378 Systemic Lupus Erythematosus

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DEFINITION AND PREVALENCE

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding autoantibodies and immune complexes. In most patients, autoantibodies are present for a few years before the first clinical symptom appears. Ninety percent of patients are women of child-bearing years; people of all genders, ages, and ethnic groups are susceptible. Prevalence of SLE in the United States is 20 to 150 per 100,000 women depending on race and gender; highest prevalence is in African-American and Afro-Caribbean women, and lowest prevalence is in white men.

PATHOGENESIS AND ETIOLOGY

The proposed pathogenic mechanisms of SLE are illustrated in Fig. 378-1. Interactions between susceptibility genes and environmental factors result in abnormal immune responses, which vary between different patients. Those responses may include (1) activation of innate immunity (dendritic cells, monocyte/macrophages) by CpG DNA, DNA in immune complexes, viral DNA or RNA, and RNA in RNA/protein self-antigens; (2) lowered activation thresholds and abnormal activation pathways in adaptive immunity cells (mature T and B lymphocytes); (3) ineffective regulatory CD4+ and CD8+ T cells, B cells, and myeloid-derived suppressor cells; and (4) reduced clearance of immune complexes and apoptotic cells. Self-antigens (nucleosomal DNA/protein; RNA/protein in Sm, Ro, and La; phospholipids) are recognized by the immune system in surface blebs of apoptotic cells; thus autoantigens, autoantibodies, and immune complexes persist for prolonged periods of time, allowing inflammation and disease to develop. Immune cell activation is accompanied by increased secretion of proinflammatory type 1 and 2 interferons (IFNs), tumor necrosis factor α (TNF-α), interleukin (IL) 17 and B cell-maturation/survival cytokines B lymphocyte stimulator (BLyS/BAFF), and IL-10. Upregulation of genes induced by