The active (or proliferative) inflammatory lesions can heal completely or lead to chronic global or segmental glomerular scarring.

- **Diffuse lupus nephritis** (class IV) is the most common and severe form of lupus nephritis. The lesions are similar to those in class III, but differ in extent; typically, in class IV nephritis half or more of the glomeruli are affected. As in class III, the lesions may be segmental or global and on the basis of this, it can be subclassified as Class IV segmental (IV-S) or Class IV global (IV-G). Involved glomeruli show proliferation of endothelial, mesangial and epithelial cells (Fig. 6-26*B*), with the latter producing cellular crescents that fill Bowman's space (Chapter 20). Subendothelial immune complex deposits may create a circumferential thickening of the capillary wall, forming "wire loop" structures on light microscopy (Fig. 6-26*C*). Immune complexes can be readily detected by electron microscopy (Fig. 6-26*D*) and immunofluorescence (Fig. 6-26*E*). Lesions may progress to scarring of glomeruli. Patients with diffuse glomerulonephritis are usually symptomatic, showing hematuria as well as proteinuria. Hypertension and mild to severe renal insufficiency are also common.
- **Membranous lupus nephritis** (class V) is characterized by diffuse thickening of the capillary walls due to deposition of subepithelial immune complexes, similar to idiopathic membranous nephropathy, described in Chapter 20. The immune complexes are usually accompanied by increased production of basement membrane-like material. This lesion is usually accompanied by severe proteinuria or nephrotic syndrome, and may occur concurrently with focal or diffuse lupus nephritis.
- **Advanced sclerosing lupus nephritis** (class VI) is characterized by sclerosis of more than 90% of the glomeruli, and represents end-stage renal disease.
- Changes in the interstitium and tubules are frequently present in lupus nephritis patients. Rarely, **tubulointerstitial lesions** may be the dominant abnormality. Discrete immune complexes similar to those in glomeruli are present in the tubular or peritubular capillary basement membranes in many lupus nephritis patients, but the clinical significance of these extraglomerular deposits is not established. Often, there are well-organized B-cell follicles in the interstitium, with plasma cells that may be sources of autoantibodies.

Skin. Characteristic erythema affects the face along the bridge of the nose and cheeks (the "butterfly" rash) in approximately 50% of patients, but a similar rash may also be seen on the extremities and trunk. Urticaria, bullae, maculopapular lesions, and ulcerations also occur. Exposure to sunlight incites or accentuates the erythema. Histologically the involved areas show vacuolar degeneration of the basal layer of the epidermis (Fig. 6-27*A*). In the dermis, there is variable edema and perivascular inflammation. Vasculitis with fibrinoid necrosis may be prominent. Immunofluorescence microscopy shows deposition of immunoglobulin and complement along the dermoepidermal junction (Fig. 6-27*B*), which may also be present in uninvolved skin. This finding is not diagnostic of SLE and is sometimes seen in scleroderma or dermatomyositis.

Joints. Joint involvement is typically a nonerosive synovitis with little deformity, which contrasts with rheumatoid arthritis.

Central Nervous System. Neuropsychiatric symptoms of SLE have often been ascribed to acute vasculitis, but in histologic studies of the nervous system in such patients significant vasculitis is rarely present. Instead, noninflammatory occlusion of small vessels by intimal proliferation is sometimes noted, which may be due to endothelial damage by autoantibodies or immune complexes.

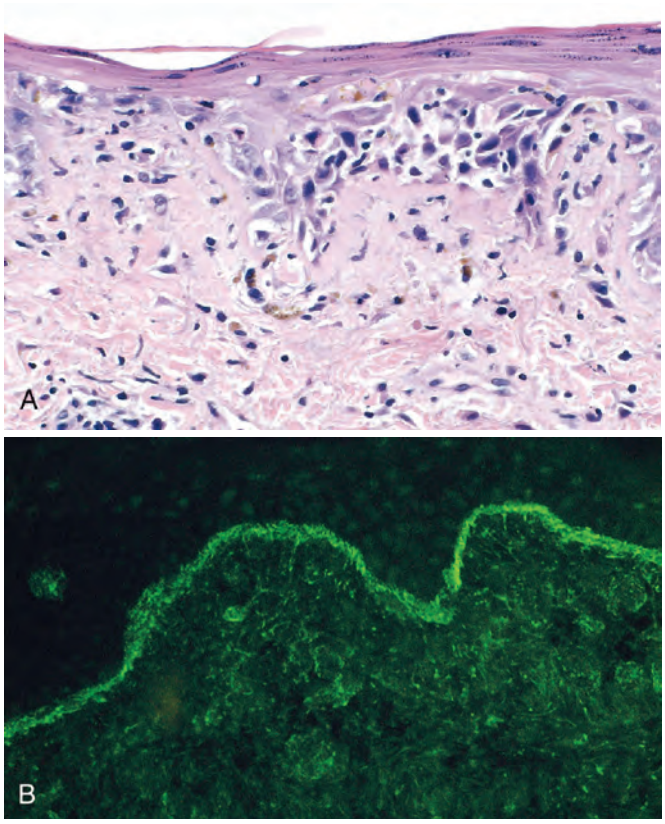

Figure 6-27 Systemic lupus erythematosus involving the skin. **A,** An H&E-stained section shows liquefactive degeneration of the basal layer of the epidermis and edema at the dermoepidermal junction. **B,** An immunofluorescence micrograph stained for IgG reveals deposits of Ig along the dermoepidermal junction. (A, Courtesy Dr. Jag Bhawan, Boston University School of Medicine, Boston, Mass. **B,** Courtesy Dr. Richard Sontheimer, Department of Dermatology, University of Texas Southwestern Medical School, Dallas, Texas.)

Pericarditis and Other Serosal Cavity Involvement. Inflammation of the serosal lining membranes may be acute, subacute, or chronic. During the acute phases, the mesothelial surfaces are sometimes covered with fibrinous exudate. Later they become thickened, opaque, and coated with a shaggy fibrous tissue that may lead to partial or total obliteration of the serosal cavity. Pleural and pericardial effusions may be present.

Cardiovascular system involvement may manifest as damage to any layer of the heart. Symptomatic or asymptomatic pericardial involvement is present in up to 50% of patients. Myocarditis, or mononuclear cell infiltration, is less common and may cause resting tachycardia and electrocardiographic abnormalities. Valvular abnormalities, primarily of the mitral and aortic valves, manifest as diffuse leaflet thickening that may be associated with dysfunction (stenosis and/or regurgitation). Valvular (or so-called Libman-Sacks) endocarditis was more common prior to the widespread use of steroids. This nonbacterial verrucous endocarditis takes the form of single or multiple 1- to 3-mm warty deposits on any heart valve, distinctively on either surface of the leaflets (Fig. 6-28). By comparison, the