Systemic Lupus Erythematosus (SLE)

SLE is an autoimmune disease involving multiple organs, characterized by a vast array of autoantibodies, particularly antinuclear antibodies (ANAs), in which injury is caused mainly by deposition of immune complexes and binding of antibodies to various cells and tissues. The disease may be acute or insidious in its onset, and is typically a chronic, remitting and relapsing, often febrile, illness. Injury to the skin, joints, kidney, and serosal membranes is prominent. Virtually every other organ in the body, however, may also be affected. The clinical presentation of SLE is so variable that the American College of Rheumatology has established a complex set of criteria for this disorder, which is helpful for clinicians and for the design and assessment of clinical trials (Table 6-9). However, the disease is very heterogeneous, and any patient may present with any number of these clinical features. SLE is a fairly common disease, with a prevalence that may be as high as 1 in 2500 in certain populations. Similar to many autoimmune diseases, SLE predominantly affects women, with a frequency of 1 in 700 among women of childbearing age and a female-to-male ratio of 9:1 during the reproductive age group of 17 through 55 years. By comparison, the female-to-male ratio is only 2:1 for disease developing during childhood or after the age of 65. The prevalence of the disease is 2- to 3-fold higher in blacks and Hispanics than in whites. Although SLE often presents in the 20s and 30s, it may manifest at any age, even in early childhood.

Spectrum of Autoantibodies in SLE

The hallmark of SLE is the production of autoantibodies. Some antibodies recognize diverse nuclear and cytoplasmic components of the cell that are neither organ- nor species-specific, and others are directed against cell surface antigens of blood cells. Apart from their value in the diagnosis and management of patients with SLE, these autoantibodies are of major pathogenetic significance, as, for example, in the immune complex-mediated glomerulonephritis so typical of this disease. Autoantibodies are found in many diseases in addition to SLE, and antibodies of different specificities tend to be associated with different autoimmune disorders (Table 6-10).

Antinuclear antibodies (ANAs). These are directed against nuclear antigens and can be grouped into four categories: (1) antibodies to DNA, (2) antibodies to histones, (3) antibodies to nonhistone proteins bound to RNA, and (4) antibodies to nucleolar antigens. Table 6-10 lists several ANAs and their association with SLE as well as with other autoimmune diseases to be discussed later. The most widely used method for detecting ANAs is indirect immunofluorescence, which can identify antibodies that bind to a variety of nuclear antigens, including DNA, RNA, and proteins (collectively called *generic ANAs*). The pattern of nuclear fluorescence suggests the type of antibody present in the patient's serum. Four basic patterns are recognized (Fig. 6-24):

Table 6-9 1997 Revised Criteria for Classification of Systemic Lupus Erythematosus*

Criterion	Definition
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
5. Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
6. Serositis	Pleuritis—convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion, or Pericarditis—documented by electrocardiogram or rub or evidence of pericardial effusion
7. Renal disorder	Persistent proteinuria >0.5 g/dL or >3 if quantitation not performed or Cellular casts—may be red blood cell, hemoglobin, granular, tubular, or mixed
8. Neurologic disorder	Seizures—in the absence of offending drugs or known metabolic derangements (e.g., uremia, ketoacidosis, or electrolyte imbalance), or Psychosis—in the absence of offending drugs or known metabolic derangements (e.g., uremia, ketoacidosis, or electrolyte imbalance)
9. Hematologic disorder	Hemolytic anemia—with reticulocytosis, or Leukopenia—$<4.0 \times 10^9$ cells/L (4000 cells/mm^3) total on two or more occasions, or Lymphopenia—$<1.5 \times 10^9$ cells/L (1500 cells/mm^3) on two or more occasions, or Thrombocytopenia—$<100 \times 10^9$ cells/L (100×10^3 cells/mm^3) in the absence of offending drugs
10. Immunologic disorder	Anti-DNA antibody to native DNA in abnormal titer, or Anti-Sm—presence of antibody to Sm nuclear antigen, or Positive finding of antiphospholipid antibodies based on (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies, (2) a positive test for lupus anticoagulant using a standard test, or (3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by negative *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with drug-induced lupus syndrome

*This classification, based on 11 criteria, was proposed for the purpose of identifying patients in clinical studies. A person is said to have SLE if any four or more of the 11 criteria are present, serially or simultaneously, during any period of observation.
From Tan EM, et al: The revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271; and Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.