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Research Progress on the Relationship between Red Blood Cell Lifespan and Rheumatic Immune System Diseases

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Abstract: *The lifespan of red blood cells (RBCs) is critical for maintaining normal blood circulation and oxygen transport. Rheumatic immune system diseases, however, can disrupt blood system functions through various immune mechanisms, potentially altering RBC lifespan. In recent years, growing evidence suggests that conditions such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) accelerate RBC destruction or modify their lifecycle via autoimmune responses and chronic inflammation. This review examines the relationship between RBC lifespan and rheumatic immune diseases, exploring the mechanisms by which these diseases affect RBC lifespan and their clinical implications. It also summarizes current research findings and technological advancements. Furthermore, the article discusses the potential of RBC lifespan as a biomarker for clinical diagnosis and disease monitoring, aiming to provide theoretical support for early diagnosis and personalized treatment of rheumatic immune diseases.*

Keywords: *Red Blood Cell Lifespan, Rheumatic Immune System Diseases, Rheumatoid Arthritis, Systemic Lupus Erythematosus*

1. Introduction

Red blood cells (RBCs) are the most abundant cell type in blood, primarily responsible for transporting oxygen and carbon dioxide to sustain normal physiological functions. Under normal conditions, RBCs have a lifespan of approximately 120 days, after which they are cleared by organs like the spleen. However, in many rheumatic immune system diseases, RBC lifespan is often compromised, leading to premature destruction or impaired function. Rheumatic immune diseases are a complex group of disorders characterized by abnormal immune responses, resulting in inflammatory damage to multiple organ systems. These include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Sjögren's syndrome, which not only affect the immune system but also impact the blood system to varying degrees.Recent studies on the pathological mechanisms of rheumatic immune diseases have revealed that chronic inflammation, immune dysregulation, and autoimmune reactions can alter RBC function, shorten their lifespan, and even affect RBC production and clearance. For instance, anemia is a common finding in RA patients, while SLE patients may experience RBC destruction accompanied by immune complex formation and RBC membrane damage. These changes not only reduce patients' quality of life but also worsen clinical outcomes and prognosis.This study aims to review the relationship between RBC lifespan and rheumatic immune system diseases, investigate the mechanisms by which these diseases affect RBC lifespan, and evaluate the potential of RBC lifespan as a biomarker for clinical applications. By analyzing existing research, we hope to offer new perspectives and theoretical foundations for early diagnosis, monitoring, and personalized treatment of rheumatic immune diseases[1].

2. Overview of Red Blood Cell Lifespan

2.1 Physiological Role and Lifecycle of Red Blood Cells

Red blood cells, also known as erythrocytes, are the most prevalent cells in blood, tasked with delivering oxygen from the lungs to tissues and transporting carbon dioxide back to the lungs for exhalation. Their primary component, hemoglobin, binds oxygen and carbon dioxide, facilitating gas exchange during circulation. The biconcave shape of RBCs provides a large surface area and flexibility,

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allowing them to navigate through tiny blood vessels, such as capillaries, to perform efficient gas exchange.The lifecycle of RBCs typically spans about 120 days, encompassing their production to clearance. RBC production, or erythropoiesis, occurs primarily in the bone marrow, where hematopoietic stem cells differentiate into erythroid progenitor cells and mature into functional RBCs. Once mature, RBCs enter the bloodstream to begin their approximately 120-day lifecycle.During circulation, RBCs undergo various physiological changes. Newly released RBCs are highly flexible and functional, capable of freely moving through blood vessels to transport oxygen. Over time, however, their shape and function deteriorate due to factors such as blood oxygen levels, RBC membrane integrity, and blood flow conditions.RBC aging typically involves membrane damage, reduced hemoglobin oxygen-binding capacity, and diminished activity of intracellular enzyme systems[2]. Eventually, aged RBCs are recognized and removed by macrophages in the spleen, liver, and bone marrow. These macrophages phagocytose senescent RBCs, breaking them down into components, with some hemoglobin metabolized into bilirubin and excreted via the liver. Beyond natural aging, RBC lifespan can be influenced by external factors such as diseases, medications, or immune system attacks. Shortened RBC lifespan can lead to clinical symptoms like anemia, making the study of RBC lifespan changes and their regulatory mechanisms vital for early diagnosis and treatment of related conditions[3].

