Aging a Growing Public Distress

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ABSTRACT

The average human age is currently 75 years, which could increase up to 85 in the coming decades. It is not clearly known if and how these additional years will be adequately satisfying and healthful. The objective was to delineate most verified insights into aging physiology in humans in serving the public awareness and public education policy-making programs. Data suggest gains in the number of healthy years but also compromised physical, mental, and social functions. Decreased oxidative capacity of aged skeletal muscle is due to impaired mitochondrial function and lowered electron transport chain complex activities. Aging coincides with reduced endocrinological functions. Diet restrictions may elongate lifespan while retarding the occurrence of age-related pathologic alterations. Immune function in the elderly may be restored by practical interventions such as vaccination. Alzheimer's disease may in part stem from poor nutritional habits at younger ages, especially with the intake of antioxidants-poor foods. Insights into mental disorders of aging are highly inadequate, thus needing novel innovative hypotheses and future experiments.

Keywords: Aging, Physiology, Endocrinology, Satisfaction, Health, Human.

INTRODUCTION

The average human age is currently about 75 years, which could potentially increase up to 85 in the coming decades (Fries, 1980; Aldwin and Gilmer, 2013). It is not however entirely known if and how these additional years will be adequately satisfying and healthful (Oswald et al., 2010). Most data suggest some gain in the number of healthy years but also a greater increase in compromised physical, mental, and social functions (Baker et al., 2013; Campion, 1994). The number of days with restricted activity and the number of hospitals and nursing homes admissions increase considerably over age 70 (Borton, 2010; Kosorok et al., 1992). Currently, > 25 million aging people suffer from physical impairment, while those requiring assistance with daily routines increases from 15% at age 65-75 to 45% at over age 85 (Aldwin and Gilmer, 2013; Moss and Parsons, 1985; Lamberts et al., 1997). The objective of this review paper is to describe most verified insights into aging physiology in humans. These are mostly to serve the public awareness and public education policy-making programs. Muscle and skin aging along with their underlying endocrinological mechanisms will be delineated. Nutritional, dietary, and endocrinological factors leading to aging will be reviewed. Aging in relation to immunity will be emphasized.

Mitochondrial Function and Apoptotic Aging

For instance, mitochondria are closely linked to the functionality of skeletal muscle (Biagi et al., 2012). These organelles supply the main energy required for contracting muscle. Decreased oxidative capacity of aged skeletal muscle is related to impaired mitochondrial function, reflected in reduced electron transport chain complex activities (Trounce et al., 1989; Conley et al., 2000; Hagen et al., 2004) or ATP synthesis (Drew et al., 2003). Several studies with isolated mitochondria have not found any deterioration in mitochondrial activity with age (Rasmussen et al., 2003). Studies examining mitochondrial adaptations to aging should take into account the potential contribution of the subsarcolemmal (SS) and intermyofibrillar (IMF) mitochondrial sub-fractions when assessing organelle composition and function (Biagi et al., 2012). It has previously been shown that each mitochondrial population displays unique

biochemical and functional properties (Takahashi and Hood, 1996; Ljubicic et al., 2004; Koves et al., 2005). Indeed, studies in cardiac muscle have reported that IMF and SS mitochondria adapt differently during the aging process, with the IMF subfraction showing a reduced capacity for oxygen consumption (VO2) concomitant with increased reactive oxygen species (ROS) production compared to SS mitochondria (Judge et al., 2005). To date, only limited evidence exists supporting the hypothesis that SS and IMF mitochondrial subfractions possess different functional characteristics in senescent skeletal muscle. Several mechanisms have been proposed as causing of age-related muscle fibre atrophy, including enhanced muscle proteolysis (Mosoni et al., 1999), the accumulation of defective mitochondria (Mosoni et al., 1999; Wanagat et al., 2001; Bua et al., 2002) and apoptosis. Recent evidence has shown that mitochondria are involved in promoting protein degradation in skeletal muscle from older compared to younger animals (Martin et al., 2007). An increased incidence of apoptosis, as well as the expression of apoptotic proteins, has been reported in aged skeletal muscle; however, the mechanisms involved in the mitochondrial-triggered apoptotic process have not been fully investigated. Reactive oxygen species may play a role in promoting apoptosis, as they are known to activate the opening of the mitochondrial permeability transition pore (mtPTP) and facilitate the release of proapoptotic proteins such as cytochrome c, endonuclease G or apoptosis inducing factor (AIF) into the cytosol. However, the levels of oxidant production, as well as the ability of ROS to initiate the opening of the mtPTP in aged skeletal muscle mitochondria, have not been fully addressed (Green et al., 2011; Biagi et al., 2012). It is hypothesized that mitochondrial function may be impaired, and that mitochondrial apoptotic susceptibility may be increased in the aging skeletal muscle, coinciding with the extent of muscle atrophy. These data suggest that the age-related sarcopenia and muscle fatigability are associated with enhanced ROS production, increased mitochondrial apoptotic susceptibility and reduced transcriptional drive for mitochondrial biogenesis (Chabi et al., 2008; Green et al., 2011).

