©IDOSR PUBLICATIONS

ISSN: 2550-794X

International Digital Organization for Scientific Research IDOSRJSR1.1.11.100
IDOSR JOURNAL OF SCIENTIFIC RESEARCH 9(1) 1-11, 2024.
https://doi.org/10.59298/IDOSRJSR/2024/1.1.11.100

# Immunological Changes with Age and Innovative Approaches to Bolster Immune Function in Older Adults

**Nkiruka R Ukibe[1], Chizoba Rita Dike [1], A.C. Ihim[1], Ezinne G. Ukibe[2], Blessing C. Ukibe[2], Victory Ezennia Ukibe[3] and *Emmanuel Ifeanyi Obeagu[4]**

**[1]Department of Medical Laboratory Science, College of Health Sciences, Nnamdi Azikiwe University, Awka, P. M. B 5025, Anambra State, Nigeria**
**[2]Department of Medicine, College of Health Sciences, Nnamdi Azikiwe University, Awka, P. M. B 5025, Anambra State, Nigeria**
**[3]Department of Radiography and Radiological Sciences, Nnamdi Azikiwe University, Awka, P. M. B 5025, Anambra State, Nigeria**
**[4]Department of Medical Laboratory Science, Kampala International University, Uganda**

***Corresponding author: Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda, emmanuelobeagu@yahoo.com, ORCID: 0000-0002-4538-0161**

## ABSTRACT

Aging is accompanied by a progressive decline in immune function, known as immunosenescence, which renders elderly individuals more susceptible to infections, reduced vaccine efficacy, and increased incidence of autoimmune diseases and cancer. This decline in immunity is characterized by alterations in both innate and adaptive immune responses, including reduced T-cell diversity, impaired function of antigen-presenting cells, and dysregulated cytokine production. Additionally, inflammaging, a chronic low-grade inflammatory state, further contributes to age-related immune dysfunction. Strategies aimed at enhancing immunity in aging individuals have garnered significant attention. Promising interventions include lifestyle modifications encompassing regular exercise, balanced nutrition, and adequate sleep, which can positively impact immune function. Furthermore, vaccination strategies tailored for the elderly, such as high-dose vaccines or adjuvanted formulations, aim to bolster vaccine efficacy. Immunomodulatory therapies, including supplementation with specific micronutrients and pharmacological interventions targeting immune senescence, hold promise for rejuvenating immune responses in older individuals. Understanding the mechanisms underlying immunosenescence and inflammaging is critical in developing targeted approaches to enhance immunity in aging populations. A holistic approach combining lifestyle interventions, vaccination strategies, and innovative immunomodulatory therapies holds potential for mitigating the impact of age-related immune decline and improving overall healthspan in the elderly.

**Keywords**: Immunosenescence, Aging, Immunity, Inflammaging, Elderly, Immunomodulation, Vaccination Strategies, Immune Rejuvenation, Geriatrics

## INTRODUCTION

Immunology began with two significant discoveries in the last quarter of the nineteenth century. The first was Elias Metchnikff's (1845-1916) discovery of phagocytic cells, which absorb and eliminate pathogens. This created the groundwork for innate immunity. The second breakthrough was the identification of antibodies that neutralize microbial poisons by Emil Behring (1854-1917) and Paul Ehrlich (1854-1915). This served as the foundation for acquired immunity [1]. The immune system exists to protect the host from harmful environmental agents, particularly pathogenic organisms such as bacteria, viruses, fungus, or parasites [2]. Immunity is an organism's ability to defend itself (and be resistant) against antigens from both the external and internal environment. In general, an antigen is any molecule capable of generating an immune system reaction [3-6]. Our body is endlessly exposed to

microbial agents and environmental noxious substances. These may cause serious illness, or toxicity to the body; therefore, they must be eliminated [7-10].

The innate immune system is the first line of host defense, recognizing invading pathogens by sensing pathogen-associated molecular patterns (PAMPs) such as foreign polysaccharides, glycoproteins, lipoproteins, and nucleic acids, as well as damaage-associated molecular patterns (DAMPs) such as molecules produced as a result of host cell and tissue damage [11-16]. Four categories of protective barriers are considered to be part of innate immunity: physiologic (temperature, low pH, and chemical mediators), endocytic and phagocytic, inflammatory, and anatomic (skin and mucous membrane) [17]. Innate immune responses limit viral entry, translation, replication and assembly, help identify and remove infected cells and coordinate and accelerate the development of adaptive immunity. The development of adaptive immunity is accelerated and coordinated by innate immune responses, which also help detect and eliminate infected cells and restrict viral entrance, translation, replication, and assembly. Using a variety of PRRs, innate immune cells, such as macrophages, monocytes, dendritic cells, neutrophils, and innate lymphoid cells (ILCs), such as natural killer (NK) cells, can trigger cells, and inflammatory signaling pathways and immune responses by identifying PAMPs, or damage-associated molecular patterns [18].

