Proceedings of the 2nd International Conference on Environmental Geoscience and Earth Ecology
DOI: 10.54254/2753-8818/48/2024PJ0121

The interplay between aging and inflammation and its role in chronic disease development

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Abstract. This paper explores the complex relationship between aging and inflammation and its impact on the development of chronic diseases. Aging is an important contributor to elevated levels of inflammation, with mechanisms including changes in immune regulatory function, chronic low-grade inflammation, cellular aging and tissue damage, changes in gene expression, and increased oxidative stress. These inflammatory processes not only accelerate aging itself, but also promote the development of chronic diseases such as cardiovascular disease (CVD) and Alzheimer's disease (AD). The article goes on to address other modern anti-inflammatory treatment approaches, such as biologics, JAK inhibitors, and nonsteroidal anti-inflammatory medications. These treatments help manage and mitigate aging-related pathologies by targeting key molecules and pathways of inflammation. A better comprehension of the relationship between inflammation and aging may serve as the foundation for the creation of novel therapeutic approaches that, in addition to reducing inflammatory reactions, may also prevent or slow the advancement of illnesses associated with age. This article aims to improve medical and scientific understanding of the relationship between inflammation and aging and to encourage the development and use of more potent therapies to lessen the burden of chronic illnesses and enhance the quality of life for the aged.

Keywords: Cardiovascular disease, Alzheimer's disease, aging, inflammation.

1. Introduction

With the intensification of the global aging trend, the relationship between aging and health has increasingly attracted the attention of the scientific and medical communities. In this context, researchers have gradually realized the close relationship between the aging process and inflammatory response. In the past few decades, significant progress has been made in research on how aging affects human inflammation, but there are still many unresolved issues that need to be further explored

Based on current studies, the human body's degree of inflammation frequently increases gradually with age, resulting in a chronic low-grade inflammatory condition described as "inflammatory aging" or "immune aging." Numerous age-related illnesses, including AD, diabetes, and CVD, are intimately linked to this inflammatory condition. Therefore, a deeper understanding of the impact of aging on human inflammation not only helps to reveal the pathogenesis of diseases, but also provides important clues for delaying the aging process and improving the quality of life of the elderly.

DOI: 10.54254/2753-8818/48/2024PJ0121

The latest research reveals key molecules responsible for the impact of military personnel on human mortality, with particular emphasis on overactivation of NF-κB vaccines, activators of NLRP3 vaccine bodies, and the role of the Soldier-Associated Form (SASP). These vaccines enhance exacerbation factor-related factors by promoting the expression of factors such as TNF-α, IL-1β, and IL-6 in vaccine cells [1]. At the same time, abnormal regulation of JAK-STAT signaling cells and changes in immune function also have an important impact on the inflammatory process. These findings provide new opportunities for understanding the complex relationship between the elderly and inflammation. Connection provides new perspectives.

Through a detailed analysis of how the elderly affects the body's inflammatory response, this study not only helps us gain a deeper understanding of the fundamental mechanism of the disease, but also provides important theoretical support for the development of sleep-enabled treatment strategies. Lowering inflammation provides several practical benefits for creating a healthy aging society, including slowing down the aging process and preventing or delaying the onset of age-related disorders. These benefits also improve older quality of life and save medical costs.

This article is to discuss the art studies on how aging affects and human inflammation response mechanisms. The content will include the molecular mechanisms of inflammatory response during aging, the relationship between inflammatory aging and age-related diseases, research progress on intervention strategies, and future research prospects. This article will offer readers a greater grasp of the most recent advancements in this subject by thoroughly evaluating pertinent literature, giving them a viewpoint that will help them find helpful references and ideas for future study and clinical practice.

2. The connection between aging and elevated inflammatory markers

2.1. Changes in immune regulatory function

Aging has a multifaceted effect on immune regulatory function and the inflammatory process, resulting in alterations to the immune system's makeup and operation as well as dysregulation of immunological responses.

As one age, the immune system's makeup drastically changes, particularly in the adaptive immune response. When people age, their thymus, which is where T cells develop, diminishes, which reduces the generation of new T cells. Additionally, the percentage of memory T cells rose while the percentage of newly developed natural T cells fell. These aged memory T cells have limited function and reduced responsiveness. Aging also has an impact on B cell renewal and function, which reduces the variety of antibodies and the effectiveness of the immune response [2].