2.2 Factors Influencing Red Blood Cell Lifespan

Several factors affect RBC lifespan, with the immune system playing a significant role. In rheumatic immune diseases, abnormal immune activation often triggers autoimmune reactions, producing autoantibodies that attack RBC membranes, causing hemolysis and shortening RBC lifespan. Oxidative stress is another key factor, as RBCs are exposed to oxidative environments during circulation, leading to damage to cell membranes and hemoglobin. With aging, RBCs' antioxidant capacity weakens, making them more susceptible to damage from free radicals and reactive oxygen species, which accelerates senescence.Mechanical stress from blood flow also contributes to RBC damage. Conditions like hypertension or vascular obstruction increase intravascular pressure, causing RBCs to sustain damage when passing through small vessels[4]. RBC membrane integrity is critical for their lifespan, but over time, membrane lipids and proteins may undergo oxidation and degradation, impairing normal function. Genetic factors also play a role, with hereditary conditions like thalassemia or sickle cell anemia causing abnormal RBC morphology or function, leading to faster destruction. Additionally, drugs and chemical toxins can affect RBC lifespan. Certain medications, such as antibiotics or antimalarials, may induce drug-related hemolytic anemia, while heavy metals and chemotherapeutic agents can suppress RBC production or cause destruction.Chronic diseases, particularly diabetes and hypertension, are often accompanied by low-grade chronic inflammation, which accelerates the shortening of RBC lifespan. In summary, immune dysregulation, oxidative stress, hemodynamic factors, membrane integrity, genetic predispositions, and drug toxicity collectively influence RBC lifespan. Understanding these factors is crucial for the early diagnosis and treatment of conditions like rheumatic immune diseases[5].

2.3 Methods and Techniques for Assessing Red Blood Cell Lifespan

Evaluating RBC lifespan involves various methods and technologies that help researchers and clinicians understand RBC aging, damage, and longevity. Common approaches include labeling techniques, hematological tests, molecular biology methods, and imaging technologies. Labeling is a traditional method for assessing RBC lifespan. By tagging RBCs with radioactive isotopes (e.g., Cr-51 labeling) or non-radioactive dyes, their survival time in the body can be tracked. Radioactive isotope labeling, while accurate, poses safety risks due to radiation exposure, limiting its clinical use. Non-radioactive dyes, such as fluorescent markers, offer a safer and effective alternative.Hematological tests are another widely used method, measuring parameters like RBC count, mean corpuscular volume (MCV), and red cell distribution width (RDW)[6]. Abnormalities in these parameters may indicate a shortened RBC lifespan. For instance, increased MCV or RDW often correlates with changes in RBC lifespan. These hematological markers provide indirect insights into RBC longevity.Molecular biology techniques offer more precise assessments. Recent advances in DNA labeling and RNA expression profiling allow researchers to observe molecular changes during RBC aging at the genetic level. For example, as RBCs age, degradation products of membrane proteins and hemoglobin accumulate, and molecular biology methods can measure these levels to estimate RBC lifespan. Additionally, changes in RBC surface molecules (e.g., CD47, CD44) can indicate whether RBCs are entering senescence. Imaging techniques, such as dynamic RBC imaging, have also been employed in recent years. Using

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technologies like fluorescence microscopy and confocal microscopy, researchers can observe RBC movement and damage in real time. These methods provide detailed data on RBC function and lifespan through dynamic tracking, particularly in laboratory settings.Overall, RBC lifespan assessment methods range from traditional labeling to advanced molecular biology and imaging techniques. Each has its strengths and limitations, and combining multiple approaches often yields more comprehensive results. Selecting appropriate techniques is critical for accurate RBC lifespan monitoring and disease diagnosis in both clinical and research contexts[7].