**Immunity and Aging**

Aging is a multimodal process that happens at multiple levels and involves significant, simultaneous remodeling of organs, tissues, and cells, traditional molecular biology techniques are limited in their ability to address this complexity. Among the main characteristics of aging are the loss of physiological integrity, disruption of tissue homeostasis, and growing decline of numerous biological systems, including the immune system [19]. Full blood counts, T and B cell counts including their subsets, the amount of immunoglobulin in the serum, and the presence of particular antibodies are among the tests that clinicians may use to assess immune competency. Although this gives a broad overview of some immune system components, unless values are significantly below the usual ranges, it does not give a useful indicator of a person's ability to respond to a particular threat. An older individual with immune parameters within the normal levels who may have immune dysfunction would thus not be easily identified. So, any attempt to restore immunity in older individuals first requires that simple methods of assessment are derived to determine the effectiveness of the process as a whole. These techniques of assessment must: (i) be related to function; (ii) yield results reasonably quickly; (iii) be relatively non-invasive; and (iv) call for relatively basic equipment [20]. Thymic atrophy, a decrease in peripheral blood naïve cells, and a relative increase in memory cell frequency are the results of aging-related declines in adaptive immune responses. These changes result in weakened immune responses to vaccinations, heightened susceptibility to infectious illnesses, reactivation of dormant viral infections like varicella-zoster virus (VZV), commonly known as chickenpox, and lowered cancer immunosurveillance. Inflammaging, a long-term state of innate immunological activation linked to aging, plays a role in the pathophysiology of the chronic immune disorders associated with aging [21]. Crucially, they also demonstrated that increased levels of CCL2, a chemokine that attracts immune cells and is recognized by the proinflammatory monocytes' CCR2 receptor, was a major factor in drawing those detrimental innate immune cells to the injection site in older people. Senescent tissue fibroblasts, which are significantly more prevalent in the elderly, produce CCL2. The well-known, largely proinflammatory senescence-associated secretory phenotype (SASP), which includes CCL2 secretion, has been linked to a number of detrimental effects of aging, such as tissue loss (sarcopenia), an increased risk of cancer, and a collection of degenerative changes in various organ systems collectively referred to as "inflammaging." [21]. One characteristic of immunological aging that is sometimes referred to as "inflammageing" is an unresolved systemic inflammation in the absence of pathogens in elderly organisms. An imbalance in the production of pro- and anti-inflammatory molecules is a hallmark of inflammation, and it is a strong predictor of death and chronic illnesses [20]. The immune system undergoes change as we age. This eventually results in a decrease in immunological function, which raises the risk of contracting infectious diseases, reduces the benefit of immunizations, and increases the risk of developing age-related inflammatory illnesses [22].

**Immunosenescence**

Immunosenescence, a process brought on by aging that affects the makeup, number, and functionality of immunological organs, immune cells, and cytokines, is the immune system's decline in function. Immunosenescence increases the risk of several age-related illnesses, such as cancer, cardiovascular disease, autoimmune disorders, neurodegenerative diseases, and COVID-19, which can ultimately lead to organ failure and death. Immunosenescence is defined by age-related reductions in coping skills and

concurrent elevations in proinflammatory state. Stress and a persistent antigen load are the root causes of this syndrome, which Claudio Franceschi initially described in 200012 and dubbed "inflammaging." Thymic involution has also been one of the most notable and pervasive modifications. Both the innate and adaptive immune systems are impacted by immunosenescence, with some immune cell types being more severely affected [23]. Immunosenescence is characterized by three main features: (i) a decreased capacity to react to novel antigens; (ii) the build-up of memory T cells; and (iii) a persistent state of low-grade inflammation known as "inflamm-aging." (Anna Aiello *et al*., 2019). Although T cells are significantly impacted, this multifactorial phenomenon—which Roy Walford named "immunosenescence"—affects both acquired and innate immunity [22].

**Cellular Senescence**

Cellular senescence is defined as the irreversible exit from the cell cycle in response to various types of stress such as uncontrolled DNA replication and genotoxic, oxidative and inflammatory stress. SnCs are characterized by evidence of telomere associate foci (TAFs), senescence-associated distension of satellites (SADS), senescence-associated heterochromatin foci (SAHF), senescence-associated ß-galactosidase (SA-ß-gal) and upregulation of at least 1 cell cycle dependent kinase inhibitor (e.g., p16INK4a, p21Cip1). Most tissues, including lymphoid tissues, have been observed to have an increase in cellular senescence, a cell fate that affects various cell types. Additionally, the quantity of senescent cells (SnCs) rises with age. The slow deterioration of a cell's capacity for division, proliferation, and physiological function over time is known as cellular senescence. Research on the molecular mechanisms and signaling pathways that influence aging has yielded significant findings for scientists. In this context, we examine and synthesise these novel developments on three fronts: molecular (genomic instability, telomere dysfunction, epigenetic modifications, proteostasis loss, autophagy compromise, mitochondrial dysfunction), cellular (cellular senescence, stem cell exhaustion, and intercellular communication), and systemic (deregulated nutrient sensing) [24].

**Impact of Immunosenescence on both Innate and adaptive system**

The innate immune system can also be stimulated by the so-called internal GARBage system. Thus, a heightened inflamm-aging state is produced as a consequence of (1) dysfunctional mitochondria, (2) defective autophagy/mitophagy (disposal of dysfunctional organelles), (3) endoplasmic reticulum stress, (4) activation of inflammasome by cell debris and misplaced self-molecules, (5) defective ubiquitin/proteasome system (misfolded/oxidized proteins), (6) activation of DNA damage response, (7) senescent T cells and their senescence-associated secretory phenotype (SASP), and (8) age-related changes in the composition of gut microbiota (dysbiosis). Intracellular alterations including altered autophagy, mitochondrial malfunction, and modifications to DNA repair processes coincide with chronic problems associated with aging.

**Chronic low-grade inflammation**

However, because of persistent low-grade inflammation, immune cells are always kept on guard. As demonstrated in the case of centenarians, anti-inflammatory chemicals may, however, counterbalance this state. As long as chronic low-grade inflammation (also known as "inflamm-aging") is kept under control, it can serve as an effective defensive mechanism in response to lifelong antigenic stress. Now once anti-inflammatory molecules are missing, as is the case with age, it is evident how detrimental this physiological state may be to the entire body [25]. Age-related changes in adaptive immunity are striking and can be boiled down to two main issues: (1) bone marrow reorganization and the pool's differentiation into the myeloid lineage, which outnumbers the lymphoid compartment; and (2) physiological thymic involution, which jeopardizes the generation of naïve T cells. The combination of these two elements can aid in the explanation of the previously documented decline in lymphocytes' ability to regenerate in older individuals when compared to myeloid-derived cells. Elderly people are more likely to contract infectious infections. The elderly are more likely than their younger counterparts to come with respiratory and urinary tract infections, and their prognosis is often worse. Mucosae's compromised barrier function and a weakened humoral and cellular adaptive immune response could be the causes of the elderly's heightened vulnerability to pathogenic microbes. Furthermore, the senescence of natural killer (NK) cells may impact the immune system's homeostasis in the elderly, raising the risk of viral infections and cancer. Finally, aging-related cell dysfunctions that result in an exhausted phenotype are a crucial aspect of the immune system remodeling process. These dysfunctions may hasten tissue damage and impair modulatory mechanisms [26]. Apart from their ability to carry out phagocytosis, neutrophils can also, in certain situations, release a structure resembling a mesh, known as neutrophil extracellular traps (NET), which help to physically confine the pathogenic

agent—mostly microorganisms—and make it easier for it to come into contact with microbicidal peptides and enzymes. Free radicals known as reactive oxygen species (ROS) are created following oxidative bursts in phagosomes and are essential to the phagocytes' microbicidal activity. In actuality, ROS can actually cause NET formation in addition to directly aiding in the removal of microorganisms. In older adults, neutrophils produce less free radicals (ROS) [26].

