



Commentary

Aging and immunity: Unraveling the complex relationship

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Abstract: The process of aging is an inherent facet of human existence, entailing various changes within the body, notably in the immune system. This article explores the profound impact of aging on immunity, elucidating its implications for healthcare, disease vulnerability and overall quality of life. Drawing inspiration from the “Aging and Immunity” special issue of *AIMS Allergy and Immunology*, this commentary provides a comprehensive perspective on the intricate interplay between aging and immunity. The immune system, a complex shield against pathogens, undergoes a decline in efficacy as individuals age, known as *immunosenescence*. This decline encompasses reduced immune cell production and communication, rendering older individuals more susceptible to infections and less responsive to vaccines. Additionally, chronic low-grade inflammation, termed *inflammaging*, emerges as a hallmark of aging and immune system alteration, contributing to age-related diseases. Recent research underscores the connection between the gut microbiota and immune aging, raising the prospect of interventions targeting gut health to enhance immunity in older individuals. Strategies for fortifying immunity in aging populations encompass optimized vaccination approaches, lifestyle modifications, anti-inflammatory interventions, targeted therapies and microbiota-based interventions. Addressing the challenges of aging and immunity necessitates collaborative efforts from policymakers, healthcare providers, researchers and communities, emphasizing healthy aging promotion, evidence-based interventions and equitable healthcare access. By delving into the multifaceted relationship between aging and immunity, this discourse envisions a future where research-driven advancements and holistic public health measures converge to enhance the well-being and resilience of older adults worldwide.

Keywords: immunosenescence; inflammaging; aging; immunity; vaccination; gut microbiota

1. Introduction

The process of aging is an inevitable part of the human experience. As we grow older, our bodies undergo a multitude of changes, including alterations in our immune system. The impact of aging on immunity is a topic of increasing significance in our aging global population, as it has far-reaching implications for healthcare, disease susceptibility, and overall quality of life. Inspired by the special issue, “Aging and Immunity” of *AIMS Allergy and Immunology*, we would like to provide a thoughtful perspective on the intricate relationship between aging and immunity, shedding light on the challenges and opportunities that arise from this complex interplay.

2. The immune system: a marvel of protection

The immune system is a highly sophisticated network of cells, tissues, and organs that work in unison to safeguard our bodies against invading pathogens and maintain overall health. Throughout our lives, the immune system acts as a vigilant shield, protecting us from infections and diseases. However, as we age, the immune system’s functionality gradually declines, leading to a phenomenon known as *immunosenescence*. Immunosenescence refers to the gradual deterioration of the immune system’s ability to respond effectively to pathogens and external threats [1,2]. One of the primary hallmarks of immunosenescence is the reduced production and function of immune cells, such as T cells, B cells, and NK cells. These cells play crucial roles in identifying and neutralizing harmful agents [3,4]. Additionally, the communication between different immune cells becomes less efficient, further compromising the body’s overall defense mechanisms. Because of immunosenescence, older individuals are more susceptible to infections, take longer to recover from illnesses and have a diminished response to vaccinations. This heightened vulnerability is particularly evident during disease outbreaks or pandemics, where older adults face an increased risk of severe outcomes and mortality [1,2].

3. Chronic inflammation and aging

Another significant aspect of aging and immunity is the rise of chronic inflammation, commonly referred to as *inflammaging*. This chronic, low-grade inflammation occurs as the immune system undergoes changes over time, resulting in the production of pro-inflammatory molecules even in the absence of infection or injury. Inflammaging is believed to contribute to the development of various age-related conditions, including cardiovascular disease, neurodegenerative disorders and certain types of cancer [5,6]. Inflammaging is a complex phenomenon that arises from the intricate interplay of various immune and non-immune cells as well as the communication between them. It involves the activation of immune cells, such as macrophages and dendritic cells, which release pro-inflammatory cytokines and other signalling molecules. These molecules, including interleukins and tumor necrosis factor-alpha (TNF- α), create a chronic inflammatory milieu that can have detrimental effects on surrounding tissues and organs [5,6]. One of the key drivers of inflammaging is the accumulation of cellular damage and debris over time. As cells age, they may become less efficient at clearing out molecular waste, leading to the release of potentially harmful substances into the surrounding environment. This triggers an immune response aimed at removing the debris, but in

the process, it can result in a chronic state of inflammation that further contributes to tissue damage and dysfunction. See Figure 1 [5,6].