Aging affects the function of immune cells, especially immune regulatory cells such as regulatory T cells (Tregs). These cells play a key role in controlling immune responses, avoiding excessive inflammatory responses and autoimmune responses. These cells' ability to operate may deteriorate with age, which would lessen their ability to regulate the inflammatory response and result in a persistent low-grade inflammatory state. Furthermore, immune surveillance function declines with age, impairing the body's capacity to eradicate infections and tumor cells and exacerbating the emergence of chronic inflammatory conditions [3].

Through the various mechanisms mentioned above, aging not only changes the composition and function of the immune system but also disrupts the fine regulation of immune responses, leading to a chronic inflammatory state that is intimately linked to the emergence of certain age-related illnesses.

2.2. Chronic low-level inflammation

Chronic low-grade inflammation is common in the aging process. Its molecular mechanism is complex and involves multiple cell types and signaling pathways. This inflammatory state, known as "inflammaging," has a major impact on the emergence of age-related illnesses. A distinctive feature of chronic low-grade inflammation is the sustained high-level expression of cytokines including IL-6, TNF-α, and CRP. IL-6 is a key inflammatory mediator that can promote B cell maturation and influence metabolic pathways. Higher levels of IL-6 have been linked to cardiovascular disease risk, attenuation

DOI: 10.54254/2753-8818/48/2024PJ0121

of muscles in the elderly, and systemic inflammatory state. By triggering the NF-κB signaling pathway, TNF-α increases inflammation and apoptosis and encourages the synthesis of additional inflammatory cytokines. Being an acute phase protein, the rise in CRP levels corresponds with the body's increased inflammatory levels and is linked to the onset of several age-related illnesses.

Numerous intracellular stress events, such as oxidative stress, ATP release, and damage to organelles, particularly mitochondria, can activate the NLRP3 inflammasome in aged cells. Once activated, NLRP3 helps convert the precursor cytokine pro-IL-1β into mature IL-1β, which is a strong inflammatory mediator that can exacerbate local and systemic inflammatory responses [4]. This process not only accelerates tissue damage but also enhances the risk of inflammatory diseases.

Among the most important transcription factors in inflammatory reactions is NF-κB. Under the influence of oxidative stress or inflammatory cytokines such as TNF-α, After being freed from the inhibitory protein, NF-κB moves into the nucleus to encourage the production of genes linked to inflammation. This includes pro-inflammatory cytokines, adhesion molecules, and MMPs, which further disrupt tissue structure and maintain an inflammatory state [5]. Furthermore, there exists a strong correlation between the development of several chronic inflammatory disorders and the prolonged activation of NF-κB.

SASP (senescence-associated secretory phenotype) involves a series of pro-inflammatory and tissue remodeling-related molecules produced via senescent cells. These molecules include IL-6, IL-8, and MMPs, which not only promote inflammatory responses through local effects but also modulate the tissue microenvironment by affecting the behavior of neighboring cells. This local and systemic inflammatory response driven by senescent cells is associated with an increased risk of tumor progression, tissue fibrosis, and chronic inflammatory diseases [6].

An in-depth understanding of these molecular mechanisms will help reveal the physiology behind aged people's persistent low-grade inflammation and provide scientific evidence for the development of targeted interventions.

2.3. Cellular aging and tissue damage

One of the main biological effects of aging is cellular senescence, which is brought on by a variety of stressors including oxidative stress, metabolic dysregulation, and damage to DNA. Although these aging cells stop proliferating, they do not die. Instead, they accumulate in tissues and promote inflammation through the following mechanism: Aging cells secrete a series of inflammation-related cytokines, chemical factors, and proteases to form the SASP [6]. This includes IL-6, TNF-α, IL-8, etc., which can trigger the surrounding cells' inflammatory response and encourage the development of a persistent inflammatory environment. SASP factors not only affect local cells, but also affect distant tissues through blood circulation, causing systemic inflammatory responses and increasing the risk of age-related diseases.

During the aging process, the decline in tissue repair capacity and the accumulation of micro-damage to cells and tissues lead to significant tissue damage. These injuries often involve the degradation of the extracellular matrix (ECM), specifically due to age-induced increases in the expression of matrix metalloproteinases (MMPs). These enzymes destroy the integrity of the ECM, leading to changes in tissue structure and function. Disruption of the ECM releases matrix components such as hyaluronic acid and elastin fragments, which can act as inflammatory signals to activate immune cells [7]. Furthermore, immune cells (like lymphocytes and macrophages) are drawn to the site of harm by inflammatory mediators generated by cells in injured tissues, such as cytokines and chemokines. These immune cells have the ability to create a vicious cycle by amplifying the inflammatory response even further.