**Thymic Involution**

Thymic involution, which is characterized by a decrease in TECs and an increase of adipose tissue within the thymus, is one of the most common changes during immune system senescence and affects most vertebrates. The thymus plays a critical role in the cellular immune system by generating T lymphocytes, which are involved in anti-tumor immunity, anti-viral, and anti-intracellular infections, as well as the establishment of self-tolerance to avoid autoimmune disorders. During the entire process of thymus organogenesis, maturation, and involution, gene regulation not only occurs at the transcriptional level via transcription factors, but is also affected at the post-transcriptional level by microRNA (miRNA) transcripts. By producing T cells, the thymus contributes significantly to the cellular immune system. T lymphocytes fight viruses, tumors, and intracellular infections. They also help build self-tolerance to prevent autoimmune diseases. Gene control happens at the transcriptional level through transcription factors and at the post-transcriptional level through microRNA (miRNA) transcripts during the whole thymus organogenesis, maturation, and involution process. One of the animal body's most active organs is the thymus. It experiences three processes: involution (cell senescence and apoptosis), development (proliferation, differentiation, and apoptosis), and organogenesis (cell migration, proliferation, and differentiation). T lymphocytes are also produced by the thymus to assist the cellular immune system. Generally speaking, during thymus growth, two key processes interact and regulate each other: T lymphocyte development, which produces functional T cells, and stromal cell development, which, mostly through TECs, builds and maintains the thymic milieu to promote T cell maturation. These two procedures show sequential or gradual developmental routes [27]. The organ grows quickly during development, reaches its maximum size during adolescence, and then starts to shrink with aging; in humans and mice, involution starts as early as birth and ends no later than the onset of puberty. Reduced thymocyte counts and naïve T cell production are the outcomes of this thymic regression, which also involves reductions in thymic bulk, loss of thymic structure, and disarray to thymic architecture. Acute atrophy of the thymus can occur during physiological stress situations, including illness, pregnancy, and cancer treatments, in addition to chronic age-related involution. Reduced naïve T cell production and weakened host immunity are the outcomes of stressed-induced thymic involution, which is typically reversible and returns to normal in terms of size and function after the insult is removed [28]. But as we age, the thymus becomes less able to create central tolerance, which leads to more self-reactive T cells escaping to the periphery and taking part in the inflammatory process. There have historically been two schools of thinking about the possible causes of diminished thymopoiesis associated with aging. The first is the notion of impaired hematopoietic stem cells, as older bone marrow (BM) produces fewer hematopoietic stem cell (HSC) progenitors. Consequently, the thymus shrinks as a result of fewer early T-cell progenitors (ETP) entering the thymus from the BM. Second is the idea of a defect in stromal niches of the BM or thymus. As a result, the thymic niche is where age-related characteristics of thymic involution predominantly manifest themselves before having an effect on the formation of ETPs [29].

**Effect of T cell development and repertoire diversity**

A wide repertory of T-cell receptors (TCRs), the main factor influencing the probability of identifying certain antigens, is necessary for the best immune response to a wide range of unknown antigens. Both chronic dysfunctions, such as those linked to age-associated involution and recurring infections, and acute immunological insults, such as those brought on by infections, stress, or antineoplastic therapy, can seriously impair thymic function and T-cell output. Highly varied TCR repertoires are necessary for effective T-cell responses because they guarantee the capacity to recognize a broad variety of Ags. Together with diversity, repertoire diversity is frequently employed as a metric of the effectiveness of the immune response. Clonality, which describes the quantity and frequency of detected TCRs within a sample, is inversely correlated with repertoire diversity [30].

**Inflammaging**

Chronic low-grade inflammation associated with aging. In order to improve species survival, the inflammatory process is a vital immunological defensive mechanism in living things. As a first line of defense against viruses, poisons, or allergens, short-term, acute inflammation is triggered. Under normal circumstances, the elimination of pathogens, infected cells, and repair of damaged tissues to restore

