PRIMEVIEW

SYSTEMIC LUPUS ERYTHEMATOSUS

nature REVIEWS DISEASE PRIMERS

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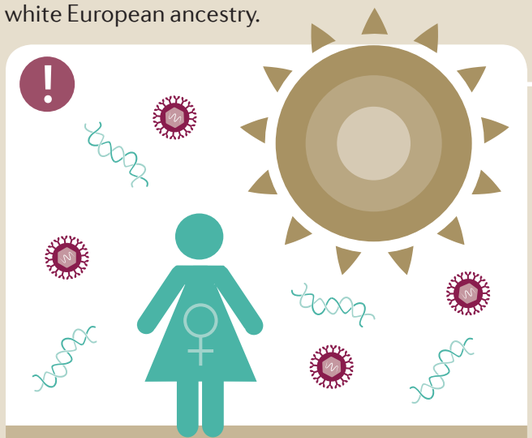
Systemic lupus erythematosus (SLE) is a serious, chronic autoimmune disorder with a heterogeneous clinical presentation potentially involving many organs.

EPIDEMIOLOGY

Prevalence, age of onset and mortality risk of SLE vary considerably. The annual incidence in the United States is 2–7.6 per 100,000 and the prevalence is 19–159 per 100,000. Women of childbearing age are particularly affected, with an estimated female to male sex ratio of 9–15 to 1. In addition to sex, ethnicity contributes to the risk of SLE. Individuals of Hispanic, Asian and African origin have a higher risk of developing SLE, develop the disease at a younger age and have more-frequent renal complications than people of white European ancestry.



Key determinants of disease progression include genetic factors that shape immune function, infection with Epstein-Barr virus, endocrine factors (for example, female sex hormones) and environmental triggers (for example, UV radiation and certain drugs). Except for cases caused by rare mutations in genes encoding proteins involved in the complement pathway, SLE is considered a polygenic disease.

DIAGNOSIS

No diagnostic criteria are available; clinicians tend to use the classification criteria proposed by the American College of Rheumatology, which were designed for research purposes

SLE is heterogeneous with considerable variability in clinical manifestations and disease severity

Early disease diagnosis and the prevention of flares are important to reduce tissue damage and long-term morbidity and mortality

Diagnosis is based on clinical manifestations and laboratory tests (including measurement of autoantibody titres)

SLE-associated mortality has improved with a 10-year survival of 60% in the second half of the twentieth century to >90% in the 1980s, at which point survival plateaued. The SLE-associated renal complication — lupus nephritis — is one of the strongest predictors of increased mortality risk. Other factors that determine mortality are an increased infection risk owing to immunosuppressive therapy and cardiovascular comorbidities.

QUALITY OF LIFE

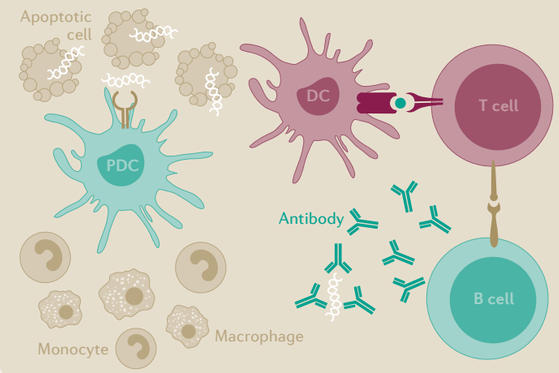
Quality of life of patients with SLE is decreased compared with healthy controls owing to disease complications and treatments, particularly glucocorticoids. Using several SLE-associated quality of life instruments, patients report higher levels of pain, fatigue, anxiety and depression.

OUTLOOK

Autoantibodies can be detected 9 years before diagnosis, which opens the door for primary prevention. Only one drug has been approved for use in SLE in the past 60 years (belimumab, a BAFF inhibitor). Better patient stratification might overcome some of the difficulties caused by disease heterogeneity and improve trial design.

MECHANISMS

SLE is characterized by an autoimmune reaction that involves the innate and adaptive immune systems. Activation of the innate immune system involves nucleic acids released from apoptotic cells, which activate Toll-like receptors (TLRs) on plasmacytoid dendritic cells (PDCs), resulting in cytokine release (type I interferons (IFNs)). Type I IFNs promote antigen presentation by dendritic cells (DCs), leading to the activation of T cells. B cells are driven to produce autoantibodies by interactions with T cells and by cytokines produced by DCs. The disease ultimately manifests as tissue damage driven by autoimmunity and excessive immune activation.



MANAGEMENT

Management of SLE involves suppression of the immune system. This is initially achieved with glucocorticoids and antimalarials, (especially hydroxychloroquine), but other immunosuppressants are also used for long-term disease control. The lowest possible dose of glucocorticoids should be used to minimize adverse effects; co-treatment with cyclophosphamide (a chemotoxic agent), mycophenolate mofetil (a purine synthesis inhibitor) or rituximab (a B cell-specific antibody) is also used for more-aggressive disease.

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