There is also a decrease in autophagy function with aging. Autophagy is an intracellular clearance mechanism responsible for removing damaged organelles and protein aggregates and maintaining cellular homeostasis. During the aging process, autophagy function is weakened, leading to intracellular protein aggregation and organelle dysfunction, thereby increasing intracellular stress levels. This stress

DOI: 10.54254/2753-8818/48/2024PJ0121

state can activate inflammatory pathways such as NF-κB, further promote the production of inflammatory cytokines, and aggravate local and systemic inflammation [8].

2.4. Changes in gene expression

DNA methylation alterations are essential for controlling inflammation as aging. Methylation is an epigenetic alteration that modifies gene expression by introducing methyl groups to cytosine on CpG islands, often in the promoter region of genes. Aging leads to changes in methylation patterns of specific genes, which may include genes associated with inflammation. For example, excessive methylation may lead to the silencing of anti-inflammatory genes, while reduced methylation levels may activate pro-inflammatory genes that are otherwise suppressed. This regulatory change can directly enhance the release of pro-inflammatory cytokines such IL-6 and TNF-α, leading to the formation and maintenance of a chronic inflammatory state, thus exacerbating aging-related inflammatory diseases.

Histone modifications, such as acetylation and methylation, are another key epigenetic mechanism regulating gene expression. Histone acetylation is generally associated with relaxation of chromatin and increased gene expression, whereas deacetylation is associated with tighter binding of chromatin and gene silencing. Aging may lead to changes in the expression or activity of histone deacetylase (HDACs), thereby affecting the expression of inflammation-related genes. In addition, site-specific methylation changes of histones H3 and H4 can also regulate the activity of inflammation-related transcription factors associated with inflammation, such NF-κB, hence modulating the inflammatory reaction [9]. These changes exacerbate the chronic inflammatory environment during aging, increasing the production of inflammatory mediators and the persistence of inflammatory responses.

Non-coding RNAs, especially miRNAs, play an important role in regulating inflammatory gene expression. By binding to the 3' untranslated region of target mRNA, miRNAs can inhibit its translation or promote its degradation, thereby affecting the inflammatory pathway. During aging, the expression patterns of certain miRNAs change, and these miRNAs may directly regulate inflammation-related signaling pathways, such as regulating key components of the NF-κB pathway or directly regulating the mRNA stability and translation of inflammatory cytokines. These changes may lead to abnormal activation of inflammatory responses and exacerbate the chronic inflammatory state associated with aging [10].

Through the combined effect of the above three epigenetic mechanisms, aging affects changes in gene expression, thereby promoting or exacerbating the inflammatory response and affecting the person's state of health. A more thorough comprehension of these processes may aid in the creation of innovative treatment plans that address chronic inflammation and aging.

2.5. Oxidative stress

Increased oxidative stress during aging is mostly caused by mitochondrial malfunction, which is primarily represented by a decline in the electron transport chain's (ETC) efficiency. Under normal circumstances, mitochondria transfer electrons to oxygen through ETC to produce water. However, as aging, the structure and function of mitochondria become damaged, causing electrons to leak and react with oxygen molecules to form superoxide radicals. These free radicals can be converted into more reactive oxygen species (ROS), such as hydrogen peroxide and hydroxyl radicals. These ROS accumulate within cells, causing damage caused by oxidation to DNA, lipids, and proteins, triggering intracellular inflammatory responses, because damaged cellular components can serve as inflammatory signals to stimulate cytokines that promote inflammation and the development of immune cells [11].

Deterioration of the body's antioxidant defense system also occurs with aging.In general, older people have reduced levels of expression and activity of important antioxidant enzymes such catalytic enzyme (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD).In addition, levels of endogenous antioxidants such as vitamins E, C, and glutathione may also be reduced [12]. These changes weaken the cells' ability to scavenge ROS, leading to the accumulation of ROS in the body and increasing oxidative stress. The accumulation of intracellular ROS not only directly damages cellular components, but also indirectly aggravates the inflammatory state by activating inflammatory pathways,

DOI: 10.54254/2753-8818/48/2024PJ0121

such as by enhancing the discharge of cytokines that induce inflammation and promoting local and systemic inflammatory responses.

