uncoupling and live longer. *Aging Cell* 3: 87-95.

Speakman, J. R. & Mitchell, S. E. (2011). Caloric restriction. *Molecular Aspects of Medicine* 32: 159-221.

Spengler, O. (1923). Der Untergang des Abendlandes. Umrisse einer Morphologie der Weltgeschichte. Nachdruck 1969, Verlag C. H. Beck, München. Deutschland.

Speth, J. D. & Spielmann, K. A. (1983). Energy source, protein metabolism, and hunter-gatherer subsistence strategies. *Journal of Anthropological Archaeology* 2: 1-31.

Squadrito, G. L., Cueto, R., Splenser, A. E., Valavanidis, A., Zhang, H., Uppu, R. M. & Pryor, W. A. (2000). Reaction of uric acid with peroxinitrite and implications for the mechanism of neuroprotection by uric acid. *Archives of Biochemistry & Biophysics* 376 (2): 333-337.

Sroufe, A. L. (2005). Attachment and development: a prospective, longitudinal study from birth to adulthood. *Attachment & Human Development* 7 (4): 349-367.

Steiniger, J., Schneider, A. & Rhode, J. (2003). Die Vitalität adipöser Patienten nach einer Gewichtsreduktion durch Fasten. *Forschende Komplementärmedizin und Klassische Naturheilkunde* 10 (1): 12-18.

Sun-Edelstein, C & Mauskop, A. (2009). Role of magnesium in the pathogenesis and treatment of migraine. *Expert Review of Neurotherapeutics* 9 (3): 369-379.

Sun Tzu, The Art of War: The Denma Translation (2009). Translation, essays and commentary by the Denma Translation Group. Shambhala Lion Editions.

Surkyn, J. & Lesthaeghe, R. (2004). Value orientations and the second demographic transition (SDT) in Northern, Western and Southern Europe: An update. *Demograhic Research* (Special Collection 3): 45-86.

Staines, A., Bodansky, H. J., McKinney, P. A., Alexander, F. E., McNally, R. J. Q., et al. (1997). Small area variation in the incidence of childhood insulin-dependent diabetes mellitus in Yorkshire, UK: Links with overcrowding and population density. *International Journal of Epidemiology* 26: 1307-1313.

Starobrat-Hermelin, B. & Kozielec, T. (1997). The effects of magnesium physiological supplementation on hyperactivity in children with attention deficit hyperactivity disorder (ADHD). Positive response to magnesium oral loading test. *Magnesium Research* 10 (2): 149-156.

Stearns, S. (1976). Life-History Tactics: A Review of the Ideas. *The Quarterly Review of Biology* 51 (1): 3-47.

Stearns, S. C. (1977). The Evolution of Life History Traits: A Critique of the Theory and a Review of the Data. *Annual Review of Ecology and Systematics* 8: 147-171.

Stefler, D., Pikhart, H., Kubinova, R., Pajak, A., Stepaniak, U., Malyutina, S., Simonova, G., Peasey, A., Marmot, M. G. & Bobak, M. (2016). Fruit and vegetable consumption and mortality in Eastern Europe: longitudinal results from the Health, Alcohol and Psychosocial Factors in Eastern Europe study. *European Journal of Preventive Cardiology* 23 (5): 493-501.

Stöckmann, T. & Tienes, G.A. (1984). Schlafe vor der Mitternacht. Die Naturzeit. 9. Auflage. Hippokrates Verlag GmbH, Stuttgart, Deutschland.

Stover, P. J. (2007). Human nutrition and genetic variation. *Food and Nutrition Bulletin* 28 (1) Supplement: S101-S115.

Strand, R. F. (1973). Notes on the Nūristāni and Dardic languages. *Journal of the American Oriental Society*, 93 (3): 297-305.

Straub, R. H., Cutolo, M., Buttgereit, F. & Pongratz, G. (2010). Energy regulation and neuroendocrine-immune control in chronic inflammatory diseases. *Journal of International Medicine* 267: 543-560.

Ströhle, A., Hahn, A. & Sebastian, A. (2010). Latitude, local ecology, and hunter-gatherer dietary acid load: implications for evolutionary ecology. *American Journal of Clinical Nutrition* 92: 940-945.