Skin Aging

Skin experiences noticeable aging. Human face modeling and animation is a complex task (Biagi et al., 2012). The complexity stems from sophisticated physical structure and psychological and behavioral dynamics (Figures 1 and 2). Natural and realistic facial animation is thus difficult. Nonetheless, many research efforts have succeeded in this regard. An earliest approach involves interpolation of expressive poses of a face. The limitation of the interpolation technique led researchers (Parke, 1974; Parke, 1982) to develop parametric models for facial animation to obtain a fairly large range of facial actions by specifying a small set of appropriate parameters. However, the parameter design depends on the personal facial topology, and therefore, obtaining a complete set of such parameters is challenging. Furthermore, the parametric model easily produces incorrect shape, unrealistic motion and other undesirable effects. The drawback of these earlier models makes researchers work on models whose parameters are based on the anatomy of the human face. There are two types of wrinkles: expressive wrinkles and micro wrinkles. Expressive wrinkles appear during facial expression at all age but become permanently visible over time. An older face has more wrinkles and the wrinkles are more pronounced. The change of skin is mainly attributed to the change of the elastic and collagen fiber. The elastic fibers of skin are stretched and make the skin less elastic, the collagen fibers gather in sheaves and make the skin less homogenous, especially at those points affected by much stress. The present system does not provide the facilities or means to generate expressive wrinkles which gradually become permanently visible. Viaud and Yohio (Viaud and Yahia, 1992) have presented a hybrid model for the formation of wrinkles, where bulges are modeled as spline segments. Given the physiological coverage of the paper, further description can be found elsewhere (Doyle et al., 2010; Wu et al., 1994).

Victorious Aging

Lifespan is a function of a balance of two opposite processes in metabolism (Oswald et al., 2010). One causes injure accumulation that leads to aging. The other includes compensatory responses that restrict and repair such metabolic injuries, which promote longevity (Figure 3) (Johnson et al., 1999). There is considerable variation in the effects of aging on healthy individuals, with some persons exhibiting extensive alteration in physiological functions with age and others little or none (Jusot et al., 2012; Nussbaum et al., 2013). It has been suggested that it might be useful to distinguish between usual and successful patterns of aging (Rowe and Kahn, 1987). Genetic factors, lifestyle, and societal investments in a safe and healthful environment are important aspects of successful aging (Hazzard, 1995). Traditionally, the aging process, including the development of physical frailty toward the end of life, has been considered to be physiological and unavoidable. In recent years, however, it has become evident that it might not be necessary to accept the grim stereotype of aging as an unalterable process of decline and loss (Rowe and Kahn, 1987; Fiatarone et al., 1994). As life expectancy increases further in coming decades, the overarching goal for the year 2000 and thereafter should be “an increase in years of healthy life with a full range of functional capacity at each stage of life” (Healthy People. 2000; Jusot et al., 2012). Such a compression of morbidity can often be

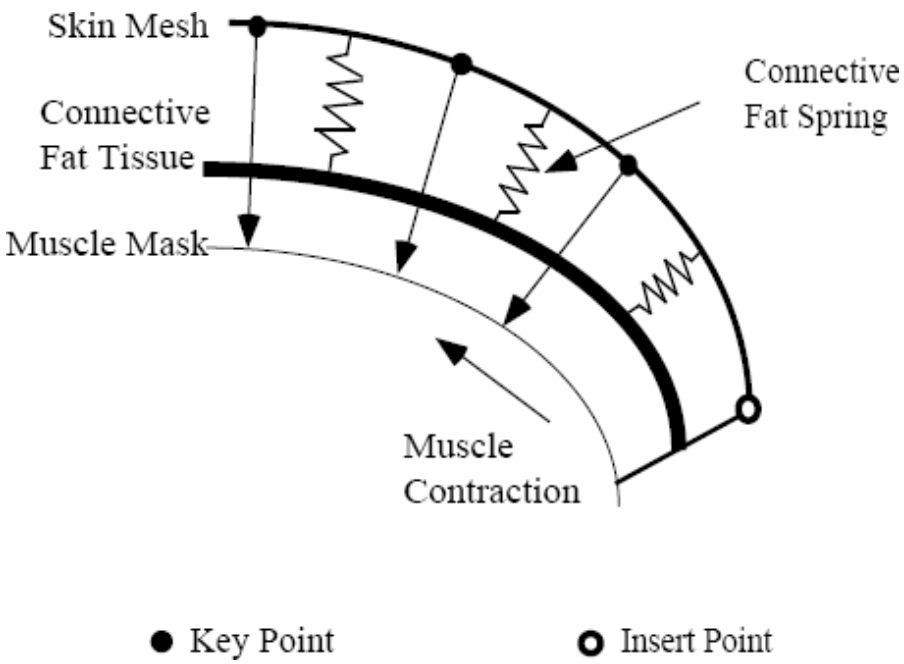

Figure1. Simplified Facial Structure (Chabi et al., 2008; Wu et al., 1994).