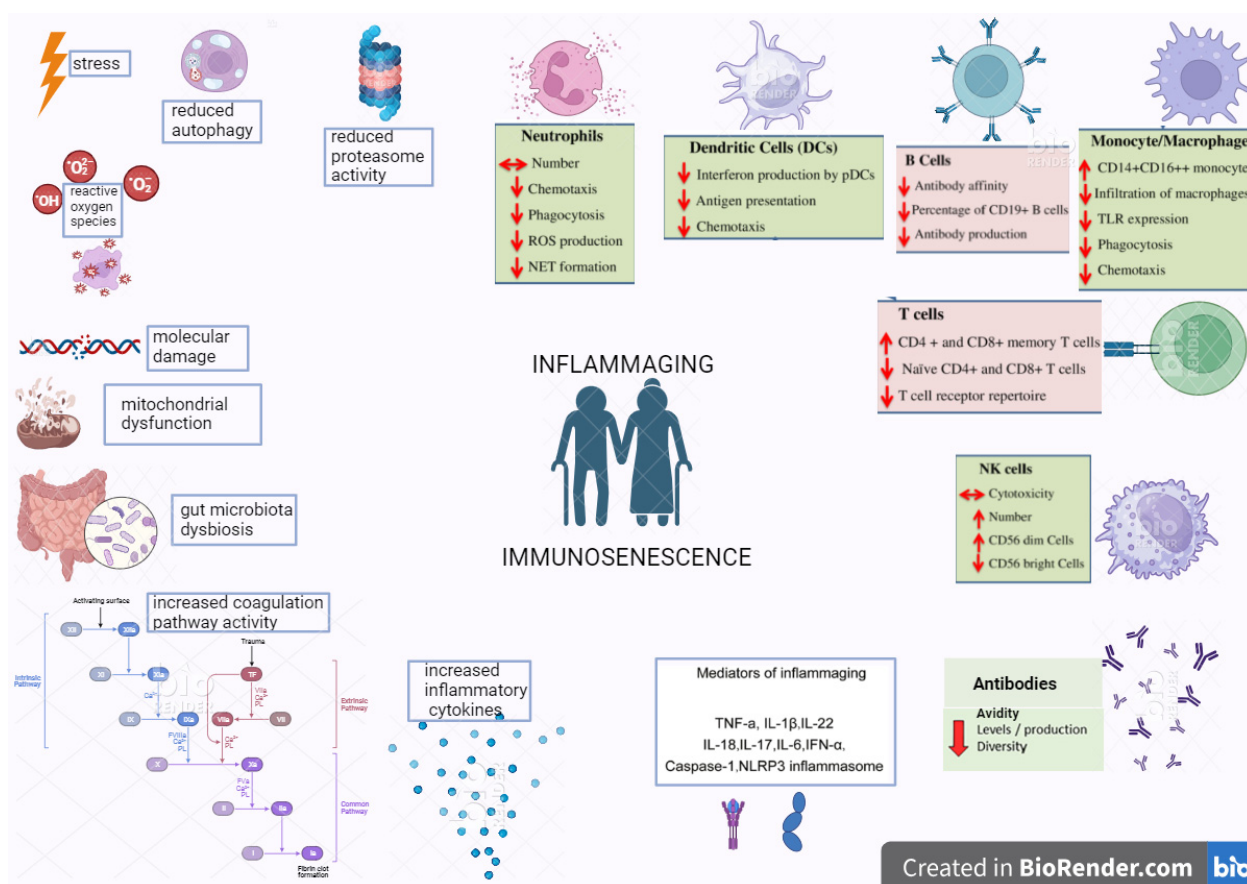


Figure 1. Illustration of elements contributing to inflammaging and immunosenescence as well as the complex cellular and non-cellular interplay between aging and the immune system. In the process of aging, disruptions in the balance of cellular equilibrium occur, leading to inflammaging, which subsequently leads to the release of pro-inflammatory cytokines [7].

Inflammaging's impact on age-related diseases is far-reaching. For example, in cardiovascular disease, chronic inflammation can damage blood vessels, leading to atherosclerosis (the buildup of fatty plaques) and increasing the risk of heart attacks and strokes. Inflammation promotes the adherence of immune cells to vessel walls and the formation of plaques, impairing blood flow and overall cardiovascular health [8]. In addition, inflammation in the brain, often referred to as neuroinflammation, has been implicated in various neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease. Inflammaging may contribute to the accumulation of abnormal protein aggregates and exacerbate neuronal damage in these conditions [9]. Furthermore, chronic inflammation can create an environment conducive to cancer development. Inflammatory molecules can promote DNA damage, cell proliferation and resistance to apoptosis (programmed cell death), all of which can contribute to the initiation and progression of certain types of cancer [10].

