Arch. Gerontol. Geriatr. Suppl. 1 (2007) 125–132
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PREVENTION OF PATHOLOGICAL AGING BY COMPREHENSIVE CLINICAL, FUNCTIONAL AND BIOLOGICAL ASSESSMENT

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SUMMARY

Parallel with global trends in population aging, numerous check-up programs of anti-aging purposes have been developed and implemented. Healthy aging and active aging are goals of the United Nations Research Agenda on Aging for the 21th century. It is necessary to have a lifelong process optimizing opportunities for improving and preserving health, physical, social and mental wellness, independence, quality of life and activity. An anti-aging check-up should point out to the factors that lead to functional decline, shifting the outcome measurement to focus on those persons who are aging well, to improve wellness. This paper discusses the principal factors of pathological aging: nutrition, physical activity, hormones, inflammation, depression, ecology and social/behavioral factors. A model of assessment is proposed based on clinical, functional and biological parameters.

Keywords: assessment of aging, check-up programs for elderly, quality of life

INTRODUCTION

The most important issue of the last century was obviously the increased longevity, and this trend persisted also during the first years of this century. The fast aging of the population has been brought to public attention, and longevity has become a major health focus. Increased longevity is a great success, but can become a danger for the people who do not realize the necessity of maintaining themselves independent, active, and healthy as long as possible. Today, the anti-aging interventions seem to be important only as the way to appear young in advanced age. The look is important, but must be associated with all type of interventions aimed at maintaining the functions at the top. A health-management strategy, regular check-ups and follow-up the medical conditions before they become problematic, are important components of maintaining our health (WHO, 2002). How old is the elderly today? Whatever age is used within different contexts, it is important to acknowledge that chronological age is not a precise marker for the changes accompanying aging. There are dramatic variations in the health status, participation, and levels of independence among older people of the same age.

Aging is a continuous, universal, progressive, intensive, deleterious, but democratic phenomenon. Preventive gerontology must help the population to fight secondary aging, i.e., pathological aging. As far as we know, good health consists of three factors: the absence of disease, the maintenance of optimal function, and the presence of an adequate support system. Good health at any age is crucial for the well being of the population. Today, we have many prognostic indexes for mortality of older adults (Salvioli, 2006), where survival is the end point. But we need to measure the effects of aging on function. Many subjects from 40, are interested in anti-aging programs. The market offers many proposals to carry out anti-aging check-ups or interventions. Scientists with poor knowledge of the aging process have developed most part of these. Nothing has been demonstrated to slow or reverse the primary aging process in human beings, instead the factors that are known to affect longevity, actually influence the disease development, that is part of secondary aging.

Preventive strategies against secondary aging are aimed at maintaining health and functional capability at any age, with many kind of interventions based on timely and comprehensive clinical, functional and biological assessment. Successful aging and longevity depend on prevention, that is crucial at any age, but particularly during adult life, in the young elderly, and in the elderly, with the purpose to avoid pathological aging. Therefore, the main question is: "How do I get old healthy?" The general answer to this question is: "Fight frailty at any age to promote active aging".

IS IT POSSIBLE TO FIGHT FRAILTY BY AN ANTI-AGING CHECK-UP?

Currently, many factors known to be associated with maintenance of functioning at older ages are considered to be determinants of successful aging. How to live to be 100 years and not to regret it? Using a health management strategy, getting a regular comprehensive assessment based on principles established by WHO (2002), taking into consideration the impact of a healthy condition on the individual according to principles of the International Classification of Functioning, Disability and Health (Wade and Halligan, 2003; Stucki and Ewert, 2005) and multiple determinants of active aging. Prevention and education are the two main ingredients inherent in health maintenance at any age, and in all countries, and in particular in countries where elderly people is a large part of the population. Measures to help adults, young elderly, and elderly people remain healthy and active are a necessity, not a luxury.