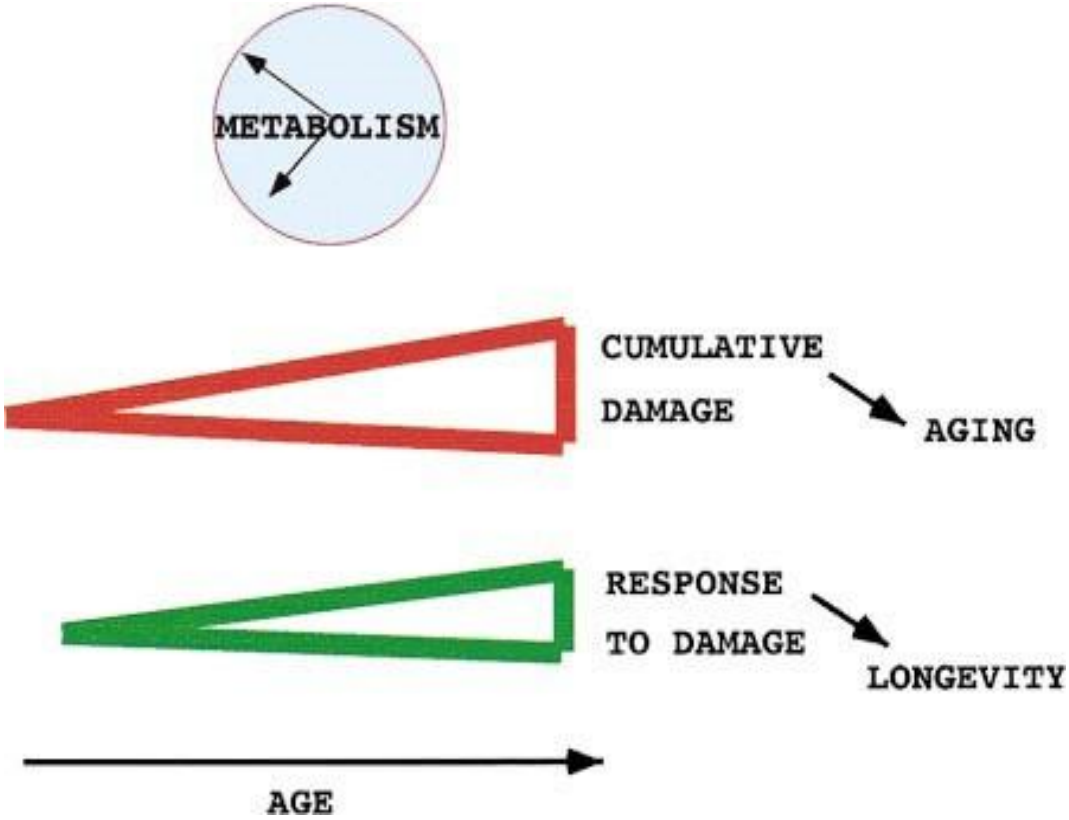

Figure2. Lifespan is a function of a balance of two opposite processes in metabolism causing injure accumulation (top triangle), and thus leading to aging. Compensatory responses (bottom triangle) restrict and repair such metabolic injuries and promote longevity (Aldwin and Gilmer, 2013; Johnson et al., 1999; Stuart-Hamilton, 2012).