Moreover, inflammaging has been linked to insulin resistance and metabolic dysfunction, contributing to the development of type 2 diabetes and obesity-related complications [11].

Understanding the mechanisms underlying inflammaging and its consequences is a burgeoning area of research. While the exact triggers and pathways involved are still being elucidated, it is becoming increasingly clear that inflammaging is not a standalone process. It interacts with other facets of aging, such as changes in the gut microbiota and cellular senescence (a state of irreversible cell cycle arrest), to collectively influence health outcomes in older individuals. Mitigating the impact of inflammaging holds promise for improving the health and well-being of aging populations. Strategies aimed at reducing chronic inflammation may involve dietary interventions, exercise regimens and medications targeting specific inflammatory pathways [12]. By unravelling the complex relationship between aging, inflammation and disease, researchers aim to develop interventions that could delay the onset or progression of age-related chronic conditions and enhance the overall quality of life in older adults.

4. Emerging research: the gut microbiota connection

Recent research has uncovered a fascinating link between the gut microbiota and the aging immune system. The gut microbiota, composed of trillions of microorganisms residing in the gastrointestinal tract, plays a vital role in maintaining immune homeostasis and overall health. With age, the diversity and composition of the gut microbiota undergo significant shifts, potentially impacting the immune system's functionality. Studies have suggested that an age-related decline in beneficial gut bacteria and an increase in harmful ones might contribute to immune dysfunction. This finding opens new avenues for therapeutic interventions that target the gut microbiota to improve immune health in older individuals [13,14]. The gut microbiota is an intricate ecosystem consisting of various bacterial species, viruses, fungi and other microorganisms. These microorganisms partake in diverse physiological processes, including aiding in the digestion of dietary components, producing essential metabolites and influencing the development and regulation of the immune system. With age, the delicate balance within the gut microbiota may be disrupted, a phenomenon known as dysbiosis. Dysbiosis can lead to an overgrowth of potentially harmful microorganisms and a decline in beneficial ones, thereby influencing immune responses [15,16]. Researchers have discerned that alterations in the gut microbiota composition during aging could impact immune function in several ways. First, the gut microbiota interacts closely with the immune cells residing in the gut-associated lymphoid tissue (GALT), shaping the immune response to various challenges. Second, the gut microbiota contributes to the maintenance of the intestinal barrier, preventing the translocation of harmful substances into the bloodstream. Dysbiosis may compromise this barrier function, potentially leading to systemic inflammation and immune activation. Moreover, the gut microbiota is engaged in a dynamic dialogue with the immune system, influencing the balance between pro-inflammatory and anti-inflammatory responses [15,16]. A disruption in this equilibrium, stemming from changes in the gut microbiota, can exacerbate inflammaging and contribute to the development of age-related diseases [17]. Strategies that target the gut microbiota to enhance immune health in older adults are currently being explored. Prebiotics, probiotics and synbiotics (combinations of pre- and probiotics) are gaining attention as potential interventions to modulate the gut microbiota composition and activity [18]. These interventions aim to promote the growth of beneficial bacteria and restore microbial diversity. Furthermore, the concept of fecal microbiota

transplantation (FMT), which involves transferring a healthy donor's fecal microbiota into a recipient's gut, is being investigated for its potential to rejuvenate the gut microbiota and consequently improve immune function in older individuals. In conclusion, the emerging link between the gut microbiota and the aging immune system presents a promising avenue for research and intervention [19]. Understanding the intricate interplay between these factors could offer insights into novel strategies to promote healthy aging and bolster immune resilience in older populations. By leveraging the potential of the gut microbiota as a therapeutic target, researchers aim to develop interventions that contribute to extending health span and improving the overall well-being of aging individuals.

5. Strategies for enhancing immunity in aging

Understanding the intricate interplay between aging and immunity lays the foundation for the development of strategies aimed at bolstering immune function and improving the overall health of older adults. Several potential approaches hold promise in addressing the challenges posed by immunosenescence and inflammaging:

Vaccination: tailoring vaccination strategies to the specific needs of the aging population is a pivotal step in enhancing immune protection. Adjuvanted vaccines, which contain additives to enhance the immune response and high-dose vaccines designed to stimulate a more robust immune reaction, have shown promise in improving vaccine efficacy in older individuals. By fine-tuning vaccines to account for age-related changes in immune function, we can enhance the body's ability to mount a strong defense against infectious diseases [20,21].