The increase in intracellular ROS activates multiple cellular stress response pathways including NF-κB. ROS can promote the release of NF-κB from the complex bound to IκB, causing it to transfer to the nucleus and activate the expression of a variety of inflammatory genes including inflammatory cytokines (such as IL-6, TNF-α). Activation of these genes enhances the synthesis of molecules involved in inflammation, attracting more immune cells to areas of injury or stress, further amplifying the inflammatory response. In addition, oxidative stress can also initiate other signaling pathways including PI3K/Akt and MAPK. These pathways are also involved in regulating cell survival, proliferation and inflammatory responses, exacerbating inflammatory damage to cells and tissues.

These three molecular mechanisms are interrelated and jointly promote the interaction between oxidative stress and inflammation during aging, forming a complex regulatory network that exacerbates aging-related inflammation and disease processes.

3. Chronic disease

3.1. CVD

3.1.1. Atherosclerosis. Aging significantly affects the progression of atherosclerosis, a long-term condition where inflammatory pathways cause lipids, inflammatory cells, and fibrous tissue to build up inside blood vessel walls. An important factor in the onset and advancement of atherosclerosis is inflammation. Here are the specific ways aging affects atherosclerosis through inflammatory mechanisms:

Aging leads to changes in the regulatory functions of the immune system, particularly the activity and the way that inflammatory cells like macrophages and monocytes work. In the context of atherosclerosis, damage or impaired function of the vascular endothelium (in part due to oxidative stress and aging) increases the expression of adhesion molecules (like VCAM-1 and ICAM-1) and chemotactic oxidizing factors (like MCP-1) in endothelial cells [13]. These molecules promote the adhesion and migration of inflammatory cells, especially monocytes, into the vessel wall. These monocytes subsequently differentiate into macrophages, which engulf oxidized low-density lipoprotein (oxLDL) and become foam cells, forming the core component of plaques.

Aging enhances the production of inflammatory mediators, such as cytokines (TNF-α, IL-6), chemical factors, and growth factors. These mediators play a key role in atherosclerosis. They not only promote the recruitment and activation of inflammatory cells, but also stimulate the migration of vascular smooth muscle cells from the vascular media to the intima, and enhance the proliferation and extracellular matrix synthesis capabilities of these cells, promoting Fibrous cap formation with reduced plaque stability.

Aging leads to the weakening of antioxidant defense mechanisms in the body and increases the production of ROS, which intensifies the oxidation of lipoproteins. Oxidized low-density lipoprotein (oxLDL) is an important pathogenic factor in atherosclerosis because it is not only phagocytosed by macrophages to form foam cells, but also has strong pro-inflammatory properties and can activate endothelial cells and smooth muscle cells to produce more multiple inflammatory mediators.

During aging, the persistence of the inflammatory response can lead to structural changes in plaques, making them more fragile and susceptible to rupture. Proteases produced by inflammatory cells such as matrix metalloproteinases (MMPs) can degrade collagen and elastin, which are the main components of the plaque fibrous cap. The fibrous cap of the plaque may rupture, increasing the risk of acute cardiovascular events including myocardial infarction and stroke by causing abrupt thrombosis.

In summary, aging aggravates the development of atherosclerosis by promoting inflammatory responses, enhancing oxidative stress, and affecting the function and response of blood vessel wall cells. Understanding these mechanisms can help develop preventive and therapeutic strategies for atherosclerosis in the elderly.

DOI: 10.54254/2753-8818/48/2024PJ0121

3.1.2. Inflammatory markers. Inflammatory markers are a group of biomolecules produced by the immune system during inflammatory states in the body and are often used to assess inflammatory activity in chronic diseases. They include various cytokines, acute phase proteins, and other molecules. These markers not only reflect the presence of inflammation but are also involved in the pathological processes of disease, especially CVD.

C-reactive protein is an acute-phase protein produced by the liver and is a sensitive marker of inflammation. Elevated CRP levels generally indicate the presence of an active inflammatory process in the body and are directly proportional to the degree of inflammation. High CRP levels are directly linked to an increased risk of cardiovascular disease (CVD). CRP can increase the adhesion of vascular endothelial cells, promote the formation of atherosclerotic plaques, and may increase the possibility of heart-related incidents by affecting platelet aggregation and accelerating the decrease in the stability of atherosclerotic plaques.