body homeostasis are made possible by the closely coordinated actions of multiple defense components, including immune cells, endogenous anti-inflammatory agents, and tissue remodeling processes. However, additional defense mechanisms are activated to produce a long-term unresolved immune response known as chronic inflammation when this complex acute inflammatory response is unable to end and continues. Leukocytes collected by macrophages and lymphocytes, together with a variety of other cellular constituents, are involved in chronic inflammation, which usually presents itself over an extended period of time in a low-grade way. It is crucial to understand that alterations in the cellular redox state and signaling pathways leading to cell death are causally related to this chronic inflammation. An ongoing state of systemic inflammation is brought on by the deregulation of the immune response, which is one of the main aging-related alterations. Cytokines and chemokines are two of the dysregulated proinflammatory mediators that play a crucial role in the development of chronic inflammation and the immunosenescence process [31]. The components of inflammatory cytoplasmic multiprotein complexes, known as inflammasomes, are adaptor apoptosis-associated speck-like (ASC) protein, procaspasce-1, and NLR protein 3 (NLRP3). When an inflammasome is activated, it causes caspase-1 expression and maintains the release of proinflammatory cytokines, such as IL-1β and IL-18. Two steps are needed for the NLRP3 inflammasome to assemble: the priming phase and the activation phase. Priming involves post-translational changes that are required for NLRP3-mediated gene expression and facilitates accurate inflammasome assembly. In order to cleave pro-IL-1β into IL-1β paired with pro-IL-18, NLRP3 polymerizes to ASC upon inflammasome activation and recruits procaspase-1. With caspase-1 activation and proinflammatory cytokine release (IL-1β/IL-18) in response to cellular injury, the NLRP3 inflammasome is a crucial component of the innate immune system. As was previously indicated, "inflammaging" (also known as "inflammaging, inflammageing") refers to the low-grade, persistent, asymptomatic inflammation that happens during aging in the absence of infection. Atherosclerosis, chronic renal disease, cardiovascular disease, adult diabetes, and Alzheimer's disease are just a few of the age-related chronic diseases that are exacerbated by inflammation and have a detrimental impact on health. The exact reasons of inflammation are still mostly unknown, but they include the following: (i) the release of damaged cells and the accumulation of altered molecules (microRNA, mitochondrial DNA, or histones), which are recognized by immune system cells and cause inflammation to activate and develop; (ii) the growth of senescent cells that release pro-inflammatory molecules into the blood; (iii) chronic stress conditions; and (iv) disruption of autophagic processes (v) alteration of the intestinal microbiota; (vi) immunosenescence, defining the steady waning of immune system function during ageing. Autophagy and microbiome homeostasis are rhythmically regulated by the biological clock and their derangement cause several pathological processes underlying inflammatory, metabolic, degenerative, and neoplastic diseases. An in-depth discussion of the involvement of these processes in pathological conditions and in age-related diseases goes beyond the boundaries of this review; therefore, we refer to exhaustive articles already present in the international scientific literature. Innate and adaptive immune response, including humoral and cellular immunity, decays during aging [32]. Increasing evidence shows that ageing significantly affects all cell compartments of the innate immune system. Numerous neutrophilic functions, for instance, phagocytic capacity, ROS production, and intracellular killing ability, are impaired in the elderly. Similarly, macrophage functions, including phagocytic activity, cytokine and chemokine secretion, antigen presentation, infiltration and wound repair and antibacterial proficiency decline with ageing. Age-related reduction in mast cell and eosinophil and alterations of functional properties have been demonstrated [33].

**Contribution of inflammaging to age-related diseases**

Decreases in cellular repair mechanisms occur with aging and age-related diseases, resulting in the build-up of damaged molecules, proteins, DNA, and lipids, ultimately leading to the loss of effective cellular function. Age-related decreases in the cell's ability to undergo autophagic breakdown may also have an impact on aging. Age-related slowdowns in both of the primary intracellular protein degradation mechanisms are accompanied by a physical decrease in autophagy-related proteins, which adds to the build-up of misfolded proteins and damaged macromolecules within the cell. Conditions including obesity, Crohn's disease, and cardiovascular disease that are linked to elevated oxidative stress also slow down cellular clearance and decrease autophagy, which exacerbates the illness [34].

## Molecular Mechanism

### Telomeres and cellular aging

The genomic regions at the ends of linear chromosomes are called telomeres. In vertebrates, telomeric DNA is composed of TTAGGG repeats that are bound by a collection of proteins that control their biological activities and prevent them from being identified as DNA damage that would otherwise set off a DNA damage response (DDR) [35]. Many writers now acknowledge that TL is a potent biomarker of aging and pathological disorders linked to aging [36]. Furthermore, the molecular mechanisms behind the age-related telomere shortening phenomenon are still unclear and the phenomenon itself is incredibly complex. Specifically, it is still uncertain if telomeric aging is a reflection of a process similar to the mitotic clock, or if it is a biomarker of stress or a biological mechanism that sends messages to the cell related to stress [37]. Because they shield chromosomes from end-to-end fusions and chromosomal instability, telomeres are essential for a variety of biological activities. At the beginning of the end and in the middle of the beginning: structure and maintenance of telomeric DNA repeats and interstitial telomeric sequences. The protective protein complex known as Shelterin binds the repeated TTAGGG sequences that make up telomeric DNA. This complex forms the telomere structure, safeguarding chromosomal ends, together with proteins that are involved in chromatin remodeling [38]. The chromosomal ends' creation of DNA loops, or T-loops, and the transcription of telomeres to produce G-rich RNA, or TERRA, are two important telomere characteristics. The 3′ end of the G-rich strand projects as the G-overhang, a single stranded overhang in the t-loop structure [39].

## Increased susceptibility to infections

### Respiratory infections

An age-related rise in viral infection susceptibility is partly due to compromised innate and adaptive immune systems. When it comes to respiratory viral infections, such as influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, aging is a significant factor that increases morbidity and death [40-52]. The number of people 65 and older worldwide will nearly treble to 1.5 billion by 2050. (Population Division of the United Nations Department of Economic and Social Affairs, 2020). This perspective calls for the creation of plans aimed at enhancing the lives of the elderly [53-59].

### Vaccine efficacy in the elderly

The best and most practical way to safeguard the health of elderly patients is through preventive medicine, and the best course of action is to vaccinate against the most prevalent infectious diseases. Three dangerous pathological conditions—seasonal influenza, pneumococcus infection, and varicella zoster virus reactivation—are major sources of morbidity and mortality for elderly individuals, who are more vulnerable than young persons [60]. The elderly should also receive regular booster shots against tetanus, diphtheria, pertussis, and polio. In certain countries (Austria, France, Liechtenstein, and Portugal), the booster intervals are shortened for those over 65 due to a faster decline in antibodies with age. The effectiveness of a vaccine, which measures its ability to prevent a particular infection, and its efficacy—a measure of its capacity to generally improve an older person's health status and prevent other related diseases—are what determine the value of vaccines for the elderly. Therefore, it is crucial to develop vaccination techniques that are especially suited for the aged population, taking into account the aging immune system and inflammatory processes in both vaccine formulations and immunization procedures. Geriatric medicine developed a number of syndromes to manage the variability of elderly physiology and pathophysiology. These syndromes enable the elderly population to be categorized based on their relative risk of developing certain diseases. These include frailty, minor cognitive impairment, and chronic obstructive pulmonary disease. The elderly must receive vaccinations while maintaining a careful balance between immunosenescence, which reduces their receptivity to immunization, and inflammation [60].