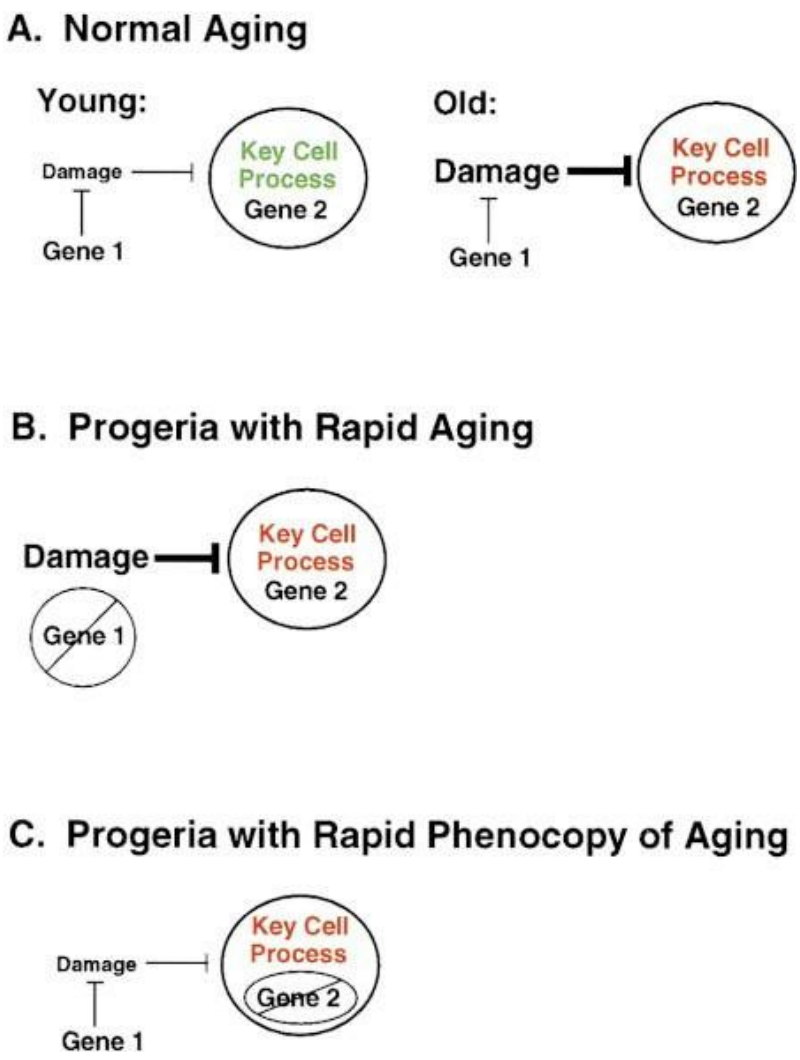

Figure3. Models of relationships between normal aging and progeroid disorders
(A). Normal aging stems from the accumulation of damage and injure with age. Such injures interfere with key cellular processes contributing to longevity. Gene 2 is an example. Gene 1 slows the rate of damage accumulation that causes a normal lifespan.
(B) A progeroid phenotype due to Gene 1 is inactivated, causing a rapid accumulation of damage and premature inhibition of key cell process.
(C) Inactivation of Gene 2 decreases activity of the key cell process and a premature aging phenotype (Aldwin and Gilmer, 2013; Johnson et al., 1999; Stuart-Hamilton, 2012).

achieved through lifestyle measures, but a number of aspects of the aging process of the endocrine system invite the development of "routine" medical intervention programs offering long-term replacement therapy with one or more hormones, to delay the aging process and to allow humans to live for a longer period in a relatively intact state (Jusot et al., 2012).

Endocrinology, Hormone Therapy, and Aging

Aging coincides with reduced activities of many hormonal regulations (Figure 4). Research findings support the hypothesis that decreased lean body mass, increased adipose-tissue mass, and skin thinning occur in older men in part by reduced growth hormone–IGF-I axis activity (Rudman et al., 1990). This can be restored partly by human growth hormone administration (Rudman, 1985; Meites, 1988). The effects of six months of human growth hormone on lean body mass and adipose-tissue mass were equivalent to the changes incurred during 10 to 20 years of aging (Rudman et al., 1990; Meites, 1988; Shuster et al., 1975). It is not yet adequately known what the benefits and what the nature and frequency of any adverse effects will be with larger numbers of elderly subjects and other doses of human growth hormone (Rudman et al., 1990). Research is needed on what

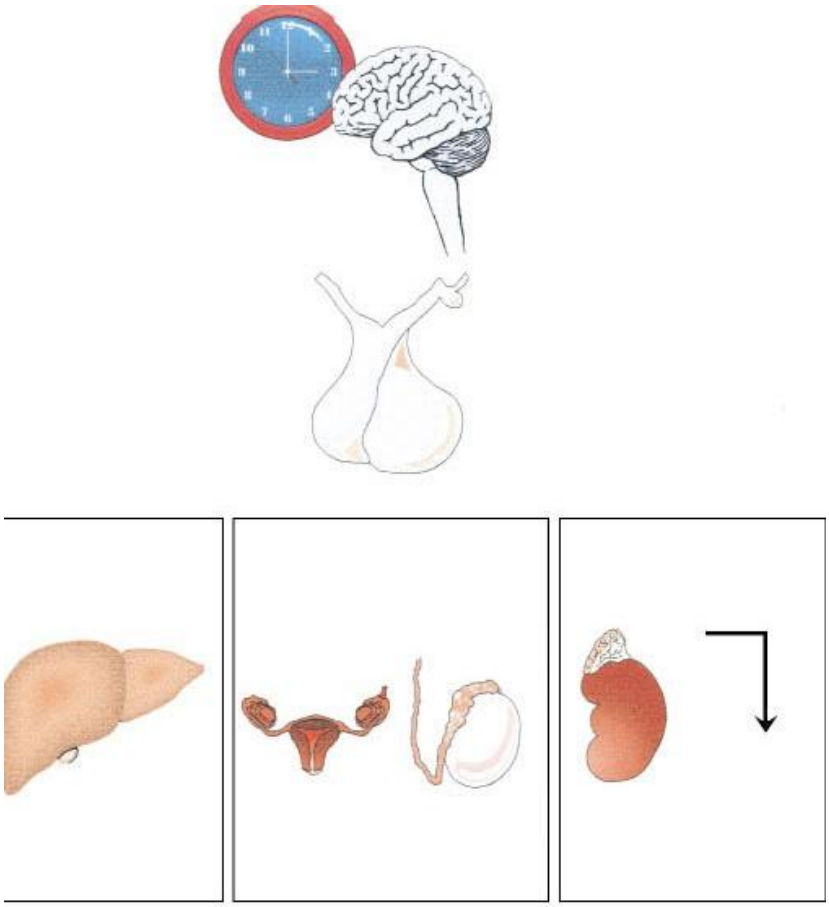

Figure4. Aging coincides with reduced activities of many hormonal regulations. Decreased pituitary gland GH release decreases IGF-I production by by the liver and other organs (somatopause) (Left). Decreased release of gonadotropin luteinizing hormone (LH) and follicle-stimulating hormone (FSH), with a decreased secretion at the gonadal level (from the ovaries, decreased E2; from the testicle, decreased T), cause menopause in women and andropause in men (Middle). The activity of adrenocortical cells responsible for the production of DHEA decreases (adrenopause) without clinically evident changes in corticotrophin (ACTH) and cortisol secretion (Right). A central pacemaker in the hypothalamus or higher brain areas is hypothesized to, together with changes in the peripheral organs such as ovaries, testicles, and adrenal cortex, regulate the aging of these endocrine processes (Lamberts et al., 1997; Stuart-Hamilton, 2012).

organs are responsible for increased lean body mass, and if their functional capacities change also (Johnson, 2013). With answers to these questions, possible benefits of human growth hormone in the elderly may be explored. Since muscle and skin atrophy contributes to the frailty of older people, the potential effects of growth hormone merit further research (Spirduso et al., 2005).