3. Overview of Rheumatic Immune System Diseases

3.1 Definition and Classification of Rheumatic Immune System Diseases

Rheumatic immune system diseases are a group of disorders caused by abnormal immune responses, characterized by the immune system attacking the body's own tissues, leading to chronic inflammation and tissue damage. These diseases present a wide range of clinical symptoms, potentially affecting multiple organ systems, including joints, skin, kidneys, and heart, and in severe cases, they can be life-threatening. The pathogenesis of these diseases is complex, involving genetic predispositions as well as environmental factors such as infections, medications, or external stimuli.Based on clinical manifestations and pathological mechanisms, rheumatic immune system diseases can be classified into various types[8]. Common conditions include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjögren's syndrome, ankylosing spondylitis, systemic sclerosis, and myositis. These diseases are typically chronic, with recurrent flares, and often have a prolonged course, significantly impacting patients' quality of life. Rheumatoid arthritis, a hallmark rheumatic disease, primarily manifests as joint inflammation and pain, potentially leading to joint deformity and loss of function. Systemic lupus erythematosus is a widespread autoimmune disease that, beyond joints, can affect the skin, kidneys, heart, and other organs. Sjögren's syndrome primarily involves damage to salivary and lacrimal glands, causing symptoms like dry mouth and eyes. Ankylosing spondylitis mainly affects the spine and large joints, resulting in persistent back pain and restricted mobility. Additionally, diseases like systemic sclerosis and myositis are characterized by skin hardening and muscle weakness, respectively.In these conditions, aberrant immune responses, including immune cell activity and autoantibody production, damage healthy tissues, triggering inflammation and organ dysfunction. As the disease progresses, inflammation often leads to fibrosis, severely affecting patients' daily lives and work. Thus, early diagnosis and effective treatment are critical for improving prognosis. Treatment for rheumatic immune diseases typically involves immunosuppressive agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and disease-modifying antirheumatic drugs (DMARDs) to control inflammation, alleviate symptoms, and prevent organ damage[9].

3.2 Immunopathological Mechanisms of Common Rheumatic Immune Diseases

The immunopathological mechanisms of rheumatic immune system diseases are complex and diverse, generally involving abnormal immune activation and attacks on the body's own tissues. Although different types of rheumatic diseases vary in presentation, they are all closely linked to immune overactivity and loss of immune tolerance. Key pathological mechanisms include dysfunctional immune cells, excessive cytokine production, autoantibody formation, and persistent inflammation. Rheumatoid arthritis, a classic rheumatic disease, is primarily driven by T-cell activation and excessive cytokine production. T cells play a central role in the inflammatory response, secreting cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1), which activate synovial cells, causing joint inflammation and damage. Additionally, rheumatoid factor, an autoantibody, binds to immune complexes on RBCs, amplifying the immune response and exacerbating joint inflammation. Systemic lupus erythematosus is a quintessential autoimmune disease characterized by the immune system producing autoantibodies that attack normal cells and tissues. Its immunopathology involves abnormal B-cell activation, leading to the production of antinuclear antibodies (ANAs) and other autoantibodies. These antibodies bind to nuclear components, forming immune complexes that deposit in tissues like the skin, kidneys, and joints, triggering chronic inflammation. Dysfunctional T cells, particularly overactive CD4+ T cells, also contribute by inducing B cells to produce more autoantibodies and causing organ damage. Sjögren's syndrome is driven by peripheral T-cell activation and autoantibody production, particularly anti-SSA/SSB antibodies. T cells secrete cytokines that activate epithelial cells in glands, leading to chronic inflammation and tissue damage. B cells also play a role by producing autoantibodies that further exacerbate gland destruction.