### Currently recommended vaccines for the elderly

#### 1. Influenza Vaccine

One of the primary causes of illness and mortality in the elderly is influenza infection. Annual influenza outbreaks are thought to cause between 3 and 5 million instances of severe illness and between 290.000 and 650.000 fatalities globally. http://www.who.int/news-room/detail/14-12-2017-up-to-650-000-people-die-of-respiratory diseases-linked-to-seasonal). The World Health Organization (WHO) considers annual influenza vaccination to be the most effective method of preventing influenza, and many high-income countries prescribe it for elderly individuals. However, compared to adults, the effectiveness of influenza vaccinations in older patients is just 30–50% [60]. There are now two varieties of influenza vaccines available: live attenuated influenza vaccine

(LAIV) and inactivated influenza vaccine (IIV). Antigens from one strain of influenza B (the Yamagata or Victoria lineages) and two subtypes of the influenza A strain (H1N1 and H3N2) are included in the trivalent inactivated influenza vaccine (TIV). The production of quadrivalent inactivated influenza vaccines (QIV), which contain two A strains and two B strains and have now been licensed in some countries, was spurred by the frequent observations of co-circulation of the two B lineages and the frequent mismatch between the vaccine component and the circulating strains. LAIV is primarily advised for use in children. It was originally licensed and used in Russia and North America in 2003. Because of a phenomenon known as "antigenic drift," which is the spontaneous change of the surface proteins neuraminidase (NA) and hemagglutinin (HA), influenza viruses are always changing [60]. Numerous tactics have been used to enhance influenza shots administered to senior citizens. These include the formulation of the inactivated vaccine using oil-in-water emulsion adjuvants, the administration of the vaccine via intradermal rather than intramuscular route, and the increase of the vaccine antigen from 15 to 60 µg of HA protein per dose. Though these responses do not reach the magnitude of those induced by the standard dose vaccine in young adults, the high dose vaccine has been linked to a stronger immune response and better effectiveness than the regular dose flu vaccine in older people. The high dose vaccine contains four times the amount of HA antigen compared to the traditional formulation [60].

**2.Pneumococcal vaccine**

Blood or cerebrospinal fluid are examples of ordinarily sterile sites where the presence of the bacteria is known as invasive pneumococcal disease (IPD), which is caused by Streptococcus pneumoniae, the most often isolated agent of community-acquired pneumonia. The incidence of pneumococcal illness rises sharply in those over 65, with the condition most common at the extremes of age. Immunosenescence and co-morbidities make people more vulnerable to pneumococcal illness in particular and community-acquired pneumonia in general. Therefore, it is advised that older adults have a pneumococcal immunization. The 23-valent pneumococcal polysaccharidic vaccine (PPV23) contains 25 µg of purified pneumococcal polysaccharide per serotype; the 13-valent conjugated vaccine (PCV13) contains 2.2 µg of each polysaccharide type, with the exception of 4.4 µg of serotype 6B, conjugated to the non-toxic mutant of diphtheria toxin CRM197 and 0.125 mg of aluminum phosphate as an adjuvant. These are the licensed pneumococcal vaccines. PCV13 is advised for use in older populations even though it covers fewer serotypes since it can cause a T-dependent response and high titers of functional (opsonophagocytic) antibodies. Even in the presence of comorbidities, PCV13 has shown to be immunogenic and safe in the elderly, however there is currently no information on the effectiveness of the vaccination in this population. Vaccination techniques using PCV13 priming and PCV13 or PPV23 boosting are also advised for the older population, as the immune response to PPV23 is not ideal in this age group and repeated administration of PPV23 may also cause hyporesponsiveness.

**3. Herpes zoster vaccine**

The latent varicella zoster virus reactivates to cause herpes zoster (HZ, or shingles). When elements of cell-mediated immunity are weakened by illness, medication side effects, or aging, viral reactivation occurs. In actuality, the incidence of HZ increases with age and is higher in the elderly (3–5/1000 persons/year in the general population, 8–12/1000 persons/year in adults over 80). With 65/100.000 hospitalizations in adults over 80 years of age, HZ is a leading cause of hospitalization for the elderly. It can also be compounded by postherpetic neuralgia, which causes debilitating pain after the rash goes away, or by eye involvement, which occurs when the ophthalmic branch of the trigeminal nerve is afflicted. Currently, there are two licensed shingles vaccines: the subunit zoster vaccine (GSK) and the HZ live attenuated zoster vaccine (Zostavax, Merck). The Oka strain, an attenuated VZV strain that was first obtained in Japan and is also used in children to prevent chickenpox, albeit at a lesser dose, is included in the live attenuated vaccine in at least 20.000 PFU form. The VZV glycoprotein E (gE), a significant part of the viral surface, is present in 50 µg of the recombinant subunit vaccine. This vaccine is prepared with the AS01B adjuvant, which is made up of 50 µg of Quillaja saponaria Molina, fraction 21, and 50 µg of 3-O-desacyl-4′-monophosphoryl lipid A from Salmonella minnesota. The live attenuated vaccine received a license in the United States in 2006. A recent meta-analysis evaluated the vaccine's performance and found that it was 33% effective in preventing HZ, but 74% effective in avoiding hospitalizations for HZ and 57% effective in preventing postherpetic neuralgia. After receiving its license in 2017, the recombinant vaccine showed a 97% efficacy in preventing HZ in adults 50 years of age and above. However, it had a moderate reactogenicity, causing discomfort at the injection site in 79.1% of recipients and myalgia in 46.3%. According to immunological study, older persons

who receive the recombinant vaccination that contains AS01B adjuvant experience a strong and long-lasting memory response.

**Strategies for enhancing immunity in aging**

We propose that lifestyle variables, including food and exercise regimens, have a major impact on the immunosenescence and inflammatory processes. Consequently, the danger of maladaptive immunological aging is reduced and effective immune aging is supported by targeted nutrition and regular exercise training.