Testosterone therapy has selectively lessened visceral fat accumulation without changing total body fat mass (Allan et al., 2008). It has also increased total body fat-free-mass and total body and thigh skeletal muscle mass (Bhasin et al., 2010; Liverman and Blazer, 2003). Allan et al. (2008) used sixty healthy but symptomatic, nonobese men aged 55 yr or older with total testosterone (TT) levels < 15 nM randomly assigned to transdermal testosterone patches or placebo for 52 wk. Body composition, by dual-energy x-ray absorptiometry (FM, fat mass, FFM, fat-free mass, skeletal muscle) and magnetic resonance imaging (abdominal subcutaneous and visceral adipose tissue, thigh skeletal muscle, and intermuscular fat) and hormonal and metabolic parameters were measured at wk 0 and 52. Serum TT increased by 30% and LH decreased by 50%. Relative to placebo, total body FFM and skeletal muscle were increased and thigh skeletal muscle loss was inhibited with testosterone therapy. Visceral fat accumulation was decreased without changing total body or abdominal subcutaneous FM. Changes in visceral fat were positively correlated with changes in TT levels. There was a trend to increasing total and low-density lipoprotein cholesterol

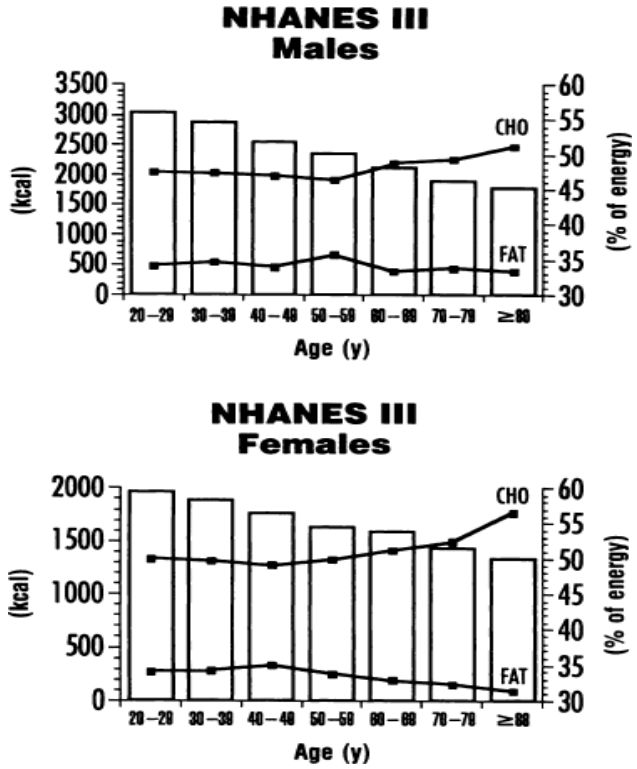

Figure5. Lifespan changes in food intake (The Third National Health and Nutrition Examination Survey, NHANES III) (Barton, 2010; Morley, 1997). CHO = carbohydrate intake. In SI units, kcal × 4.184 = kJ.

Figure 6. Calorie restriction (CR) increases average lifespan in multiple species. Data shown are the average ages (in years) from selected published longevity studies in which animals were fed ad libitum (AL; black bars) or CR (»60% of AL intake, except for the cow and dog, which were restricted to»75%–80% of AL intake; white bars), beginning at weaning and continuing throughout life. The value provided with each bar is the percentage increase in lifespan in response to CR. The p53¡=¡ mice have both alleles of the p53 tumor suppressor gene knocked out; the p53C=C mice are their wild-type littermates (Pinney et al., 1972). The other studies used C3B10RF1 mice (Kealy et al., 2002); Sprague-Dawley rats (Hursting et al., 1997); Fischer 344 rats (Weindruch et al., 1986); Labrador retrievers (Berg and Simms, 1961); and Hereford cows (Yu et al., 1982).