Any program of anti-aging check-up must be carried out not only considering esthetic problems, but the way to promote well being at any age and to fight frailty and any factor of pathological aging. Pathological aging depends on many factors, like gender, ecology, pre-

morbid status, financial status, disease, age, genetic, systemic disorders, cognitive reserves, education. This is a puzzle of interacting factors where prevention is based on comprehensive assessment, clinical history and measures of functioning, and of self-rated evaluations. Items of the comprehensive assessment should consider age, sex, civil status, smoking habits, alcohol drinking, physical activity, muscular strength, nutritional habits, build, cognition, depression, sex, anthropometric parameters, body image, occupation and used measures of prevention screenings. The compression of morbidity hypothesis suggests that it may be possible to reduce cumulative lifetime morbidity (Vita et al., 2006). Since chronic illness and disability occur late in life, cumulative lifetime disability could be reduced if primary prevention measures are timely taken with the purpose to counteract frailty and pathological aging and to postpone the onset of chronic illnesses, and particularly of those responsible of dependency.

PREVENTION AND EDUCATION

Prevention and education are the two main ingredients inherent in health maintenance, that is true anti-aging intervention, and is based on fighting frailty at any time of life, taking into consideration all possible determinants of frailty (Table I).

Table I
A LIST OF DETERMINANTS OF FRAILTY

Ecological environment
Behavior and clinical history
Compliance to changes
Socio-economic and nutritional status
Existing functional capacity
Healthy life-expectancy
Running intervention programs

Frailty has different effects on functional dependency in adults, younger and older elderly. In the older population, measures of frailty can be based on the ability to use the stairs, to walk outside, bathing, dressing, eating, but those parameters have a floor or ceiling effect in younger age classes. The assessment should always be based on a holistic, human-ecological model, where health related quality of life (HRQoL) is the gold standard.

Global physical efficiency decreases with age. Particularly after 45, maximum aerobic power, lactacidic and alactacidic capabilities, muscular strength and power decrease. Among the causes are the decrease of the cardiac reserve, of the enzymatic systems speed, and of the muscular mass (sarcopenia). This functional decline, that is genetically determined, can be counteracted in part by physical activity. Various experimental

evidences show that a personalized program of physical activity can counteract the decline or improve significantly both muscular strength and cardiac efficiency.

A life style that includes in itself a regular physical activity helps to prevent metabolic syndromes increasing thermo-genesis, often underestimated, and, above all avoiding the spontaneous decrease in energy consumption that is associated to a hypocaloric diet. Today "empowerment" is a commonly used word in referring to the necessity to make people more conscious of the importance of a regular physical activity. Jogging, walking, cycling, swimming slowly are some of the classical physical exercises suggested for regular practice, as they are aerobic, thus able to improve insulin resistance without increasing the feeling of hunger. (Haveman-Nies et al., 2003; Peel et al., 2005; Rejeski et al., 2005). Baseline and outcome assessments of walking capacities should be made in order to quantify the subject's functional ability, to prescribe an adequate exercise regimen and to evaluate free radicals production due to moderate exercise (Leung et al., 2006).

Progressive, incremental tests using treadmill or cycle ergometry with online monitoring of cardiac and ventilatory functions are the gold standard for the diagnosis of disease, or measurement of maximum oxygen intake. In the past few years, walking tests have gained prominence in both clinical practice and research: these tests are used in clinical practice for measuring functional capability, monitoring treatment effectiveness, and establishing prognosis (Solway et al., 2001).

The most commonly used tests are the 6-min walk test (6 MWT) and the 12- min walk test (12 MWT). These tests have been proven to be responsive to improvements in physical functioning after treatment or rehabilitation; however, they cannot give enough information in the evaluation of performance in normal subjects of different sex and age. However, these technically intense and relatively expensive measures are of questionable benefit when predicting physical functioning for daily living or to assess what happens in the subject under evaluation during usual, or almost usual activities. The real world in a program of anti-aging check-ups is different from the one that is specific to make diagnosis or treatment and rehabilitation.