TNF-α is a strong pro-inflammatory cytokine secreted by immune cells such as macrophages, which is essential for controlling inflammatory and immunological responses. In the cardiovascular system, TNF-α guides the migration of inflammatory cells such as monocytes into the vessel wall by promoting the expression of adhesion molecules on vascular endothelial cells. The accumulation and activation of these cells promote the development of atherosclerosis. Long-term increased TNF-α expression is closely associated with the development of CVD, particularly through its pro-inflammatory properties that exacerbate vascular damage and inflammatory responses.

IL-6 is a multifunctional cytokine that can not only promote inflammatory responses but also participate in immune regulation and metabolic processes. In CVD, the role of IL-6 is particularly important, as it increases systemic inflammatory status by stimulating the liver to generate additional acute-phase proteins, such as CRP. Atherosclerosis and other vascular diseases are mostly caused by the increased activity of vascular smooth muscle cells, which are also migrated and multiplied by IL-6.

The white blood cell count in whole blood is a broad indicator of inflammatory activity in the body, and changes in the number and type of white blood cells can reveal different types and degrees of inflammatory states. In the context of CVD, A higher risk of CVD is linked to elevated white blood cell numbers. Leukocytes, particularly neutrophils and monocytes, are essential for the development and breaking down of atherosclerotic plaques. They not only participate in the amplification of inflammatory responses, but also promote plaque formation by secreting various enzymes and cytokines. of instability and rupture.

3.2. Increased risk of AD

3.2.1. Neuroinflammation. Aging is one of the major risk factors for the development of AD, and an important factor in this process is neuroinflammation. Neuroinflammation is a common feature of the development of AD, which involves multiple immune cells, cytokines, enzymes, and signaling pathways, all of which may accelerate the onset of the disease.

Microglia are the main immune cells in the brain, responsible for monitoring and responding to pathological changes within the central nervous system (CNS). With age, microglia tend to be overactivated due to long-term exposure to multiple damaging signals such as β-amyloid deposition, neuronal damage, and oxidative stress. Because of this ongoing active state, microglia emit proinflammatory cytokines such as IL-1β, TNF-α, and IL-6, which can exacerbate neuronal injury and encourage amyloid accumulation [14].

In AD, two indicators include hyperphosphorylation of Tau protein and aberrant aggregation of amyloid β protein. These abnormal proteins are not only toxic to neurons, but also activate microglia and glial cells, which produce more inflammatory factors and aggravate the inflammatory environment. This inflammatory response further damages nerve cells, leading to decreased neuronal function and increased neurodegeneration.

Aging is also associated with blood-brain barrier dysfunction, which can enhance the brain's inflammation by facilitating the immune system's and inflammatory mediators' penetration. The

DOI: 10.54254/2753-8818/48/2024PJ0121

inflammatory decline of the blood-brain barrier may be caused by the combined effects of oxidative stress, persistent activation of microglia, and increased inflammatory mediators. Damage to the blood-brain barrier makes it easier for the immune system, such as T cells and monocytes, to enter the brain, and these cells release more inflammatory factors in the brain, forming a vicious cycle [15].

With aging, the levels of neurotrophic factors (such as nerve growth factor NGF) that support nerve growth and maintain neuronal function may decrease. Neuroinflammation further deteriorates the survival environment of neurons by affecting the production and function of these trophic factors, reduces the ability of nerve regeneration, and accelerating the neurodegenerative process [16].

3.2.2. Inflammatory mediators. Tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), interleukin-6 (IL-6), and other inflammatory factors are important in the development of AD. They are not only involved in the regulation of inflammatory responses, but also directly and indirectly affect AD-related pathological changes, such as neuronal damage, amyloid β protein (Aβ) deposition, and Tau protein pathology.

IL-1β is a key inflammatory factor that plays an important role in microglial activation in AD. This activation prompts microglia to release more pro-inflammatory mediators, exacerbating the inflammatory environment of the brain and directly affecting the health of neurons. In addition, IL-1β accelerates the generation and aggregation of amyloid beta protein (Aβ) by increasing the expression of amyloid precursor protein (APP) and promoting β-secretase activity, which is a core part of AD pathological changes and exacerbates the progression of the disease.