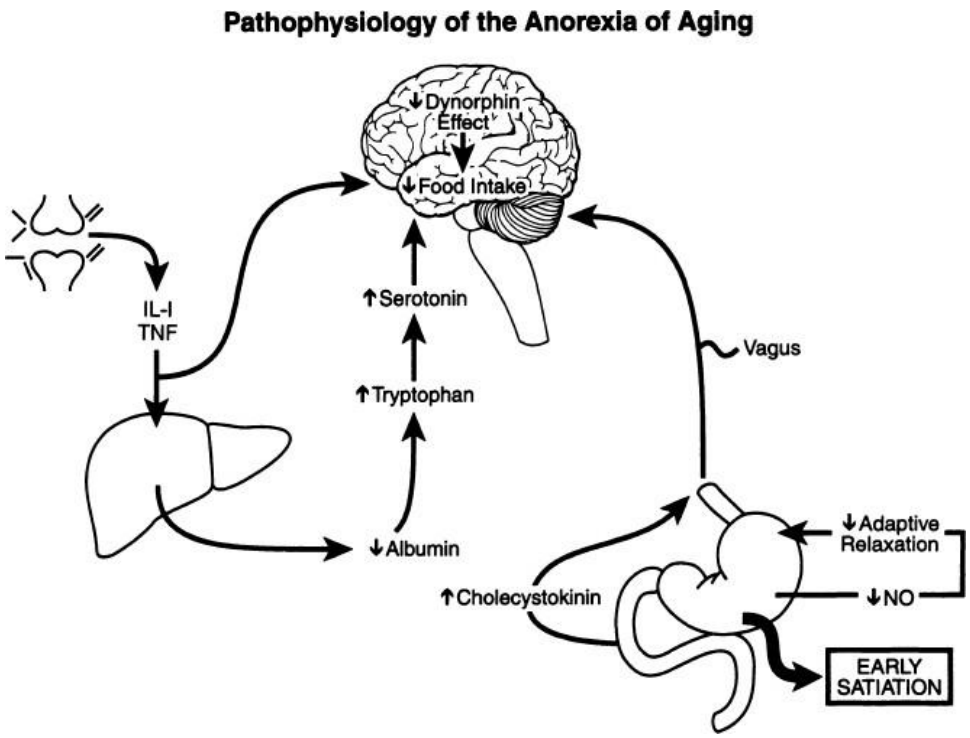

Figure7. Postulated factors involved in the pathogenesis of the physiologic anorexia of aging. IL-I, insulin-like growth factor I; TNF, tumor necrosis factor; NO, nitric oxide.

with placebo. Therefore, Testosterone therapy selectively reduced visceral fat accumulation without changing total body FM, and increased total body FFM and total body and thigh skeletal muscle mass. Further studies will be needed to determine the impact of these body compositional changes on markers of metabolic and cardiovascular risk (Allan et al., 2008).

Nutritional Programs and Aging

Aging has been verified to be highly closely related to the amount, type and nature of nutrition (Figures 5, 6, 7 above). To evaluate impacts of dietary restriction (under-nutrition without malnutrition) on aging, female mice from a long-lived strain were fed post-weaning in one of six groups (Weindruch et al., 1986). The groups included 1) a non-purified diet ad libitum; 2) 85 kcal/wk of a purified diet (25% restriction); 3) 50 kcal/wk of a restricted purified diet enriched in protein, vitamin and mineral to provide nearly equal intakes of these essentials as in group 2 (55% restriction); 4) similar to group 3, but also restricted pre-weaning; 5) 50 kcal/wk of a vitamin- and mineral-enriched diet but with protein intake gradually reduced with age; and 6) 40 kcal/wk of the diet fed to groups 3 and 4 (65% restriction). Mice from groups 3-6 had average and maximal life spans of 35-65% greater than for group 1 and 20-40% greater than for group 2. Mice from group 6 lived longest. The longest-lived 10% of mice from group 6 lived on average for 53.0 months, exceeding reported values for any mice of any strain. The most noticeable were beneficial effects on tumor patterns and on declines with age in T-lymphocyte proliferation for group 6. Significant positive correlations were found between adult body weight and longevity in groups 3-5, which suggest that increased metabolic efficiency may be linked to longevity in restricted mice. The groups 3-6 consumed 30% more calories per gram of mouse over the life span than the group 2. These findings demonstrate profound anti-aging effects of dietary restriction (Weindruch et al., 1986).

Diet restrictions in mice and rat models have repeatedly and firmly elongated life span while retarding the occurrence of age-related pathologic changes (Weindruch, 1996; Hursting et al., 2003). The majority of rodent studies have applied calorie restriction (CR) early in life or 1-3 months of age. Nonetheless, CR initiated in mid-adulthood or at about 12 months of age also increases life span in mice. Evidence suggests that CR may attenuate age-related oxidative damages. Studies on rhesus monkeys and the limited human epidemiological data support such CR effects. Elongated life span and improved health in rodents by CR has implications in toxicologic pathology, and can seriously questions ad libitum intake in humans of all ages (Weindruch, 1996; Hursting et al., 2003).

Coronary heart disease (CHD) risk increases manifestly with age. In addition to diet and lifestyle, factors such as age, family history of CHD, smoking, hypertension, diabetes, elevated low-density-lipoprotein (LDL) cholesterol (4.1 mmol / L, or 160 mg / dL), and

decreased high-density lipopnotein (HDL) cholesterol (< 0.9 mmol/L, on 35 mg/dL) contribute to increased CHD risks. A diet with 30% of energy from fat, < 10% from saturated fat, and < 300 mg cholesterol/d for reduced CHD risks, and even further < 7% of energy from saturated fat and < 200 mg cholesterol/d for hypercholesterolemic subjects are recommended. When adjusted for age, CHD mortality rates have declined by 50% over the last four decades, likely due to reduced dietary animal fats, controlled hypertension, and/or decreased smoking (Schaefer et al, 1995).