Ströhle, A. & Hahn, A. (2011). Diets of modern hunter-gatherers vary substantially in their carbohydrate content depending on ecoenvironments: results from an ethnographic analysis. *Nutrition Research* 31: 429-435.

Takahashi, R. & Goto, S. (2002). Effect of dietary restriction beyond middle age: accumulation of altered proteins and protein degradation. *Microscopy Research and Technique* 59 (4): 278-281.

Takaya, J., Yamato, F. & Kaneko, K. (2006). Possible relationship between low birth weight and magnesium status: from the standpoint of fetal origin hypothesis. *Magnesium Research* 19 (1): 63-69.

Tappy, L. & Le, K. A. (2010). Metabolic effects of fructose and the worldwide increase in obesity. *Physiological Reviews* 19: 23-46.

Tappy, M. D., Lê, K. A., Tran, C. & Paquot, N. (2010). Fructose and metabolic diseases: New findings, new questions. *Nutrition* 26: 1044-1049.

Tarín, J. J., Brines, J. & Cano, A. (1998). Long-term effects of delayed parenthood. *Human Reproduction* 13 (9): 2371-2376.

Taylor, R. (1964). Hunza Health Secrets for Long Life and Happiness. Prentice-Hall, Englewood Cliffs, New Jersey.

Terman, A. (2006). Catabolic insufficiency and aging. *Annals of the New York Academy of Sciences* 1067: 27-36.

Testa, M. R. (2007). Childbearing preferences and family issues in Europe: Evidence from the Eurobarometer 2006 survey. *Vienna Yearbook of Population Research* 2007: 357-379.

Thonon, B. (1983). Tonsillektomie: Kritische Überlegungen und Alternativen. *Mikroökologie und Therapie* 13: 67-73.

Thapar, A., Cooper, M., Eyre, O. & Langley, K. (2013). Practitioner review: what have we learnt about the causes of ADHD? *Journal of Child Psychology and Psychiatry* 54 (1): 3-16.

Torroni, A., Bandelt, H. J., D'Urbano, L., Lahermo, P., Moral, P., Sellitto, D., Rengo, C., Forster, P., Savontaus, M. L., Bonne-Tamir, B. & Scozzari, R. (1998). mtDNA analysis reveals a major late Paleolithic population expansion from southwestern to northeatern Europe. *American Journal of Human Genetics* 62: 1137-1152.

Toynbee, A. J. (1946). A Study of History. Abridgement of Volumes I-VI by D.C. Somervell. Oxford University Press, United Kingdom.

Toynbee, A. J. (1957). A Study of History. Abridgement of Volumes VII-X by D.C. Somervell. Oxford University Press, United Kingdom.

Trudel, E. (1983). Mayr-Kur und Symbioselenkung. (Mayr cure and microbiological therapy). *Mikroökologie und Therapie* 13: 89-94.

Turner, B. L. & Thomson, A. L. (2013). Beyond the Paleolithic prescription: incorporating diversity and flexibility in the study of human diet evolution. *Nutrition Reviews* 71 (8): 501-510.

Ujfalvy, K. E. v. (1884). Aus dem westlichen Himalaja, Erlebnisse und Forschungen. Leipzig, Deutschland.

UN (2000). Replacement Migration: Is it a Solution to Declining and Ageing Populations? Department of Economic and Social Affairs, Population Division, United Nations, Geneva and New York.

Vaiserman, A. M. & Voitenko, V. P. (2003). Early programming of adult longevity: demographic and experimental studies. *Journal of Anti-Aging Medicine* 6 (1): 11-20.

Vaiserman, A. M., Carstensen, B., Voitenko, V. P., Tronco, M. D., Kravchenko, V. I., M. Khalangot, M. D. & Mechova, N. (2007). Seasonality of birth in children and young adults (0-29 years) with type 1 diabetes in Ukraine. *Diabetologia* 50: 32-35.

Vaiserman, A. M., Khalangot, M. D, Carstensen, B., Tronco, M. D., Kravchenko, V. I., Voitenko, V. P., Mechova, L. V., Koshel, N. M. & Grigoriev, P. E. (2009). Seasonality of birth in adult type 2 diabetic patients in three Ukrainian regions. *Diabetologia* 52: 2665-2667.

Vaiserman, A. (2011). Early-life origin of adult disease: evidence from natural experiments. *Experimental Gerontology* 46: 189-192.