IL-6 has a complex role in AD, which can play a neuroprotective role at low concentrations and may also cause neurological damage and inflammation at high concentrations. High levels of IL-6 affect neuronal survival by regulating synaptic function and plasticity. Studies have also shown that IL-6 is involved in the phosphorylation process of Tau protein, and hyperphosphorylated Tau is associated with the formation of neurofibrillary tangles in AD, further promoting the development of the disease.

TNF-α is a strong pro-inflammatory cytokine. Its high expression in AD not only activates a variety of inflammatory reactions, including microglia and astrocytes, but also may affect the metabolism of Aβ by regulating the expression of enzymes related to Aβ clearance. The pro-inflammatory effect of TNF-α not only aggravates neuronal damage, but also may promote Aβ deposition by affecting the aggregation and clearance mechanism of Aβ, forming a vicious cycle of inflammation and neurodegenerative damage, accelerating the pathological process of AD.

4. Response strategies

4.1. Drug therapy

4.1.1. Non steroidal anti-inflammatory drugs (NSAIDs). An extensive family of medications known as NSAIDs is used to treat inflammation, fever, and discomfort. Their main anti-inflammatory mechanism of action is achieved by inhibiting the synthesis of prostaglandins. Prostaglandins are a significant family of inflammatory mediators that the cyclooxygenase (COX) enzyme synthesises from arachidonic acid.

The main target of NSAIDs is COX, a key enzyme responsible for catalyzing the production of prostaglandins. COX has two main forms: COX-1 and COX-2

COX-1 is expressed in most tissues and is involved in normal physiological processes such as protecting the gastric mucosa, supporting renal function and platelet aggregation. COX-2 is mainly overexpressed under inflammatory conditions due to the stimulation of cytokines and growth factors and is the main source of inflammation and pain.

Most traditional NSAIDs (such as aspirin and ibuprofen) inhibit both COX-1 and COX-2, reducing the production of prostaglandins, thereby reducing inflammation, pain and fever. However, because these drugs also inhibit COX-1, they may lead to a reduction in gastric mucosal protective prostaglandins, causing gastric side effects such as indigestion and gastric ulcers.

DOI: 10.54254/2753-8818/48/2024PJ0121

In order to reduce the impact on COX-1, selective COX-2 inhibitors (such as celecoxib and rofecoxib) have been developed. These drugs inhibit COX-2 more specifically, thereby reducing side effects on the gastric mucosa while maintaining anti-inflammatory effects.

By inhibiting the production of prostaglandins, NSAIDs reduce the concentration of these compounds at the site of inflammation, thereby reducing inflammation, redness, pain and fever. Prostaglandins not only increase the permeability of blood vessels and promote the migration of inflammatory cells to the site of inflammation, but also directly stimulate pain receptors, resulting in increased pain.

NSAIDs exert their anti-inflammatory, analgesic, and antipyretic effects by inhibiting the synthesis of prostaglandins, but they should be used with caution to avoid possible gastrointestinal and cardiovascular side effects.

4.1.2. Biological agents (tumor necrosis factor inhibitors or interleukin inhibitors). Biologics are a highly specialized class of drugs used to treat a variety of inflammatory and autoimmune diseases, such as rheumatoid arthritis, psoriasis, Crohn's disease, and ankylosing spondylitis. These drugs work by specifically targeting and modulating key molecules and pathways in the immune system.

TNF inhibitors are biologics targeting tumor necrosis factor-α (TNF-α), a proinflammatory cytokine that plays a key role in autoimmune and inflammatory diseases. TNF inhibitors such as infliximab, adalimumab, and etanercept inhibit TNF-α-induced inflammatory signaling by binding to free TNF-α in the blood and blocking its interaction with TNF receptors on the cell surface. This mechanism helps reduce the activation and tissue infiltration of inflammatory cells, significantly reduces swelling and pain associated with inflammation, and improves patients' symptoms and quality of life.

A wide range of essential interleukins, including IL-1, IL-6, IL-17, and others, are targeted by interleukin inhibitors because they are crucial for the development of autoimmune and inflammatory disorders. For example, Anakinra specifically inhibits IL-1, Tocilizumab targets the IL-6 receptor, and Secukinumab targets IL-17. These drugs effectively interrupt the key pathways of the inflammatory response by blocking the binding of specific interkines to their receptors and interfering with their biological activity. This targeted intervention can significantly reduce leukocyte activation and tissue damage caused by interkinesis, thereby effectively controlling inflammation and alleviating the symptoms of related diseases.

