



**SYSTEMIC LUPUS ERYTHEMATOSUS: MULTISYSTEM INVOLVEMENT AND
MODERN IMMUNOSUPPRESSIVE THERAPY**

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Abstract

Systemic lupus erythematosus (SLE) is a chronic, autoimmune, multisystem inflammatory disease characterized by the production of autoantibodies and immune complex deposition, leading to tissue damage across multiple organ systems. The disease predominantly affects women of reproductive age and demonstrates a highly heterogeneous clinical presentation ranging from mild mucocutaneous manifestations to life-threatening renal, neurological, and hematological involvement. The pathogenesis of SLE involves genetic susceptibility, environmental triggers, hormonal influences, and immune dysregulation, particularly involving B cells, T cells, and type I interferon pathways. Advances in immunopathogenesis have led to the development of targeted immunosuppressive therapies, including biologic agents aimed at B-cell modulation and cytokine inhibition. This article reviews the mechanisms of multisystem involvement, diagnostic principles, and contemporary immunosuppressive treatment strategies for SLE, highlighting recent therapeutic innovations and challenges in long-term disease management.

Keywords

Systemic lupus erythematosus, autoimmunity, immune complexes, lupus nephritis, biologic therapy, B-cell inhibition, immunosuppressive treatment.

Introduction

Systemic lupus erythematosus (SLE) is a prototypical systemic autoimmune disease characterized by the loss of immune tolerance to nuclear antigens. It affects multiple organs, including the skin, joints, kidneys, cardiovascular system, lungs, central nervous system, and hematopoietic system. The disease follows a relapsing-remitting course and varies significantly in severity.



SLE primarily affects women, particularly during reproductive years, suggesting hormonal influences in disease development. Epidemiological data indicate higher prevalence in certain ethnic populations, reflecting genetic predisposition. Advances in immunology have significantly improved understanding of disease mechanisms, enabling development of more targeted therapeutic approaches.

Pathophysiology

The pathogenesis of SLE is multifactorial and involves a complex interaction between genetic, environmental, and immunological factors.

Genetic and Environmental Factors

Susceptibility genes affecting immune regulation increase the risk of autoimmune responses. Environmental triggers such as ultraviolet radiation, infections, and certain medications may initiate or exacerbate disease activity.

Autoantibody Production and Immune Complex Formation

A hallmark of SLE is the production of autoantibodies against nuclear components, including anti-dsDNA, anti-Smith, and antiphospholipid antibodies. These autoantibodies form immune complexes that deposit in tissues, activating complement pathways and inducing inflammation.

Role of B Cells and T Cells

B-cell hyperactivity plays a central role in SLE pathogenesis. Abnormal T-cell regulation further amplifies autoantibody production. Increased activity of type I interferons contributes to immune dysregulation and chronic inflammation.

Multisystem Involvement

SLE can affect virtually any organ system.

Musculoskeletal System

Arthralgia and non-erosive arthritis are common manifestations and may resemble rheumatoid arthritis.

Cutaneous Manifestations

The classic malar rash, photosensitivity, and discoid lesions are characteristic skin findings.

Renal Involvement

Lupus nephritis is one of the most serious complications and a major predictor of morbidity and mortality. Immune complex deposition in glomeruli leads to proteinuria, hematuria, and progressive renal impairment.

Cardiovascular System

Patients have an increased risk of pericarditis, myocarditis, accelerated atherosclerosis, and thrombotic events.



Central Nervous System

Neuropsychiatric lupus may present with seizures, psychosis, cognitive dysfunction, or cerebrovascular events.

Hematological Abnormalities

Anemia, leukopenia, thrombocytopenia, and antiphospholipid syndrome are frequent hematologic features.

Diagnosis

Diagnosis is based on clinical findings supported by immunological testing. Classification criteria developed by the European League Against Rheumatism (EULAR) in collaboration with the American College of Rheumatology emphasize the presence of antinuclear antibodies (ANA) as an entry criterion, followed by weighted clinical and immunologic domains.

Laboratory evaluation includes:

1. Antinuclear antibodies (ANA)
2. Anti-dsDNA antibodies
3. Anti-Smith antibodies
4. Complement levels (C3, C4)
5. Urinalysis for renal involvement

Modern Immunosuppressive Therapy

Treatment of SLE depends on disease severity and organ involvement.

Conventional Therapy

Glucocorticoids remain central in controlling acute inflammation.

Hydroxychloroquine is recommended for most patients due to its immunomodulatory and protective effects.

Immunosuppressive agents such as azathioprine, mycophenolate mofetil, and cyclophosphamide are used in moderate to severe disease, especially lupus nephritis.

Biologic Therapy

Recent advances have introduced targeted biologic agents:

Belimumab, a monoclonal antibody targeting B-lymphocyte stimulator (BLyS), reduces disease activity.

Rituximab, a B-cell depleting agent, is used in refractory cases.

Novel therapies targeting interferon pathways show promising results.



These therapies aim to reduce corticosteroid dependence and prevent long-term organ damage.

Discussion

SLE is a highly heterogeneous disease requiring individualized management. Early diagnosis and aggressive treatment of organ-threatening manifestations significantly improve outcomes. The emergence of biologic therapies represents a major advancement in SLE management, offering targeted immunomodulation with improved safety profiles.

Long-term management must balance disease control with minimization of treatment-related toxicity. Multidisciplinary care involving rheumatologists, nephrologists, cardiologists, and neurologists is essential for optimal patient outcomes.

Despite therapeutic progress, challenges remain in predicting disease flares, managing refractory cases, and preventing cumulative organ damage.

Conclusion

Systemic lupus erythematosus is a complex autoimmune disease characterized by multisystem involvement and diverse clinical manifestations. Immune dysregulation, autoantibody production, and immune complex deposition underlie tissue damage across multiple organs. Modern immunosuppressive therapy, including conventional agents and targeted biologic treatments, has significantly improved survival and quality of life. Early recognition, personalized treatment strategies, and multidisciplinary care remain fundamental in optimizing long-term outcomes for patients with SLE.

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