Vallejo, F., Tomás-Barberán, F. A. & García-Viguera, C. (2003). Phenolic compound contents in edible parts of broccoli inflorescences after domestic cooking. *Journal of the Science of Food and Agriculture* 83: 1511-1516.

Van de Kaa, D. J. (2001). Postmodern fertility preferences: from changing value orientation to new behaviour. *Population and Development Review* 27: 290-331. Supplement Global Fertility Transition.

Vertuani, S., Angusti, A. & Manfredini, S. (2004). The antioxidants and pro-oxidants network: an overview. *Current Pharmaceutical Design* 10: 1677-1694.

Vierhaus, R. (1984). Deutschland im Zeitalter des Absolutismus (1648-1763). 2. Auflage. Deutsche Geschichte Band 6. VR Kleine Vandenhoeck Reihe, Vandenhoeck & Ruprecht, Göttingen, Deutschland.

Vink, R. & Nechifor, M. (2011). Magnesium in the Central Nervous System. University of Adelaide Press, University of Adelaide. Australia.

Vitetta, L., Briskey, D., Hayes, E., Shing, C. & Peake, J. (2012). A review of the pharmacobiotic regulation of gastrointestinal inflammation by probiotics, commensal bacteria and prebiotics. *Inflammopharmacology* 20: 251-266.

Voigt, M. (1933). Kafiristan. (Landeskunde auf Grund einer Reise im Jahre 1928). Inaugural-Dissertation zur Erlangung der Doktorwürde. Naturwissenschaftliche Fakultät, Universität Halle-Wittenberg. Verlag Ferdinand Hirt, Breslau. Deutschland.

Vogtmann, H. (1985). Qualität und Quantität. In: Ökologischer Landbau. Landwirtschaft mit Zukunft. Herausgeber H. Vogtmann. Seiten 31-53. Pro Natur Verlag, Stuttgart und Eden-Stiftung, Bad Soden. Deutschland.

Voland, E. (1998). Evolutionary ecology of human reproduction. *Annual Review of Anthropology* 27: 347-374.

Voland, E. (2000). Contributions of family reconstitution studies to evolutionary reproductive ecology. *Evolutionary Anthropology* 9: 134-146.

Von Wagner-Jauregg, J. (1927). The treatment of dementia paralytica by malaria inoculation. In *Nobel Lectures: Physiology of Medicine 1922-1941*: 159-169. Elsevier Publishing Company, New York.

Wachter, K. W. & Bulatao, R. A. (2003). (Editors). *Offspring: Fertility behaviour in biodemographic perspective*. Washington DC: National Academic Press.

Wakefield, A. P., House, J. D., Ogborn, M. R., Weiler, H. A., & Aukema, H. M. (2011). A diet with 35% of energy from protein leads to kidney damage in female Sprague-Dawley rats. *British Journal of Nutrition* 106: 656-663.

Wald, A. & Adibi, S. A. (1982). Stimulation of gastric acid secreted by glycine and related oligopeptides in humans. *American Journal of Physiology. Gastrointestinal and Liver Physiology* 242 (2): G85-G88.

Walker, B. R. (2006). Cortisol – cause and cure for metabolic syndrome? *Diabetic Medicine* 23 (12): 1281-1288.

Walker, R., Gurven, M., Hill, K., Migliano, A., Chagnon, N., De Souza, R., Djurovic, G., Hames, R., Hurtado, M., Kaplan, H., Kramer, K., Oliver, W. J., Valeggi, C. & Yamaguchi, T. (2006). Growth rates and life histories in twenty-two small-scale societies. *American Journal of Human Biology* 18: 295-311.

Walker, M. (2017). Why we sleep. The new science of sleep and dreams. Allen Lane.

Wallace, D. C. (1999). Mitochondrial diseases in man and mouse. *Science* 283: 1482-1488.

Wallace, D. C. (2005). A mitochondrial paradigm of metabolic and degenerative diseases, aging, and cancer: a dawn for evolutionary medicine. *Annual Review of Genetics* 39: 359.

Wallace, D. C. (2010). Bioenergetics and the epigenome: interface between the environment and genes in common diseases. *Developmental Disabilities Research Review* 16: 114-119.