THE AGING PROCESS AND NUTRITION

The aging process strongly depends on nutrition and food intake. Nutrients, vitamins, drug-nutrient interactions play an important role and there is the necessity of a personally oriented intervention program that takes into consideration aging and anti-aging factors.

The main goal in structuring a personalized nutritional profile is to preserve the individual health status at the top and to prevent pathological aging. Chemical molecules

contained in foods can act on genome, both directly and indirectly, and alter the gene-expression and the messenger structure. In some cases and in certain individuals, diet can represent a serious risk factor for various diseases. Some genes that are regulated by the diet, and their possible variants, appear to play a determinant role in the etiology, the incidence, the progression, and the severity of numerous chronic pathologies. Prior disability is important determinant of the likelihood of functional transitions (Hardy et al., 2006).

The grade at which diet influences the balance between health and illness status could depend on the genetic "make-up" of any individual. Eating is a highly complex activity during life, influenced by a wide range of factors, like individual cooking skills, knowledge about nutritional principles, socioeconomic factors, living environment, social relationships, and so forth. The importance of nutrition on activities of daily living (ADL), or instrumental ADL (IADL), depression, and cognition is well known. "A brain that cannot function normally because of lack of an essential nutrient is like trying to run a 220 Volt electrical appliance on a 120 Volt system" (Horrobin, 2002). All strategies against pathological aging must fight malnutrition and related syndromes, such as sarcopenia and sarcopenic obesity. Sarcopenia is the loss of muscle protein mass that occurs with advancing age and grows worse in elderly subjects. Consequences are: impaired muscular strength and endurance, reduced physical function, decrease in the HRQoL, increased vulnerability, risk of falls as demonstrated by studies of our group (Cucinotta et al., 2004, 2006). It is necessary to counteract underweight and overweight in time and also frequent variations of body weigh during lifetime. The optimal body mass index (BMI) must be defined for each age class, and sex.

THE AGING PROCESS, HORMONES, INFLAMMATION AND DEPRESSION

The connection of hormone levels to aging is very important in evaluating the risk of frailty or of disability. Inverse correlation between leptin and testosterone in man, effects of hypo-estrogenism due to menopause on leptin-binding, abdominal obesity, sarcopenia, anemia, dyslipidemia, sarco-obesity due to growth-hormone (GH) deficiency have been demonstrated. If frailty can be considered as a "Vulnerable sate of health, arising from the complex interaction of medical and social problems, resulting in a decreased ability to respond to stress and associated with a decline in functional performance" (Rockwood et al., 2000), any kind of anti-aging program must consider all causal factors, such as inflammation at the onset, which is subclinical and takes place at a cellular level. It triggers free radical production, which accelerates aging by damaging cells. The causes are: a pro-inflammatory diet, environmental stressors, weakened immune system, excessive exposure to ultraviolet light, hormonal changes, stress and circulating factors, such as cytokines,

among which are tumor necrosis factor-α (TNFα), interleukin-1 (IL-1), interle-ukin-6 (IL-6), and interferon-γ (IFN-γ). High serum levels of TNFα, IL-1, IL-6 are highly indicative of frailty and of poor prognosis. In these cases we observe not only impaired quality of life, but also a reduction in life expectancy (Fried et al., 2004).

Chronic stress adversely affects hormone production and blood levels. During aging per se, and in pathological aging, there will be a substantial reduction of sex hormones, growth hormone, free triiodothyroxine, insulin-like growth factor-1, dehydroepiandrosterone and melatonin, as partially demonstrated by previous studies carried out by some of our group (Ravaglia et al., 2000). Depression can worsen any disease typical of middle age and favor the expression of a phenotype of pathological or accelerated aging. The "happy brain" has a powerful influence on the rest of the body, on life expectancy, and on physical competence. People who rated best in psychological tests react better to any disease. Hopefully, optimized moods, and contentment appear to reduce the risk or limit the severity of cardiovascular and pulmonary disorders, diabetes, hypertension, infections, tumors, and cognitive impairment as well. Also loneliness is a risk factor for cardiac diseases, because this social condition is frequently associated with other risk factors, such as smoking, alcohol consumption and depression.