**1. Diet and nutrition**

**2. Physical activity**

Engaging in regular physical activity has been linked to several significant health advantages, such as a lower risk of mortality, sarcopenia, diabetes, stroke, and cardiovascular illnesses. However, the amount and intensity of physical activity decrease sharply with age, and most older persons do not achieve the minimum standards of 150 minutes per week of aerobic exercise set by the World Health Organization (WHO). Lower levels of pro-inflammatory cytokines including IL6 and TNFα have been linked to exercise in older persons. Several methods allow physical activity to have an anti-inflammatory impact. Age-related increases in fat mass have been linked to low-grade chronic inflammation. Immune system performance is directly impacted by physical activity, even in elderly persons. According to a recent study, adults who engage in high levels of physical activity had better thymic output. This impact is probably due to an improved thymic microenvironment, which includes higher levels of IL7 and lower levels of IL6. Furthermore, we discovered that the active older adults maintained a frequency of peripheral naïve T cells, which was linked to greater serum IL15 levels. All things considered, engaging in regular physical activity is a non-invasive, largely cost-neutral anti-aging and anti-immunesenescence treatment.

**CONCLUSION**

The age-related decline in immune function poses significant challenges to the health and well-being of the elderly population. Immunosenescence and inflammaging contribute to increased susceptibility to infections and reduced responsiveness to vaccinations. However, research efforts focused on understanding the underlying mechanisms have paved the way for the development of strategies to enhance immunity in aging individuals. Interventions targeting lifestyle modifications, specialized vaccination approaches, and innovative immunomodulatory therapies hold promise for rejuvenating immune responses in the elderly. A multidisciplinary approach that integrates knowledge from immunology, geriatrics, and nutrition sciences is crucial in devising effective strategies to counteract age-related immune decline and promote healthy aging. Implementation of these strategies may lead to improved health outcomes and quality of life in aging populations.

**REFERENCES**


1. Kaufmann S. H. E. (2019). Immunology's Coming of Age. *Frontiers in immunology*, 10, 684.
2. Calder P. C. (2020). Nutrition, immunity and COVID-19. *BMJ nutrition, prevention & health*, *3*(1), 74–92.
3. Obeagu, E. I., Muhimbura, E., Kagenderezo, B. P., Nakyeyune, S., & Obeagu, G. U. (2022). An Insight of Interleukin-6 and Fibrinogen: In Regulating the Immune System. *J Biomed Sci*, *11*(10), 83.
4. Obeagu, E. I., & Obeagu, G. U. (2017). Occult Hepatitis B infection and immunity. *Int. J. Curr. Res. Med. Sci*, *3*(8), 89-100.
5. Obeagu, E. I., Obeagu, G. U., Obiezu, J., Ezeonwumelu, C., Ogunnaya, F. U., Ngwoke, A. O., & Ugwu, O. P. C. (2023). Immunomodulatory Effects of Transfusions on Maternal Immunity in Pregnancy.NEWPORT INTERNATIONAL JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES (NIJBAS) *3*(3):1-8. https://doi.org/10.59298/NIJBAS/2023/1.1.11000
6. Alum, E. U., Obeagu, E. I., Ugwu, O. P., Samson, A. O., Adepoju, A. O., & Amusa, M. O. (2023). Inclusion of nutritional counseling and mental health services in HIV/AIDS management: A paradigm shift. *Medicine*, *102*(41), e35673.
7. Maeda, K, Caldez, MJ, Akira, S. (2019). Innate immunity in allergy. *Allergy*, 74, 1660–1674
8. Obeagu, E. I., & Onuoha, E. C. (2023). Tuberculosis among HIV Patients: A review of Prevalence and Associated Factors. *Int. J. Adv. Res. Biol. Sci*, *10*(9), 128-34.
9. Ibebuike, J. E., Nwokike, G. I., Nwosu, D. C., & Obeagu, E. I. (2018). A Retrospective

Study on Human Immune Deficiency Virus among Pregnant Women Attending Antenatal Clinic in Imo State University Teaching Hospital. *International Journal of Medical Science and Dental Research*, *1*(2), 08-14.