Wallach, J. D. & Lan, M. (1996). Rare Earths, Forbidden Cures. Double Happiness Publishers.

Warburton, D. E. R., Nicol, C. W. & Bredin, S. S. W. (2006). Health benefits of physical activity: the evidence. *Canadian Medical Association Journal* 174 (6): 801-809.

Wasser, S. K. (1994). Psychosocial stress and infertility. Cause or effect? *Human Nature* 5 (3):

Waterland, R. A. & Jirtle, R. L. (2004). Early nutrition, epigenetic changes at transposons and imprinted genes, and enhanced susceptibility to adult chronic diseases. *Nutrition* 20: 63-68.

Waterland, R. A., Kellermayer, R., Laritsky, E., Rayco-Solon, P., Harris, R. A., Travisano, M., Zhang, W., Torskaya, M. S., Zhang, J., Shen, L., Manary, M. J. & Prentice, A. M. (2010). Season of conception in rural Gambia affects DNA methylation at putative human metastable epialleles. *PLOS Genetics* 6 (12): e1001252.

Weaver, I. C. G., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckle, J. R., Dymov, S., Szyf, S. & Meaney, M. J. (2004a). Epigenetic programming by maternal behavior. *Nature Neuroscience*, 7 (8): 847-854.

Weaver, I. C. G., Dioro, J., Seckle, J. R., Szyf, S. & Meaney, M. J. (2004b). Early environmental regulation of hippocampal glucocorticoid receptor gene

expression. Characterization of intracellular mediators and potential genomic target sites. *Annals of the New York Academy of Sciences* 1024: 182-212.

Weil, A. (1985). Health and Healing. Understanding Conventional and Alternative Medicine. Paperback. Houghton Mifflin Company. USA.

Weil, A. (1995). Spontaneous Healing. How to discover and enhance your body's natural ability to maintain and heal itself. Warner Books, United States of America. (Spontanheilung. Die Heilung kommt von innen. 2. Auflage. C. Bertelsmann Verlag GmbH, München. Deutschland).

Weiss, H. (1990). Kranker Darm – kranker Körper. 2. Verbesserte Auflage. Karl F. Haug Verlag, Heidelberg. Deutschland.

Weinstock, M. (2008). The long-term behavioural consequences of prenatal stress. *Neuroscience and Biobehavioral Reviews*, 32:1073-1086.

Wendt, L. (1985). Krankheiten verminderter Kapillarmembranpermeabilität. Ernährung – Diät – Therapie. Karl F. Haug Verlag, Heidelberg. Deutschland.

Westendorp, R.-G. & Kirkwood, T. B. L. (2001). Maternal and paternal lines of familial longevity. In: Population. Biodemographic perspectives on human longevity. pp. 223-235.

Whitehead, M., Pennington, A., Orton, L., Nayak, S., Petticrew, M., Sowden, A. & White, M. (2016). How could differences in 'control over destiny' lead to socio-economic inequalities in health? A synthesis of theories and pathways in the living environment. *Health and Place* 39: 51-61.

WHO-Europe (2012). The European Health Report. Charting the way to well-being. World Health Organization, Regional Office for Europe, Copenhagen, Denmark.

Wiederkehr, M. & Krapf, R. (2001). Metabolic and endocrine effects of metabolic acidosis in humans. *Swiss Medical Weekly* 131: 127-132.

Willcox, D. C., Willcox, B.J., Todoriki, H., Curb, J. D. % Suzuki, M. (2006). Caloric restriction and human longevity: what can we learn from the Okinawans? *Biogerontology* 7: 173-177.

Willcox, B. J., Willcox, D. C., Todoriki, H., Fujiyoshi, A., Yano, K., He, Q., Curb, J. D. & Suzuki, M. (2007a). Caloric restriction, the traditional Okinawan diet, and healthy aging. *Annals of the New York Academy of Sciences* 1114: 434-455.

Willcox, B. J., Willcox, D. C., Todoriki, H., Fujiyoshi, A., Yano, K., He, Q., Curb, J. D. & Suzuki, M. (2007b). Caloric restriction, energy balance and healthy aging in Okinawans and Americans: biomarker differences in septuagenerians. *The Okinawan Journal of American Studies* 4: 62-74.