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Persistent immune and inflammatory responses eventually cause gland fibrosis, resulting in hallmark symptoms like dry mouth and eyes.In summary, the immunopathological mechanisms of rheumatic immune diseases involve not only abnormal immune cell activity but also excessive cytokine production, immune complex deposition, and autoantibody formation. These aberrant immune responses collectively damage the body's tissues, causing chronic inflammation and organ dysfunction. As research progresses, therapeutic strategies targeting these immune mechanisms continue to evolve, with immunosuppressive and anti-inflammatory treatments offering new hope for managing these conditions[10].

3.3 Impact of Rheumatic Immune Diseases on the Blood System

Rheumatic immune diseases have profound and widespread effects on the blood system, often manifesting as anemia, leukocyte abnormalities, and thrombocytopenia. Abnormal immune activation and chronic inflammation directly impair the production, function, and survival of blood cells, leading to various hematological issues. Different rheumatic diseases cause distinct hematological abnormalities through specific immune mechanisms, and these changes are often key clinical indicators of disease activity. Rheumatoid arthritis, one of the most common rheumatic diseases, affects not only joints but also the blood system, frequently causing anemia. RA-associated anemia, often termed "anemia of chronic disease," results from chronic inflammation, which reduces erythropoietin (EPO) production, disrupts iron utilization, and shortens RBC lifespan. Chronic inflammation also disturbs iron metabolism, inhibiting iron absorption and utilization, leading to iron deficiency anemia. Additionally, RA patients often exhibit mild to moderate leukocytosis, particularly during active disease phases, reflecting systemic inflammation.Systemic lupus erythematosus, a systemic autoimmune disease, commonly presents with anemia, leukopenia, and thrombocytopenia. Anemia in SLE is often hemolytic, driven by immune-mediated RBC destruction. Patients may produce anti-RBC antibodies that bind to RBCs, promoting their destruction. Leukopenia, particularly neutropenia, and thrombocytopenia are linked to immune complex deposition, vascular endothelial damage, and abnormal immune activation. These hematological abnormalities are closely associated with disease activity and prognosis, serving as critical markers for assessing SLE's clinical course. Sjögren's syndrome, another rheumatic disease, frequently leads to hemolytic anemia and leukopenia. Chronic inflammation and immune complex deposition impair blood cell function, particularly shortening RBC lifespan and causing anemia. The disease is also associated with positive antinuclear antibodies (ANA) and anti-SSA/SSB antibodies, which may exacerbate blood system damage.Overall, the impact of rheumatic immune diseases on the blood system is multifaceted, typically presenting as anemia, leukopenia, or thrombocytopenia. These changes are closely tied to abnormal immune responses and reflect disease activity and patients' overall health. Consequently, hematological assessments are vital for the diagnosis, treatment monitoring, and prognosis evaluation of rheumatic immune diseases.

4. Relationship Between Red Blood Cell Lifespan and Rheumatic Immune Diseases

4.1 Impact of Rheumatic Immune Diseases on Red Blood Cell Lifespan

Rheumatic immune diseases significantly affect red blood cell (RBC) lifespan through various immune mechanisms. Abnormal immune activation and chronic inflammation often accelerate RBC destruction, thereby shortening their lifespan. For example, in rheumatoid arthritis (RA), inflammatory responses trigger the release of cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1). These cytokines not only cause joint damage but also disrupt normal RBC production and maintenance. Chronic inflammation reduces erythropoietin (EPO) levels, inhibiting RBC production. Additionally, patients with rheumatic immune diseases frequently experience iron metabolism disorders, leading to iron deficiency anemia, which makes RBCs more susceptible to destruction. In diseases like systemic lupus erythematosus (SLE), anti-RBC antibodies produced by the immune system directly attack RBCs, causing hemolytic destruction and further shortening their lifespan.