10. Obeagu, E. I., Obeagu, G. U., Akinleye, C. A., & Igwe, M. C. (2023). Nosocomial infections in sickle cell anemia patients: Prevention through multi-disciplinary approach: A review. *Medicine*, *102*(48), e36462.
11. Etido, A., Obeagu, E. I., Okafor, C. J., Chijioke, U. O., Vincent, C. C. N., & Mojo-Eyes, G. C. (2021). The Dynamics of Innate and Adaptive Immune Response to Sars Cov-2 Infection and Its Limitations in Human Beings. *Journal of Pharmaceutical Research International*, *33*(45A), 10-25.
12. Obeagu, E. I., Obeagu, G. U., Igwe, M. C., Alum, E. U., & Ugwu, O. P. C. (2023). Neutrophil-Derived Inflammation and Pregnancy Outcomes. *Newport International Journal of Scientific and Experimental Sciences*, *4*(2), 10-19.
13. Obeagu, E. I. (2023). Tuberculosis diagnostic and treatment delays among patients in Uganda. *Health Science Reports*, *6*(11), e1700.
14. Obeagu, E. I., Babar, Q., Vincent, C. C. N., Anyanwu, C. O., & Uduchi, I. O. (2021). Advances in Therapeutic Strategies of Immunotherapy in Cancer Treatment. *World Journal of Pharmacy and Pharmaceutical Sciences*, *10*(8), 2144-2164.
15. Obeagu, E. I., & Obeagu, G. U. (2018). Utilization of Antioxidants in the management of diabetes mellitus patients. *J Diabetes Clin Prac*, *1*(102), 2.
16. Obeagu, E. I., Babar, Q., Uduchi, I. O., Ibekwe, A. M., Chijioke, U. O., Okafor, C. J., & Vincent, C. C. N. (2021). An Update on Transfusion Related Immunomodulation (TRIM) in a Time of COVID-19 Pandemic. *Journal of Pharmaceutical Research International*, *33*(42A), 135-146.
17. Marshall, J.S., Warrington, R., Watson, W. (2018). An introduction to immunology and immunopathology. *Allergy Asthma Clin Immunol* 14 (2), 49.
18. Diamond, M.S., Kanneganti, TD (2022). Innate immunity: the first line of defense against SARS-CoV-2. *Nat Immunol* 23, 165–176.
19. Mogilenko, D.A., Shchukina, I. & Artyomov, M.N. (2022). Immune ageing at single-cell resolution. *Nat Rev Immunol 22*, 484–498.
20. Aspinall, R., Lang, P.O. (2018). Interventions to restore appropriate immune function in the elderly. *Immun Ageing* 15, 5.
21. Kasler, H., Verdin, E. (2021). How inflammaging diminishes adaptive immunity. *Nat Aging* 1, 24–25.
22. Anna Aiello, Farzin Farzaneh, Giuseppina Candore, Calogero Caruso, Sergio Davinelli, Caterina Maria Gambino, Mattia Emanuela Ligotti, Nahid Zareian, Giulia Accardi (2019). *Front. Immunol.*, 10.
23. Liu, Z., Liang, Q., Ren, Y. (2023). Immunosenescence: molecular mechanisms and diseases. *Sig Transduct Target Ther* 8, 200.
24. Guo, J., Huang, X., Dou, L. (2022). Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. *Sig Transduct Target Ther* 7, 391.
25. Tamas Fulop, Anis Larbi, Gilles Dupuis, Aurélie Le Page, Eric H. Frost, Alan A., Cohen Jacek, Witkowski M., Claudio Franceschi (2018). Sec. Inflammation. *Front. Immunol.*, 8.
26. Lucas Leite Cunha, Sandro Felix Perazzio, Jamil Azzi, Paolo Cravedi, Leonardo Vidal Riella (2020). Sec. Cytokines and Soluble Mediators in Immunity. *Front. Immunol.*
27. Minwen Xu, Tao Gan, Huiting Ning, and Liefeng Wang (2018). *Front Immunol.* MicroRNA Functions in Thymic Biology: Thymic Development and Involution
28. Jennifer E. Cowan, Yousuke, Takahama, Avinash Bhandoola, Izumi Ohigashi (2020). Postnatal Involution and Counter-Involution of the Thymus. *Front. Immunol.*, *Sec. T Cell Biology*, 11
29. Thomas, R., Wang, W. & Su, DM. (2020). Contributions of Age-Related Thymic Involution to Immunosenescence and Inflammaging. *Immun Ageing* 17, 2.
30. Antonella Cardinale, Carmen Dolores De Luca, Franco Locatelli, Enrico Velardi (2021). Thymic Function and T-Cell Receptor Repertoire Diversity: Implications for Patient Response to Checkpoint Blockade Immunotherapy. *Front. Immunol.*, *Sec. Cancer Immunity and Immunotherapy.*
31. Hae Young Chung, Dae Hyun Kim, Eun Kyeong Lee, Ki Wung Chung, Sangwoon Chung, Bonggi Lee, Arnold Y. Seo, Jae Heun Chung, Young Suk Jung, Eunok Im, Jaewon Lee, Nam Deuk Kim, Yeon Ja Choi, Dong Soon Im, and Byung Pal Yu (2019). Redefining Chronic Inflammation in Aging and Age-Related Diseases: Proposal of the

Senoinflammation Concept. *Aging Dis.* 10(2), 367–382.
32. Ferrucci L., Fabbri E. (2018). Inflammageing: Chronic inflammation in ageing, cardiovascular disease, and frailty. *Nat. Rev. Cardiol.* 15, 505–522.
33. Barbara Colombini, Monica Dinu, Emanuele Murgo,Sofia Lotti, Roberto Tarquini, Francesco Sofi and Gianluigi Mazzoccoli (2022). Ageing and Low-Level Chronic Inflammation: *The Role of the Biological Clock*, 11(11).
34. Irene Maeve, Rea David, S. Gibson, Victoria McGilligan, Susan E. McNerlan, H. Denis Alexander, Owen A. Ross (2018). The Aging Immune System and Health. Age and Age Related Diseases: Role of Inflammation Triggers and Cytokines. *Front. Immunol.* Sec. Inflammation, 9.
35. Rossiello, F., Jurk, D., Passos, J.F. (2022). Telomere dysfunction in ageing and age-related diseases. *Nat Cell Biol* 24, 135–147.
36. Fasching, C. L. (2018). Telomere length measurement as a clinical biomarker of aging and disease. *Crit. Rev. Clin. Lab. Sci.* 55, 443–465.
37. Koliada, A. K., Krasnenkov, D. S., and Vaiserman, A. M. (2015). Telomeric aging: mitotic clock or stress indicator? *Front. Genet.* 6, 82. And Notterman, D. A., and Schneper, L. (2020). Telomere Time-Why We Should Treat Biological Age Cautiously. *JAMA.*
38. Tomita, K. (2018). How long does telomerase extend telomeres? regulation of telomerase release and telomere length homeostasis. *Curr. Genet.* 64, 1177–1181.
39. Turner, K. J., Vasu, V., and Griffin, D. K. (2019). Telomere biology and human phenotype. *Cells* 8, 73
40. Ogar CO, Okoroiwu HU, Obeagu EI, Etura JE, Abunimye DA. Assessment of blood supply and usage pre-and during COVID-19 pandemic: a lesson from non-voluntary donation. Transfusion Clinique et Biologique. 2021;28(1):68-72.
41. Obeagu EI, Babar Q. Covid-19 and Sickle Cell Anemia: Susceptibility and Severity. J. Clinical and Laboratory Research. 2021;3(5):2768-0487. links/617acdd03c987366c3f8b3f1/Covid-19-and-Sickle-Cell-Anemia-Susceptibility-and-Severity.pdf.
42. Obeagu EI. COVID 19: Factors Associated with Implementation and Practice of Covid-19 Prevention. Int. J. Adv. Multidiscip. Res. 2022;9(9):37-42.DOI: 10.22192/ijamr.2022.09.09.004
43. Nnodim J, Njoku-Obi T, Ohalete C, Obeagu EI. Perspective of Covid 19 Hesistancy. Madonna University journal of Medicine and Health Sciences. 2022;2(1):235-8.
44. https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/50.
45. Obeagu EI, Babar Q, Vincent CC, Anyanwu CO. INFANTS IMMUNIZATION: CHALLENGES OF OTHER VACCINES DUE TO COVID-19 PANDEMIC. Journal of Bioinnovation. 2021;10(4):1056-66. links/6105aef21e95fe241a9e607a/INFANTS-IMMUNIZATION-CHALLENGES-OF-OTHER-VACCINES-DUE-TO-COVID-19-PANDEMIC.pdf.
46. Obeagu EI, Scott GY, Amekpor F, Ofodile AC, Chukwueze CM. A Systematic Review on the role of untreated inflammation of the genital tract in SARS COV 2 transmission. Madonna University journal of Medicine and Health Sciences. 2023;3(1):19-24. https://www.journal.madonnauniversity.edu.ng/index.php/medicine/article/view/98.
47. Obeagu EI, Hamisi S, Bunu UO. An update on cytokine storm in covid-19 infection: Pivotal to the survival of the patients. Int. J. Adv. Res. Biol. Sci. 2023;10(3): 171-80.DOI: 10.22192/ijarbs.2023.10.03.020
48. Obeagu EI. Mental Health Care during the COVID-19 Pandemic. Journal of Public Health and Nutrition. 2020;3(5). links/6012dc1792851c2d4dfebad6/Mental-Health-Care-during-the-COVID-19-Pandemic.pdf.
49. Asogwa EI, Obeagu EI, Abonyi OS, Elom CO, Udeoji DU, Egbumike CJ, Agunwah EU, Eze CN, Akamike IC, Esimai BN. Mitigating the Psychological Impacts of COVID-19 in Southern Nigeria; Public Awareness of Routine Exercises and Preventive Measures. Journal of Pharmaceutical Research International. 2021;33(30A):72-83.
50. Obeagu EI, Babar Q, Vincent CC, Okafor CJ, Eze R, Chijioke UO, Ibekwe AM, Uduchi IO. Pulmonary Embolism in Covid-19 Pandemic: A Threat to Recovery of the Infected Patients. Journal of Pharmaceutical Research International. 2021;33(42A):90-98.
51. Obeagu EI, Babar Q, Uduchi IO, Ibekwe AM, Chijioke UO, Okafor CJ, Vincent CC. An Update on Transfusion Related Immunomodulation (TRIM) in a Time of COVID-19 Pandemic. Journal of

