

# Inflammaging in the pathogenesis of chronic non-communicable diseases

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According to the World Health Organization estimates, from 1950 to 2020, the average life expectancy increased ~2 times — from 47 to 73,2 years. It is predicted that the proportion of older people in the population will increase from 12% to 22% by 2050. The increase in the proportion of elderly population naturally draws attention to healthy aging. It includes the prevention (or late onset) of age-related diseases, disabilities, the maintenance of cognitive and physical functions and social activity throughout life. Unfortunately, at present, healthy life expectancy significantly lags behind the general life expectancy, and noncommunicable diseases have become the leading cause of death in the world [1].

Aging is a multifactorial process characterized by a decrease in body functionality over time and accompanied by an increased risk of developing noncommunicable diseases [2]. Seven key mechanisms leading to aging have been identified. These include disorders of stem cell regeneration, metabolism, proteostasis, macromolecular damage, stress, epigenetic modifications, and inflammation. These mechanisms are interconnected, modulating each other and forming an integrated network. All mechanisms converge on inflammation, since disorganization of each of them causes an inflammatory response, which, in turn, disrupts the regulation of other pathways [3].

In contrast to acute inflammation caused by infectious agents, inflammaging is a chronic, aseptic, mild, asymptomatic inflammation caused by endogenous signals. It is a complex and systemic process that is likely the result of several factors. As a result of

the accumulation of molecules secreted by senescent and damaged cells (for example, micro-ribonucleic acid, mitochondrial deoxyribonucleic acid, or histones), innate immune cells are activated, leading to an inflammatory response. With age, the number of senescent cells increases, and they secrete a large number of proinflammatory cytokines, which leads to senescence associated secretory phenotype (SASP). The main role is played by following cytokines: interleukin-6, tumor necrosis factor- $\alpha$ , and C-reactive protein [4]. Other factors leading to inflammation include poor nutrition, altered gut microbiota and epithelial permeability, chronic stress, and cytomegalovirus infection. Obesity makes a significant contribution to increased inflammation, since adipose tissue is a large endocrine organ that actively and bidirectionally interacts with the nervous and immune systems [5].

It is noteworthy that simultaneously with activation of innate immunity during aging, suppression of the adaptive immune response occurs, which leads to infectious disease vulnerability and a reduced response to vaccination with a general proinflammatory status — a phenomenon called immunoaging [6]. It is believed that the increase in inflammation with age is a particular example of the so-called antagonistic pleiotropy, where the same trait is useful for adaptation at an early age, but has a negative effect in the post-reproductive period, when the natural selection pressure is weakened [7]. For example, it was found that cardiovascular mortality in old age was much higher among those with a high proinflammatory ratio of tumor necrosis factor to interleukin-10. It was hypothesized that this status was associated with high resistance to pathogens

in youth, but turned out to be a greater predisposition to cardiovascular diseases in old age [8]. More and more evidence accumulates that it is inflammaging that plays a key role in the development of cardiovascular and musculoskeletal diseases, cancer, type 2 diabetes and depression [3, 5].

The article by Krivoschapova K. E., et al. "Osteosarcopenic obesity in cardiovascular patients. Controversial and open issues" discusses a new geriatric syndrome, the components of which (atherosclerosis, obesity, osteoporosis and sarcopenia) are usually considered separately. Understanding these conditions as a complex, united by one mechanism of chronic systemic inflam-

mation, will allow the practitioner to take a differentiated approach to the diagnosis and treatment of such a patient and avoid polypharmacy.

Currently, methods are being actively developed aimed at reducing chronic inflammation as a universal method for the prevention and treatment of age-related diseases. The use of low-dose aspirin, statins, physical activity and calorie reduction are already widely used methods [9]. Potential therapies in the future include senolytic drugs, pro- and prebiotics, fecal microbiota transplant, and cytomegalovirus vaccine [5].

**Relationships and Activities:** none.

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