ANTI-AGING CHECK-UP: MYTH OR REALITY?

Only an intense and multi-dimensional evaluation and management based on criteria coming from preventive gerontology can fight frailty and prevent pathological aging. The anti-aging check-up used in our laboratory covers the following factors: clinical history and global clinical exam, check of preventive medicine screenings, nutritional habits, self-assessment of mood, depressive symptoms, and body image, body uneasiness test, anthropometrics, bio-electrical impedance analysis of body composition (the assessment of electrical conductivity enables to prioritize intervention on nutritional aspects, based on estimations of body cell mass, intracellular and extracellular water, lean body mass, basal metabolic rates), spirometrc tests, cardiovascular evaluation, hand grip strength evaluation, laboratory tests (homocysteine, fibrinogen, C-reactive protein, etc.), free radical blood levels, demographic and socioeconomic evaluation of risk factors of stress, disease, and pathological aging, evaluation of sexual competence, screening for memory and cognition problems (Cucinotta et al., 2004).

The assessment of oxidative stress is carried out at rest, during, and after an aerobic cardiovascular mini-stress test using a "tapis roulant". Using an empiric method, we carried out many experiments in different groups of free-living volunteers of different ages, of both

sexes, all Caucasians, and the walk test was modified many times according to the results. The data from this research made clear the necessity to apply different levels of speed, of time of walk and of slope, according to age and sex.

The results of the tests were not used for clinical diagnosis, but as tests of performance and are based on monitoring of heart rate, blood pressure, and free radical levels. Free radicals are deeply associated with the aging process. In normal conditions, the body can handle free radicals, but if their production becomes excessive, oxidative damage can occur, that is an imbalance between oxidants and antioxidants. The measuring of oxygen free radicals in capillary blood is now available for health care professionals. Using a photometer, it is possible to measure the level of blood total hydroperoxidase, expressed in units. Stop free radicals was a message used in the past, but it is not always useful if not targeted to subjects who can benefit it.

It is well known that in animals the influence of nutritional intake on antioxidants promotes longevity only, if it starts during the first part of life, whereas the effects would be poor when it starts during middle age. In theory, antioxidants could regulate the interaction between the immune system and endothelial cells, decreasing the risk of cardiovascular diseases that are the main cause of morbidity and mortality in the elderly. Nevertheless, all trials failed to demonstrate the efficacy of antioxidants. Why this occurred? Probably because it is necessary to verify in each subject the free radical production in basal conditions, and during aerobic exercise and to treat only subjects with pathological values.

Thus we conclude that the anti-aging evaluation should be tailored on the physical characteristics and on the age of any subject. The first goal of any anti-aging check-up is to precisely evaluate individual capabilities, the presence of pathologies (hypertension, obesity, vertebral pathologies), to establish the opportunity or the intensity of overload and also the kind of physical activity. Any anti-aging program should promote healthy aging and active aging, evaluating all determinants of this complex phenomenon.

The final message will be: promoting active aging by a program based on comprehensive, clinical, functional, social, psychological, ecological assessment. The anti-aging check-up must accomplish a program of social medicine, which includes preventive, curative, and rehabilitating medicine. The main goals will be an improvement of the HRQoL, life satisfaction, physical and psychological balance. This activity must be based on a constant education program of either mental, physical or nutritional aspects, to enable each individual to deal with their biological heritage, to prevent diseases, the possible consequences of psycho-physical impairment. Every person is aware of the psychosomatic

disturbances that occur in an individual due to age-related disorders, but it is first of all important to increase the interest on functional capability.

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