4.2 Manifestations of Shortened Red Blood Cell Lifespan in Rheumatic Immune Diseases

Shortened RBC lifespan in rheumatic immune diseases manifests as various clinical symptoms, with anemia—particularly anemia of chronic inflammation—being the most common. Patients with RA and SLE often develop hemolytic anemia, characterized by accelerated RBC destruction and reduced

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hemoglobin levels. Concurrently, chronic inflammation impairs iron absorption and utilization, contributing to iron deficiency anemia. Symptoms such as fatigue, pallor, and palpitations are prevalent, and severe cases can significantly impact patients' quality of life and treatment outcomes. Moreover, shortened RBC lifespan may reduce circulating RBC counts, exacerbating tissue oxygen deficiency and leading to weakness and reduced exercise tolerance. Another manifestation is morphological changes in RBCs, often observed in anemia associated with rheumatic immune diseases. These changes include increased RBC volume or wider distribution width, indicating abnormal physiological or pathological alterations in RBCs.

4.3 Research Progress on the Interaction Between Red Blood Cell Function and the Immune System

In recent years, the interaction between RBC function and the immune system has emerged as a key focus in rheumatic immune disease research. Beyond their role in gas transport, RBCs play a significant part in immune responses. Studies have identified that RBC surfaces express immune-related molecules, such as CD47, which interacts with the SIRPα receptor on macrophages to inhibit phagocytosis, thereby supporting RBC survival. However, in rheumatic immune diseases, immune system dysregulation may disrupt these immunosuppressive molecules, leading to excessive recognition and clearance of RBCs. Additionally, under oxidative stress or immune complex formation, RBC membranes may expose signals that promote immune responses, a phenomenon commonly observed in SLE. RBCs are not limited to oxygen transport; they also act as "messengers" in the immune system, modulating immune responses. The interplay between RBCs and the immune system offers new perspectives and directions for treating rheumatic immune diseases. For instance, modulating this interaction could become a potential therapeutic strategy in the future.In summary, shortened RBC lifespan in rheumatic immune diseases manifests as anemia and hematological abnormalities, driven by aberrant immune responses. As research deepens, the role of RBCs in immune responses is increasingly recognized, and their interaction with the immune system may provide novel insights and approaches for clinical management.

5. Clinical Observations and Experimental Studies

5.1 Correlation Between Red Blood Cell Lifespan and Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a common rheumatic immune disease characterized by chronic joint inflammation and destruction. In RA patients, RBC lifespan is often shortened, leading to anemia. RA-associated anemia arises primarily from two factors: first, chronic inflammation disrupts iron metabolism, impairing iron absorption and utilization; second, immune responses trigger RBC destruction. Cytokines such as TNF-α and interleukin-6 (IL-6) in chronic inflammation suppress EPO secretion and reduce iron availability, exacerbating anemia. Additionally, the presence of rheumatoid factor may directly induce immune-mediated hemolysis, increasing RBC destruction rates and shortening their lifespan. Clinical studies show that anemia in RA patients is often correlated with disease duration, joint damage severity, and disease activity. Thus, monitoring RBC lifespan and anemia can serve as a key indicator for assessing RA activity.

5.2 Correlation Between Red Blood Cell Lifespan and Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease often accompanied by multi-organ damage. In SLE patients, shortened RBC lifespan is closely linked to abnormal immune responses. The immune system frequently produces autoantibodies, such as anti-RBC antibodies, which bind to RBCs, forming immune complexes that prompt their clearance by macrophages in the spleen and liver, leading to hemolytic destruction. This significantly shortens RBC lifespan. Research indicates that hemolytic anemia is common in SLE, often accompanied by leukopenia and thrombocytopenia. Beyond immune-mediated hemolysis, chronic inflammation in SLE also causes iron metabolism abnormalities, further worsening anemia. The degree of SLE activity is closely tied to changes in RBC lifespan, making clinical monitoring of anemia, RBC lifespan, and immune markers valuable for assessing disease activity and patient prognosis.