4.1.3. JAK inhibitor. JAK inhibitors are a relatively new class of anti-inflammatory drugs used to treat many autoimmune and inflammatory conditions, including psoriatic arthritis, rheumatoid arthritis, and some types of leukemia. The anti-inflammatory mechanism of JAK inhibitors is mainly achieved by targeting Janus Kinases (JAKs), which are key proteins that transmit signals from cell surface receptors to the cell nucleus.

The conversion of cell surface receptors' responses to cytokines and growth factors into genetic responses in the cell nucleus is largely attributed to the JAK/STAT signaling pathway. When this pathway is activated, specific cytokines such as interleukins and interferons bind to their corresponding cell surface receptors, causing receptor aggregation and activation of the associated JAKs. Signal transducers and activators of transcription (STATs) are phosphorylated by activated JAKs. After becoming dimers, phosphorylated STATs go to the cell nucleus, directly participating in regulating the expression of related genes and affecting cell proliferation, differentiation and immune response [17].

JAK inhibitors inhibit the JAK/STAT signaling pathway by blocking the activity of Janus kinases, thereby reducing the production of inflammatory mediators and the intensity of immune responses. These drugs can reduce the signaling of proinflammatory cytokines, including interferon, IL-6, and IL-12, and reduce inflammatory responses. At the same time, JAK inhibitors also regulate the activity of immune cells such as T cells, B cells and natural killer cells, reducing their aggressiveness or inflammatory contribution in autoimmune diseases and inflammatory conditions, thereby effectively controlling inflammation [18].

DOI: 10.54254/2753-8818/48/2024PJ0121

In clinical practice, JAK inhibitors such as Tofacitinib, Baricitinib and Upadacitinib have been widely used to treat moderate to severe rheumatoid arthritis and are being studied for other autoimmune and inflammatory diseases. These drugs inhibit the JAK/STAT pathway, which not only reduces the inflammatory response, but also improves the patient's symptoms and quality of life. Although JAK inhibitors provide an effective treatment option, potential side effects such as increased risk of infection need to be noted when using them, so the patient's health status needs to be carefully monitored during treatment [19].

4.2. Other strategies

In addition to drug treatment, there are a variety of non-drug strategies that can effectively fight inflammation, including lifestyle adjustments, dietary changes, physical therapy, and psychological intervention. Regular physical exercise and stress management such as meditation and yoga can help reduce inflammation levels. Adopting an anti-inflammatory diet rich in Omega-3 fatty acids, natural antioxidants, and fiber, as well as appropriate supplementation of anti-inflammatory nutrients such as curcumin and vitamin D, have also shown good anti-inflammatory effects. Physical therapy methods such as warm therapy, cold therapy, massage, and acupuncture can improve blood circulation and relieve muscle pain. In addition, cognitive behavioral therapy and good social support can help manage the mental stress associated with inflammation, thereby indirectly reducing inflammation levels. These non-drug methods can not only reduce the inflammatory response, but also improve the patient's overall health and quality of life, especially in the long-term management of chronic inflammatory diseases, combined with drug treatment, can provide a more comprehensive treatment effect.

5. Conclusion

This article explored how aging promotes elevated inflammation through multiple biological pathways, including changes in immune regulation, the persistence of chronic low-grade inflammation, cell aging and tissue damage, changes in gene expression, and increased oxidative stress. Together, these factors exacerbate the inflammatory response that occurs with age, which in turn affects physical health and disease susceptibility.

Not only is inflammation a sign of age, but it also serves as a trigger for the onset of many chronic illnesses. Inflammation plays a central role in conditions such as CVD and AD. In CVD, inflammation increases the risk of cardiac events by promoting atherosclerosis and endothelial dysfunction; in AD, neuroinflammation accelerates neurodegenerative changes such as the abnormal accumulation of amyloid beta and tau proteins.

In terms of treatment strategies, a variety of drug approaches to combat inflammation, including biologics, JAK inhibitors, and nonsteroidal anti-inflammatory medications, which offer therapies for various inflammatory routes and causes. These treatment strategies not only help reduce inflammatory symptoms, but may also delay or improve the progression of chronic diseases associated with aging.

In summary, understanding the complex interactions between aging and inflammation is essential for developing new treatments and improving the quality of life of older adults. Future studies should further explore the specific details of these mechanisms and develop more precise and personalized treatment options to address the challenges posed by aging and inflammation

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