Lifestyle modifications: encouraging healthy lifestyle habits can exert a positive influence on immune function and overall well-being in older adults. Regular physical activity has been shown to enhance immune responses by promoting the circulation of immune cells and reducing chronic inflammation. Adopting a balanced diet rich in nutrients, antioxidants and fiber supports immune health by providing the necessary building blocks for immune cells and regulating inflammation. Additionally, stress management techniques, such as mindfulness and relaxation, can help mitigate the detrimental effects of chronic stress on the immune system [22].

Anti-inflammatory interventions: addressing the consequences of inflammaging is a critical aspect of enhancing immunity in aging. Exploring the use of anti-inflammatory medications or natural compounds with anti-inflammatory properties could potentially dampen the chronic inflammation associated with aging. These interventions might not only alleviate the burden of age-related diseases but also contribute to extending health span [23].

Targeted therapies: developing innovative therapies that specifically target age-related immune changes holds considerable potential. Researchers are investigating various approaches to restore immune function in older individuals. These therapies could range from immune-modulating drugs that target key pathways involved in immunosenescence to regenerative strategies that rejuvenate the production of immune cells [24].

Microbiota-based interventions: recognizing the influence of the gut microbiota on immune health has paved the way for microbiota-based interventions. Probiotics, which are beneficial microorganisms, and prebiotics, which nourish beneficial gut bacteria, are being explored for their potential to positively impact the gut microbiota composition and immune responses in older adults.

Additionally, the innovative approach of fecal microbiota transplantation (FMT) is being studied to restore a more youthful gut microbiota profile and potentially enhance immune function [19,25].

These multifaceted strategies underscore the potential to address the challenges posed by immunosenescence and inflammaging. As our understanding of the aging-immunity nexus evolves, implementing these approaches could contribute to maintaining the health and quality of life of older adults. By adopting a comprehensive approach that encompasses vaccination optimization, lifestyle modification, anti-inflammatory interventions, targeted therapies and microbiota-based interventions, we can work towards extending the period of healthy aging and promoting immune resilience in the aging population.

6. The role of public health

Effectively addressing the challenges presented by the intricate relationship between aging and immunity demands a comprehensive and collaborative approach encompassing policymakers, healthcare providers, researchers and the community at large [26,27]. Public health initiatives play a pivotal role in shaping the well-being of aging populations by focusing on several key aspects. Public health efforts should center on advocating for and facilitating healthy aging practices. This involves disseminating information about lifestyle modifications, nutrition, physical activity and stress management that can positively impact immune function and overall health in older adults. Next, a vital component of public health efforts involves supporting and conducting research into age-related immunological changes. By fostering a deeper understanding of these changes, evidence-based interventions can be developed to enhance immune resilience and mitigate the effects of immunosenescence and inflammaging. In addition, healthcare systems must ensure that older adults have equitable access to essential healthcare services. This includes not only medical treatments but also vaccinations, preventive screenings and tailored healthcare services designed to address the unique needs of aging individuals [28–30]. Moreover, public health agencies should orchestrate comprehensive vaccination campaigns targeted at older adults. These campaigns should not only focus on routine vaccines but also highlight the importance of specialized vaccines designed to optimize immune response in aging individuals. Furthermore, raising awareness among older adults about the significance of maintaining a healthy lifestyle and seeking timely medical attention is paramount. Empowering them with knowledge about the impact of lifestyle choices on immune resilience can motivate healthier behaviors and encourage proactive healthcare-seeking behaviors. Finally, community involvement is crucial in promoting healthy aging. Community programs and initiatives can provide opportunities for social engagement, physical activity and educational sessions that promote immune health and overall well-being [28–30].

By aligning efforts across these domains, public health initiatives can create a synergistic effect that results in enhanced immune resilience and improved quality of life for older adults. As the global population continues to age, it becomes increasingly imperative to invest in policies and interventions that foster healthy aging and fortify immune health. Such efforts not only benefit individual older adults but also contribute to the broader goal of building more resilient and vibrant aging societies [26,27].

7. Conclusions

Aging and immunity form a complex and dynamic relationship that profoundly influences the health and well-being of older adults. As our global population continues to age, understanding the mechanisms behind immunosenescence and inflammaging becomes ever more critical. We believe this special issue of *AIMS Allergy and Immunology* is one the perfect venues to spark evidence-based discussion on this topic. By fostering research, investing in targeted therapies and implementing public health strategies, we can strive to enhance the quality of life for older adults and promote healthy aging across societies. Embracing the challenges and opportunities presented by aging and immunity will be crucial in shaping a healthier and more resilient future for the aging world.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The author declares no conflict of interest in this paper.

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