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Editorial

Inflammaging: Significance and intervention

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The year 2000 marked a revolutionary shift in the way we think about aging and longevity, thanks to the groundbreaking work of Professor Franceschi and his colleagues. Their concept of "inflammaging" challenged our entire understanding of the aging process, not just in immunology but across all fields. Through their research, we were able to recognize the critical role that inflammation plays in the aging of the immune system and its consequences.[1] Inflammaging, or inflamm-aging, is an undeniable reality that develops in the human body with advanced age. This low-grade inflammation is an upregulated inflammatory response that can significantly accelerate aging and worsen specific age-related symptoms and diseases. Acknowledging the existence of inflammation is crucial to tackling the challenges of aging and finding practical solutions to mitigate its adverse effects on our bodies. Inflammation is a condition where the immune system produces excessive inflammatory cytokines, leading to chronic inflammation. This condition is influenced by various factors, such as genetics, environmental factors, and aging. If not addressed, it can result in increased cytokine production and inflammation, a reduced ability of the body to eliminate damaged cells, and an increased risk of obesity. Moreover, inflammaging can contribute to various age-related health issues, leading to functional decline and even mortality.[2-4]

It is a fact that aging is a natural process we all go through. Nevertheless, the research shows that simple measures like calorie restriction and regular exercise can extend our lifespan. Furthermore, we must acknowledge the concept of inflammaging, which emphasizes the chronic damage resulting from high levels of inflammation within our bodies. While it is a typical aspect of aging, it is crucial to recognize that inflammation can severely damage the immune system, ultimately leading to immunosenescence during the aging process. It is interesting to note that studies have shown that women tend to live longer than men. Research has also shown that inflammation-related modules are more active in older men, and their naive T and B cells decrease more dramatically than in older women. This indicates that inflammation and immunity play a significant role in aging.[5]

Immunosenescence is an inevitable process associated with aging that severely impairs immune function, making it highly responsible for inflammation. Multiple age-associated events cause immunosenescence, including thymic involution, which reduces the pool of naïve T cells and amplifies the oligo-clonal expansion of memory T cells. This leads to reduced immune repertoire diversity, severely weakening the ability to fight infections and increasing cancer incidence. Thymic involution also results in an amplified release of self-reactive T cells. It reduces the capacity of T-regulatory (reg) cells to suppress these self-reactive T cells and preserve immune homeostasis. Consequently, these events enhance tissue damage through autoimmunity and chronic inflammation, essential contributors to inflammation. Understanding the severity of these effects is crucial to devising effective strategies to combat inflammation and promote healthy aging. Immunosenescence also affects the bone marrow, the primary site of blood cell production. The bone marrow gradually replaces normal cells with fat cells and produces more myeloid cells, negatively impacting the activity of T and B lymphocytes, critical immune cells. Furthermore, the degeneration of the bone marrow increases the production of pro-inflammatory cytokines, further impacting immune cell activity.[6]

As we age, the immune system undergoes changes that significantly impact its ability to function effectively. Neutrophils and macrophages lose their capacity for phagocytosis, and natural killer cells become less effective at secreting cytotoxic molecules. In addition, macrophages increasingly polarize toward M2 cells. These changes lead to the accumulation of senescent somatic cells, which, in conjunction with the pro-inflammatory molecules produced by senescent cells, are known as the senescence-associated secretory phenotype (SASP) and contribute to inflammation. The SASP further promotes inflammation, accelerating the aging process and leading to the development of cancer. The accumulation of senescent cells and the SASP also enhance cellular senescence and inflammation in neighboring non-senescent cells. The interplay between immunosenescence and inflammaging creates a feedback loop that solidifies their roles in developing age-related diseases. Notably, this dynamic duo contributes to a range of conditions, including cancer, neurodegenerative diseases, metabolic disorders, and cardiovascular diseases.[6,7]

Extensive research shows that various factors can contribute to and sustain inflammation as we age. These factors include pathogens, endogenous cells, misplaced molecules, the gut microbiota, and nutrients. If our body's receptors detect these factors, they can trigger the body's natural immune response, leading to metainflammation. Avoiding overnutrition can prevent low-grade chronic inflammation, the root cause of accelerated age-related and chronic disease development. A study on aging has found a significant link between inflammation and oxidative stress. It is essential to understand the impact of this connection on the development and acceleration of age-related and chronic diseases so that we can take preventive measures to avoid and effectively handle these health conditions.[4]

The immune system possesses an exceptional ability to recognize and respond to diverse stimuli and experiences, resulting in significant variations in immunosenescence among individuals. Such heterogeneity can be attributed to differences in the type, dose, intensity, and temporal sequence of antigenic stimuli exposed to each person. To address this issue, Franceschi *et al*. (2017) introduced the "immunobiography" concept, which provides a comprehensive framework for understanding immune aging.[8] However, it fails to consider other crucial factors, such as genetics and social factors, which can influence the accumulation of inflammation and aging. A more comprehensive approach that considers multiple factors may be required to fully understand the complexities of immunosenescence and inflammaging fully.[5,7]

As we grow older, our bodies become more susceptible to chronic diseases. Recent advancements in aging research have demonstrated that regular exercise can significantly decrease the risk of age-related chronic diseases. In a recent study, researchers aimed to investigate the effectiveness of exercise in delaying or reducing the onset of age-associated chronic inflammation, commonly known as inflammation. The study included older adults who had maintained a regular exercise regimen. Results showed that these individuals were more likely to prevent or delay inflammation. The researchers found that exercise can be a natural anti-inflammatory, which may help protect against age-associated inflammation. These findings suggest that exercise can be crucial in promoting healthy aging. Therefore, incorporating regular exercise into our daily routines can help us stay healthy, active, and independent as we age.[9]

Aging is an intricate process, and there is strong evidence that inflammation significantly contributes to the progression of many age-related chronic diseases. The gradual increase in age is accompanied by a subtle but chronic low-grade inflammation, which scientists appropriately call "inflammaging". A mashup of inflammation and aging, this buzzword initially referred to inflammation's overall effect on health. The ultimate goals of aging research are to prevent and alleviate age-related diseases while improving the quality of life. Therefore, it is imperative to conduct thoughtful research in order to understand the exact causality between inflammation and aging, which will enable efficient intervention in aging-associated diseases and enhance well-being.

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