Editor's Page

Aging, Genes and Environment: Lessons from the Ikaria Study

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Since the beginning of human history people have looked for methods to extend their lifespan and their quality of life. Hippocrates (400 BC) said *"All parts of the body which have a function if used in moderation and exercised in labors in which each is accustomed, become thereby healthy, well developed and age more slowly; but if unused and left idle they become liable to disease, defective in growth and age quickly."* Various "healthy" foods, herbs, potions and behaviors have been suggested over the centuries to promote longevity; however, so far any scientific confirmation is lacking. It is a fact that longevity is a very complex attribute, where various environmental, genetic, behavioral, and socio-demographic factors may also influence the physiological pathways of life expectancy.

Aging can be defined as a decline in performance and fitness with advancing age, creating difficulty in adapting to new situations. It is an almost universal feature of living organisms. Increasing age is fraught with increasing morbidity. The list of diseases associated with aging is long and includes diabetes, cardiovascular disease, dementia and cancer. There are a number of theories that explain aging in terms of progressive failures in cellular mechanisms, which lead to accumulating damage and systemic dysregulation. The accumulation of free radicals, mitochondrial dysfunction, and telomere damage are the most appealing theories for the aging process.[1]

Hormones have also been recognized to play a significant role during aging. Among them, serum total testosterone, which is synthesized in the interstitial Leydig cells of the testis, is associated with bone mineral density, body composition, mood aggression, cognitive function, and sexual function, and has also been linked with visceral obesity, atherosclerosis and type 2 diabetes mellitus in men.[2] Recently, in a sample of in 467 elderly individuals (mean age 75 ± 6 years), from the Ikaria Study, low serum testosterone was associated with the prevalence of metabolic syndrome in elderly men, while lipid levels, body-mass index, high-sensitivity C-reactive protein (hs-CRP) and insulin resistance marker levels seemed to explain this relationship, suggesting a potential mediating effect.[3]

Environmental factors have long been linked with disease and survival. Among them exercise, diet, and education have been recognized as factors contributing to long-term survival. Exercise is believed to enhance brain neurotrophic factors and modify apoptosis; it can preserve muscle mass, optimal cardiovascular function, prevent stroke and microvascular disease, while diet has been shown in several studies to provoke antiarrhythmic, anti-inflammatory and antioxidative mechanisms that decrease cardiovascular morbidity and cancer incidence[4,5] This is more relevant with aging, as inflammation is a key factor in the progressive loss of lean tissue and impaired immune function observed in advanced age. In particular, interleukin-6 and CRP, known as "geriatric cytokines," are multifunctional cytokines produced in situations of trauma, stress, and infection, and become elevated during the aging process. In that way, both exercise and a healthy diet preserve immune function and lean tissue mass during the aging process.

One other environmental factor that influences human health is radiation. Since 1977, a theory of a linear correlation between radiation and health risk has been adopted, following the observations from atomic bomb accidents. Recently, radiation is be-

ing discussed as a factor that has bipolar effects on life expectancy and morbidity. Cameron[6] refers to a previous study of the annual level of natural background radiation in the three Rocky Mountain States (Idaho, Colorado and New Mexico). The author describes that, although radiation in this specific area is 3.2 times more than that in three Gulf Coast States (Louisiana, Mississippi and Alabama), the overall age-adjusted cancer death rate in the Gulf States is 1.26 times higher. Additionally, there is much evidence that radiation induction of cancer is not linear with dose and that a threshold dose rate of the order of 1 Gy per year must be exceeded to induce cancer. The biological effects of low-dose radiation have been found to be similar to that of moderate exercise in animal studies, in that they stimulate the production of antioxidants and enhance the immune system, reducing the endogenous DNA damage and increasing DNA repair capacity.[7] Furthermore, this U- or J-shaped effect has also been described, along with many other factors, as an adaptation mechanism to environmental hazards and toxins. On the other hand, several other meteorological conditions, such as temperature variations, winds, humidity and altitude, have also been discussed as possible factors affecting the morbidity and mortality of populations. Those observations and theories might contribute to the design of prospective human epigenetic studies focused on long-living populations, which will illustrate the interactions between genetic variation, lifestyle factors, and environmental influence on human health and quality of life.

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