Pharmaceutical Research International. 2021;33(42A):135-46.

52. Okorie N, Adeniran OC, Adimabua OP, Obeagu EI, Anastasia E. Pathological Changes among Norvegicus Rattus Exposed on Novel Smoked Bambusa Vulgaris (Bamboo) Leaf: Cigarette Substitute during COVID-19 Lockdown in Nigeria. Journal of Advances in Medical and Pharmaceutical Sciences. 2022;24(7):30-39.
53. Nakyeyune S, Ikpenwa JN, Madekwe CC, Madekwe CC, Tolulope AA, Ajayi DT, Obeagu EI, Hassan AO. COVID 19 Omicron: The Origin, Presentation, Diagnosis, Prevention and Control. Asian Journal of Research in Infectious Diseases. 2022:25-33.
54. Obeagu EI, Obeagu GU, Chukwueze CM, Ngwoke AO. Inappropriate use of personal protective equipment among health workers: A review of associated factors. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(8): 27-34.DOI: 10.22192/ijcrcps.2023.10.08.004
55. Obeagu EI, Nwosu DC, Obeagu GU. Interleukin-6 (IL-6): A Major target for quick recovery of COVID-19 patients. **Int. J. Curr. Res. Biol. Med. (2022). 7(2): 1-19. DOI:** 10.22192/ijcrbm.2022.07.02.001
56. Ifeanyi OE, Mercy OH, Prayer NN, Chijindu OH. Cytokines, coagulation profile and haematological changes in covid 19 patients as indicators of their health staus: A review. European Journal of Biomedical. 2020;7(7):7249.links/5f083f4e299bf188161034aa/CYTOKINES-COAGULATION-PROFILE-AND-HAEMATOLOGICAL-CHANGES-IN-COVID-19-PATIENTS-AS-INDICATORS-OF-THEIR-HEALTH-STATUS-A-REVIEW.pdf.
57. Obeagu EI, Scott GY, Amekpor F, Ugwu OP, Alum EU. Covid-19 Infection and Diabetes: A Current Issue. International Journal of Innovative and Applied Research. 2023;11(1):25-30.
58. Hassan AO, Obeagu EI, Ajayi DT, Tolulope AA, Madekwe CC, Madekwe CC, Ikpenwa JN, Nakyeyune S. COVID 19 Omicron: The Origin, Presentation, Diagnosis. Prevention and Control. Asian Journal of Research in Infectious Diseases. 2022;11(1):25-33.
59. Ifeanyi OE. Emerging clinical & medical challenges and appropriate solutions during COVID-19 pandemic times. Med Clin Rev. 2020;6(5):108.10.36648/2471-299X.6.5.108 links/6012db46299bf1b33e30a9ec/Emerging-Clinical-Medical-Challenges-and-Appropriate-Solutions-during-Covid-19-Pandemic-Times.pdf
60. Annalisa Ciabattini, Christine Nardini, Francesco Santoro, Paolo Garagnani, Claudio Franceschi, Donata Medaglini (2018). Vaccination in the elderly: The challenge of immune changes with aging. *Seminars in Immunology* 40, 83-94.

**CITE AS: Nkiruka R Ukibe, Chizoba Rita Dike, A.C. Ihim, Ezinne G. Ukibe, Blessing C. Ukibe, Victory Ezennia Ukibe and Emmanuel Ifeanyi Obeagu (2024). Immunological Changes with Age and Innovative Approaches to Bolster Immune Function in Older Adults. IDOSR JOURNAL OF SCIENTIFIC RESEARCH 9(1) 1-11. https://doi.org/10.59298/IDOSRJSR/2024/1.1.11.100**