5.3 Impact of Other Rheumatic Immune Diseases on Red Blood Cell Lifespan

Beyond RA and SLE, other rheumatic immune diseases also significantly affect RBC lifespan.

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Sjögren's syndrome, another prevalent rheumatic condition, involves immune complex deposition and immune cell activation, which can accelerate RBC destruction. Patients with Sjögren's syndrome often exhibit anemia, particularly hemolytic or chronic inflammatory anemia. Due to prolonged inflammation, iron metabolism disruptions shorten RBC lifespan, aggravating anemia symptoms. Diseases like ankylosing spondylitis may also hasten RBC aging through chronic inflammation, though overt anemia is less common, with patients typically showing mild RBC functional abnormalities. Similarly, conditions such as systemic sclerosis and dermatomyositis demonstrate immune dysregulation and shortened RBC lifespan, particularly under prolonged immune activation and inflammation, negatively impacting RBC production and longevity. In conclusion, RBC lifespan is consistently shortened across various rheumatic immune diseases, driven by chronic inflammation, immune dysregulation, and iron metabolism disorders. Clinical observations and experimental studies elucidating these effects not only aid in early diagnosis and treatment but also provide critical insights for developing individualized therapeutic strategies.

6. Conclusion

Changes in RBC lifespan in rheumatic immune diseases are multifaceted, influenced by immune dysregulation, chronic inflammation, and iron metabolism disorders. Diseases like RA and SLE significantly shorten RBC lifespan through immune responses and cytokine activity, leading to anemia and other hematological abnormalities. These changes not only impair patients' quality of life but also reflect disease activity. The interplay between RBCs and the immune system highlights new research avenues, potentially offering novel therapeutic targets for rheumatic immune diseases. Clinically, monitoring RBC lifespan and related hematological markers can help assess disease progression and treatment efficacy, supporting personalized therapeutic approaches.

References

[1] Rybtsova, Natalia, Tatiana N. Berezina, and Stanislav Rybtsov. "Molecular markers of blood cell populations can help estimate aging of the immune system." International Journal of Molecular Sciences 24.6 (2023): 5708.

[2] Da Silva, Rose Mary Ferreira L., and Lucas Espindula Borges. "Neutrophil-lymphocyte ratio and red blood cell distribution width in patients with atrial fibrillation and rheumatic valve disease." Current Vascular Pharmacology 21.6 (2023): 367-377.

[3] Guder, Christian, et al. "Osteoimmunology: a current update of the interplay between bone and the immune system." Frontiers in Immunology 11 (2020): 58.

[4] Qu, Jiling, et al. "Correlation analysis of hemoglobin-to-red blood cell distribution width ratio and frailty in elderly patients with coronary heart disease." Frontiers in cardiovascular medicine 8 (2021): 728800.

[5] Bianchi, Marzia, et al. "Preclinical and clinical developments in enzyme-loaded red blood cells: An update." Expert Opinion on Drug Delivery 20.7 (2023): 921-935.

[6] Ren, Yijun, Chengkai Yan, and Huan Yang. "Erythrocytes: Member of the immune system that should not be ignored." Critical Reviews in Oncology/Hematology 187 (2023): 104039.

[7] Cabling, Marven G., et al. "Cardiovascular disease and bone health in aging female rheumatic disease populations: A review." Women's Health 19 (2023): 17455057231155286.

[8] Luo, Ting-Ting, et al. "The involvement of glucose and lipid metabolism alteration in rheumatoid arthritis and its clinical implication." Journal of Inflammation Research (2023): 1837-1852.

[9] Jang, Sunhee, Eui-Jong Kwon, and Jennifer Jooha Lee. "Rheumatoid arthritis: pathogenic roles of diverse immune cells." International journal of molecular sciences 23.2 (2022): 905.

[10] Dooley, Leanne M., et al. "Rheumatic heart disease: a review of the current status of global research activity." Autoimmunity reviews 20.2 (2021): 102740.