Deficiency of the prohormone calcidiol (25OH vitamin D3) may be related to aging-related chronic diseases and cancer. Research data show that calcidiol is responsible for differentiation homeostasis, whereas calcitriol could be more involved in calcium homeostasis. An imbalance of calcidiol is a risk factor for cancer and chronic diseases. Calcidiol insufficiency and insufficient solar exposure increase risks of several cancers. A vitamin D3 deficiency and a high calcidiol density may increase cancer risk. Aging phenomena show a U-shaped link with vitamin D bioactivity. These suggest that aging-related chronic diseases and cancers could be potentially prevented by optimal concentrations of serum calcidiol, which requires further quantification (Tuohimaa, 2008).

Immunity, Diseases, and Aging

Age-related morbidity pattern can be described three situations (Stuart-Hamilton, 2012). First, in a progressive illness, such as Alzheimer's disease, a relatively rapid functional decline occurs. Second, in a catastrophic event, such as a stroke or hip fracture, a decline in function occurs that improves with following rehabilitation. Third, normal aging occurs with gradual progressive functional decline. Results from the New Mexico Aging Process Study provide unique insights into aging effects on the nutritional status of healthy elderly people. Between 1979 and 1989, anthropometric and biochemical markers and dietary intakes remained relatively constant in this healthy elderly population. Thus, the aging process alone may have little or no important effect on the nutritional status of healthy elderly individuals. However, the adaptation of pancreatic and intestinal function to under-nutrition and re-feeding may easily be perturbed in such individuals (Vellas et al., 1992).

Immune function changes with increasing age (Stuart-Hamilton, 2012). There is an increasing incidence of several cancers with aging. It has been a question how altered immunity causes cancer related morbidity and mortality in the elderly. Despite a statistical relationship between diseases incidence and immune dysfunction, evidence for a direct causal-and-effect association has been scarce. Theoretically, the immune system provides surveillance against cancer, and monitors malignant cells transformation for removal. Thus, any failure in such monitoring task could contribute to increased malignancy risk. Possibly age-related changes in immunity affect malignant conditions. In vitro and in vivo animal and human data demonstrate age-related changes in cellular and humoral components of the immune system. However, little evidence exists for direct cause-and-affect relationships. Reduced immune surveillance causes cellular and DNA mutations buildup potentially developing malignancy and programmed apoptosis as observed in the elderly (Edith et al., 2000).

Cancer is mainly a disease of older ages. The median age for cancer diagnosis in developed countries is about 70 years that is expected to increase (Gloeckler Ries et al., 2003). Prolonged duration of carcinogenesis and the susceptibility of aging cells to carcinogens with aging may be among reasons for the higher cancer incidence with aging (Serrano and Blasco, 2007; Campion, 1994; Kosorok et al., 1992). Reduced immune function, "immunosenescence", in the elderly may also in part explain carcinogenesis. The importance of the immune system in preventing tumor formation (i.e., immune-surveillance) has been demonstrated in animal models. This has been further supported by an increased frequency of cancer with immunosuppression (Finn, 2006; Smyth et al., 2006; Moss and Parsons, 1985; Lamberts et al., 1997). Immune function is reflected in responsiveness to vaccination. Immune function in the elderly may be restored and empowered by practical interventions including vaccination. Vaccination against common pathogens such as influenza is a realistic example (Aspinall et al., 2007; Trounce et al., 1989). The increasing application of immunotherapy for cancer in the elderly is another example. Such immunotherapies have mild or negligible side effects, making them preferable over chemotherapy to combat cancer, particularly in frail older cancer patients (Derhovanessian, 2008).

Endogenous Mutagens and Causes of Aging

Metabolism involves major oxidative damages to DNA. In each rat cell, about 10^5 new adducts are formed daily. This endogenous DNA damage is a major cause of aging its degenerative diseases, such as cancer. Such oxidative damages occur more noticeably in mammalian species with a high metabolic rate, short life span, and high age-specific cancer rate, when compared to humans a long-lived creature with a lower metabolic rate and a lower age-specific cancer rate. Micronutrients deficiency, inadequate dietary antioxidants and folate are among major contributors to human cancer. Understanding the role of mitogenesis in mutagenesis is critical for clarifying the mechanisms of carcinogenesis. High-dose animal cancer tests have been done on synthetic industrial chemicals, yet almost all of the chemicals humans are exposed to are natural. About half of natural chemicals tested in high-dose animal cancer tests are rodent carcinogens. The high- dose tests frequently increase

mitogenesis rates. Animals have numerous defenses against toxins that keep them buffered against low doses of almost all toxins, whether synthetic or natural (Ames et al., 1993).

