(secondary to consumption of complement proteins) and granular deposits of complement and immunoglobulins in the glomeruli further support the immune complex nature of the disease. T cell infiltrates are also frequently seen in the kidneys, but the role of these cells in tissue damage is not established.

- **Autoantibodies specific for red cells, white cells, and platelets opsonize these cells and promote their phagocytosis and lysis.** There is no evidence that ANAs, which are involved in immune complex formation, can penetrate intact cells. If cell nuclei are exposed, however, the ANAs can bind to them. In tissues, nuclei of damaged cells react with ANAs, lose their chromatin pattern, and become homogeneous, to produce so-called LE bodies or hematoxylin bodies. Related to this phenomenon is the *LE cell*, which is readily seen when blood is agitated in vitro. The LE cell is any phagocytic leukocyte (blood neutrophil or macrophage) that has engulfed the denatured nucleus of an injured cell. The demonstration of LE cells in vitro was used in the past as a test for SLE. With new techniques for detection of ANAs, however, this test is now largely of historical interest. Sometimes, LE cells are found in pericardial or pleural effusions in patients.
- **Antiphospholipid antibody syndrome**. Patients with antiphospholipid antibodies may develop venous and arterial thromboses, which may be associated with recurrent spontaneous miscarriages and focal cerebral or ocular ischemia. This constellation of clinical features, in association with lupus, is referred to as the *secondary antiphospholipid antibody syndrome*. The mechanisms of thrombosis are not defined, and antibodies against clotting factors, platelets and endothelial cells have all been proposed as being responsible for thrombosis (Chapter 4). Some patients develop these autoantibodies and the clinical syndrome without associated SLE. They are said to have the *primary antiphospholipid antibody syndrome* (Chapter 4).
- The neuropsychiatric manifestations of SLE have been attributed to antibodies that react with neurons or receptors for various neurotransmitters and cross the blood brain barrier. However, this is not established and mechanisms involving other immune factors, such as cytokines, may also underlie the cognitive dysfunction and other CNS abnormalities that are associated with SLE.

MORPHOLOGY

The morphologic changes in SLE are extremely variable. The frequency of individual organ involvement is shown in Table 6-11. The most characteristic lesions result from immune complex deposition in blood vessels, kidneys, connective tissue, and skin.

Blood Vessels. An acute necrotizing vasculitis involving capillaries, small arteries and arterioles may be present in any tissue. The arteritis is characterized by fibrinoid deposits in the vessel walls. In chronic stages, vessels undergo fibrous thickening with luminal narrowing.

Kidney. Up to 50% of SLE patients have clinically significant renal involvement. All of the glomerular lesions described later are the result of deposition of immune complexes that are regularly present in the mesangium or along the entire basement membrane and sometimes throughout the glomerulus. Both in situ formation and deposition of preformed circulating immune complexes may contribute to the injury, but the reason for the wide spectrum of histopathologic lesions (and clinical manifestations) in patients with lupus nephritis remains uncertain.

The kidney virtually always shows some evidence of renal abnormality if examined by electron microscopy and immunofluorescence. According to the currently accepted classification, six patterns of glomerular disease are seen in SLE. It should be noted that there is some overlap within these classes and over time lesions may evolve from one class to another. Thus, the exact percentage of patients with each of the six classes of lesions is difficult to determine. Suffice it to say that Class I is the least common and class IV is the most common pattern.

- **Minimal mesangial lupus nephritis** (class I) is very uncommon, and is characterized by immune complex deposition in the mesangium, identified by immunoflourescence and by electron microscopy, but without structural changes by light microscopy.
- **Mesangial proliferative lupus nephritis** (class II) is characterized by mesangial cell proliferation, often accompanied by accumulation of mesangial matrix, and granular mesangial deposits of immunoglobulin and complement without involvement of glomerular capillaries.
- **Focal lupus nephritis** (class III) is defined by involvement of fewer than 50% of all glomeruli. The lesions may be segmental (affecting only a portion of the glomerulus) or global (involving the entire glomerulus). Affected glomeruli may exhibit swelling and proliferation of endothelial and mesangial cells associated with leukocyte accumulation, capillary necrosis, and hyaline thrombi. There is also often extracapillary proliferation associated with focal necrosis and crescent formation (Fig. 6-26*A*). The clinical presentation ranges from mild hematuria and proteinuria to acute renal insufficiency. Red cell casts in the urine are common when the disease is active. Some patients progress to diffuse glomerulonephritis.

Table 6-11 Clinical and Pathologic Manifestations of Systemic Lupus Erythematosus

Clinical Manifestation	Prevalence in Patients (%)*
Hematologic	100
Arthritis, arthralgia or myalgia	80-90
Skin	85
Fever	55-85
Fatigue	80-100
Weight loss	60
Renal	50-70
Neuropsychiatric	25-35
Pleuritis	45
Pericarditis	25
Gastrointestinal	20
Raynaud phenomenon	15-40
Ocular	5-15
Peripheral neuropathy	15

*Percentages are approximate and may vary with age, ethnicity, and other factors. Table compiled with the assistance of Dr. Meenakshi Jolly, Rush Medical Center, Chicago.