Willcox, D.C., Willcox, B.J., Todoriki, H. & Suzuki, M. (2009). The Okinawan Diet: Health implications of a low-calorie, nutrient-dense, antioxidant-rich dietary pattern low in glycemic load. *Journal of the American College of Nutrition* 28 (4): 500S-516S.

Wilson, M. I. & Daly, M. (1997). Life expectancy, economic inequality, homicide, and reproductive timing in Chicago neighbourhoods. *British Medical Journal* 314: 1271-1274.

Wilson, P. H. (2008). The causes of the Thirty Years War 1618-48. *The English Historical Review* CXXIII (502): 554-586.

Wilson, J. L. (2014). Clinical perspective on stress, cortisol and adrenal fatigue. *Advances in Integrative Medicine* 1: 93-96.

Winje, E. (2007). Season of Birth Bias and Eating Disorders – Fact or Fiction? Dissertation. Institute of Psychology, University of Oslo, Norway.

Winje, E., Willoughby, K. & Lask, B. (2008). Season of birth bias in eating disorders - fact or fiction? *International Journal of Eating Disorders* 41 (6): 479-490.

Wolffe, A. P. & Matzke, M. A. (1999). Epigenetics: regulation through repression. *Science* New Series 286 (5439): 481-486.

Worthman, C. M. & Kuzura, J. (2005). Life history and the early origins of health differentials. *American Journal of Human Biology* 17: 95-112.

Wrangham, R. W., Jones, J. H., Laden, G., Pilbeam, D. & Conklin-Brittain, N.L. (1999). The raw and the stolen: cooking and the ecology of human origins. *Current Anthropolgy* 40: 567-594.

Wrench, G.T. (1938). The Wheel of Health. A Study of a Very Healthy People. C.W. Daniel Company Ltd., Forty Great Russel Street, W.C.1., United Kingdom.

Wright, J. V. & Lenard, L. (2001). Why stomach acid is good for you. Natural relief from heartburn, indigestion, reflux, and GERD. M. Evans, The Rowman & Littlefield Publishing Group, Inc., Lanham, Maryland 20706. USA.

Wrigley, E. A. (1985a). The fall of marital fertility in nineteenth-century France: Exemplar or exception? (Part I). *European Journal of Population* 1 (1): 31-60.

Wrigley, E. A. (1985b). The fall of marital fertility in nineteenth-century France: Exemplar or exception? (Part II). *European Journal of Population* 1 (2/3): 141-177.

Wu, J. L., Quijano, C., Chen, E. et al. (2009). Mitochondrial dysfunction and oxidative stress mediate the physiological impairment induced by the disruption of autophagy. *Aging* 1 (4): 425-437.

Wu, J., Xiao, H., Sun, H., Zou, L. & Zhu, L. (2012). Role of dopamine receptors in ADHD: a systematic meta-analysis. *Molecular Neurobiology* 45: 605-620.

Yablon, L. A. & Mauskop, A. (2011). Magnesium in headache. In: Vink, R. & Nechifor, M. (eds) Magnesium in the Central Nervous System. University of Adelaide Press, Adelaide, Australia. Chapter 8: 125-134.

Zakharov, S. (2008). Russian Federation: From the first to the second demographic transition. *Demographic Research* 19: 907-972.

Zambrano, E., Rodríguez-González, G. L., Guzman, C., García-Becerra, R., Boeck, L., Díaz, L., Menjivar, M., Larrea, F. & Nathanielsz, P. W. (2005a). A maternal low protein diet during pregnancy and lactation in the rat impairs male reproductive development. *Journal of Physiology* 563 (Pt 1): 275-284.

Zambrano, E., Martínez-Samayoa, P. M., Bautista, C. J., Deás, M., Guillén, L., Rodríguez-González, G. L., Guzman, C., M., Larrea, F. & Nathanielsz, P. W. (2005b). Sex differences in transgenerational alterations of growth and

metabolism in progeny (F_2) of female offspring (F_1) of rats fed a low protein diet during pregnancy and lactation. *Journal of Physiology* 566 (Pt 1): 225-236.

Zanchi, A. & Gaetani, M. (2011). The geology of the Karakorum range, Pakistan: the new 1: 100,000 geological map of Central-Western Karakorum. *Italian Journal of Geosciences* 130 (2): 161-262.