Systemic Lupus Erythematosus (SLE)

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Systemic lupus erythematosus (SLE) is a severe, relapsing, remitting multisystem **autoimmune disease**. The name systemic lupus implies that almost any organ or system within the body might be affected and lupus is perhaps the classical multi-symptom illness. Onset can occur at any age however it most typically presents in young adult females at a female to male ratio of 9:1.

Juvenile onset SLE

Juvenile-onset SLE (JSLE) is the childhood form of SLE. It is a relatively rare condition with an unclear prevalance in the UK. Although the annual incidence of juvenile SLE is estimated to be 0.36–0.9 per 100,000 children per year, and is generally higher in non-Caucasian children, especially black, Hispanic, and Asian populations. Onset occurs prior to the age of 18, typically between 12–16 years and accounts for up to 20% of all cases of SLE.

The complexity of this disease is reflected in the diverse clinical and immunological symptoms upon which diagnosis is based. The diagnosis is based upon the revised American College of Rheumatology classification criteria for adult onset SLE which has been adopted to be used in a juvenile population. It consists of 11 criteria (which include malar rash, oral or nasal ulceration, nephritis and a positive test for nuclear antibodies) of which four have to be met, simultaneously or periodically before a diagnosis can be fulfilled.

A complex interplay between genetic and environmental factors appears to contribute towards its immunopathogenesis, resulting in activation of all components of both the innate and acquired immune system.

Immune system dysfunction

The disease is characterised by the production of 'self' (auto) antibodies (directed against nuclear 'self' (auto) antigens), inflammation and organ damage. The presence of antinuclear antibodies has been detected in the serum of a majority of patients before the onset of clinical disease symptoms, and levels of certain auto-antibodies have been found to correlate with disease activity supporting a role for these antibodies in mediating disease pathology. It is thought that these antibodies form antibody-nuclear antigen immune complexes, which deposit in tissues and trigger local inflammation, thereby contributing to tissue injury.

Increased **apoptosis** (programmed cell death) and defective clearance of apoptotic material are characteristic of human SLE. Autoantigens typical of lupus cluster in surface blebs of apoptotic cells, increasing their immune-exposure. Saturation of physiological processes to safely remove apoptotic debris amplifies autoantigen exposure.

Neutrophils are the most abundant leukocytes in human blood and one of the first immune subsets to respond to a microbial insult. However dysregulation in both their function and cell death has been reported in SLE. The increased formation and decreased dismantling of Neutrophil Extracellular Traps (NETs) is also thought to be a source of autoantigen exposure. A granulocyte gene signature which may relate to the presence of an inflammatory subset of neutrophils called low density granulocytes has also been shown in JSLE patients.

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The innate immune systems role in the development of SLE is supported by the observation that a majority of patients with SLE display an increased expression of type I Interferon (IFN)–regulated genes (referred to as an IFN signature).

Plasmacytoid dendritic cells (pDC) are the main producers of Type I IFN's in response to viral infections, in SLE, these cells are also induced to synthesize IFN via Toll-like receptor (TLR) ligation by endogenous derived nucleic acids, a source of which may be increased apoptosis and NETs.

Type I IFN contributes to loss of tolerance and activation of autoreactive T and B cells with production of autoantibodies.

B lymphocytes are the cells of the immune system that make antibodies; inappropriate activation and proliferation of autoreactive memory B cells in the periphery are also characteristic of SLE.

T lymphocytes are also thought to contribute to disease progression and pathology.
T cells that are reactive with several nuclear autoantigens have been isolated from the peripheral blood of SLE patients. T cells from SLE patients also display abnormal signalling and secrete cytokines that promote inflammation. Regulatory T cells (cells important in maintaining cell tolerance) have been shown to be low in SLE and their suppressive function impaired.