Metabolism also involves tradeoffs. Oxidant by-products during metabolism cause extensive damage to DNA, protein, and lipid. The damage contributes to aging and its degenerative diseases, such as cancer, cardiovascular disorders, immune malfunction, brain dysfunction, and cataracts. Antioxidants protect cells against such damages and include ascorbate, tocopherol, and carotenoids (Ames et al., 1993; Graham et al., 1985; Masoro, 1985). Fruits and vegetables are rich in these antioxidants. As such, reduced intake of fruits and vegetables increases the risk of most cancer, heart diseases, and cataracts. For instance, only 9% of Americans eat the recommended five daily servings of fruits and vegetables. Thus, great opportunity exists for improving human health by enriching diets with fruits and vegetables (Ames et al., 1993).

Despite the increase in body fat and obesity that occurs with aging, there is a linear decrease in food intake over the life span. This conundrum is explained by decreased physical activity and altered metabolism with aging. Thus, older persons fail to adequately regulate food intake and develop a physiologic anorexia of aging. This physiologic anorexia depends not only on decreased hedonic qualities of feeding with aging (an area that remains controversial) but also on altered hormonal and neurotransmitter regulation of food intake. Findings in older animals and humans have provided clues to the causes of the anorexia of aging. An increase in circulating concentrations of the satiating hormone, cholecystokinin, occurs with aging in humans. In addition, animal studies suggest a decrease in the opioid (dynorphin) feeding drive and possibly in neuropeptide Y and nitric oxide. The physiologic anorexia of aging puts older persons at high risk for developing protein-energy malnutrition when they develop either psychologic or physical disease processes. Despite its high prevalence, however, protein-energy malnutrition in older persons is rarely recognized and even more rarely treated appropriately. Screening tools

for the early detection of protein-energy malnutrition in older persons have been developed. Multiple treatable causes of pathologic anorexia have been identified. There is increasing awareness of the importance of depression as a cause of severe weight loss in older persons. Approaches to the management of anorexia and weight loss in older persons are reviewed. Although many drugs exist that can enhance appetite, none of these are ideal for use in older persons currently (Morley, 1997).

Lifestyle, tobacco products, excessive alcohol intake, intake of health-promoting foods and drinks, and anti-obesity exercise are determinants of a life length and health. The benefits of the investments made by governments and research agencies such as the National Institutes of Health, Centers for Disease Control and Prevention, the Food and Drug Administration, and the Department of Agriculture, and the private American Cancer Society have improved public health and life quality in North America. Nonetheless, some groups including lower-income people tend to maintain poor lifestyle habits. It is important to reach everyone with appropriate encouragement for a healthy life (Baudisch and Vaupel, 2012). Optimal public education is a key to increased retirement age of 65 y to about 70 y or perhaps 75 y in the coming years. It is psychologically important since retirement brings frustrations, boredom and poor lifestyle, usually related to consuming imbalanced diets and obesity. Federal, state, and voluntary agencies will further work to persuade the public to pursue updated nutritional regimen and lifestyles to celebrate healthy lives. Following habitual regimes that recommend consuming vegetables, fruits, soy, and antioxidant-rich tea and other products will favor the aging groups (Weisburger, 2000; Parke et al., 1996).

An Alzheimer's Disease Perspective

Mental function often deteriorates with age. Residents of senior citizens and nursing homes often lack adequate mental capabilities to be considered validly normal. Geographic pathology suggests that there are fewer individuals with Alzheimer's disease in Japan and Korea (Haqqi et al., 1999; Yamada et al., 1999). People in the Far East consume more vegetables, fruits, and tea, suggesting that Alzheimer's disease may in part stem from poor nutritional habits at younger ages, especially with the intake of antioxidants-rich foods. Insightful knowledge in these areas is highly inadequate, thus needing novel innovative hypotheses and future experiments.

Changes in biological systems causing death could be considered a consequence of aging when diseases are superimposed and intertwined. These may be at least in part be due to random endogenous free radicals producing reactions. The free radical reaction inhibitors, such as 2-mercaptoethylamine hydrochloride and butylated hydroxytoluene, have increased mice age. This may be a result of an inhibiting effect of 2-MEA on neoplasia induction, and an inhibition of amybid formation. Adding free radical reaction inhibitors to normal natural diets, to minimize the intake of substances that might reasonably lead to random in vivo free radical reactions, may increase man's age by a minimum of 7 along with improved life health status (Harman, 1972; Johnson et al., 1999).

CONCLUSIONS AND IMPLICATIONS

Lifespan is a function of a balance of two opposite processes that cause injure accumulation and aging on the one hand, and induce compensatory responses that

restrict and repair such metabolic injuries for promoted longevity on the other hand. Aging is an increasing apprehension for the healthful postmodern lifespan. Data suggest increases in the number of healthy years but also compromised physical, mental, and social functions. Mitochondria are closely linked to skeletal muscle and skin cells functions. Decreased oxidative capacity of aged skeletal muscle is due to impaired mitochondrial function. Aging coincides with reduced endocrinological activities. Diet restrictions in rodent models have repeatedly and firmly elongated lifespan while retarding the occurrence of age-related pathologic alterations. Mental complexities including Alzheimer's disease will host the next generation of revisited and refined research hypotheses on aging. Nutritional habits at younger ages, especially related to the intake of antioxidants, will be of increasing importance. Advances in understanding aging physiology will determine the efficiency whereby aging related apprehension can be managed. Prolonged lifespan should guarantee prolonged life satisfaction to be favorably pursued.

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