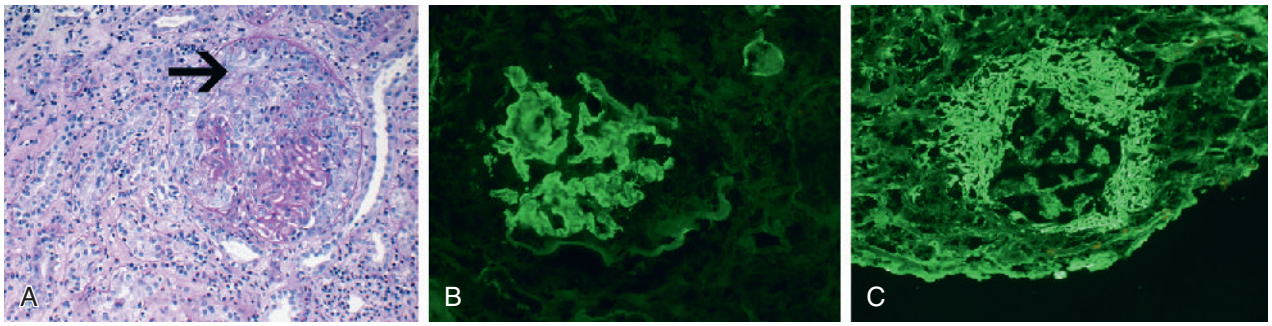

FIGURE 28-10 Anti–glomerular basement membrane–mediated disease. **A,** Light microscopy shows a large, circumferential crescent *(arrow)*, with collapse of the glomerular capillary tufts and many infiltrating neutrophils in the crescent (periodic acid–Schiff, ×20). Immunofluorescence microscopy shows linear staining for anti–immunoglobulin G antibody (**B**) along the glomerular capillary walls and bright staining for fibrinogen in the Bowman's tuft (**C**), indicating crescent formation and fibrinoid necrosis (both, ×40).

TABLE 28-4 ABBREVIATED INTERNATIONAL SOCIETY OF NEPHROLOGY/RENAL PATHOLOGY SOCIETY 2003 CLASSIFICATION OF LUPUS NEPHRITIS

TYPE	MORPHOLOGIC CLASS	RENAL MANIFESTATION
I	Minimal mesangial lupus nephritis	Normal urinary sediment
I	Mesangial proliferative lupus nephritis	Low-grade hematuria and/or proteinuria Normal renal function
III.	Focal lupus nephritis	Active sediment, proteinuria <3 g/1.73 m^2/day
IV	Diffuse segmental (IV-S) or global (IV-G) lupus nephritis	Nephritic and nephrotic syndromes Hypertension; progressive renal failure
V	Membranous lupus nephritis	Nephrotic syndrome
VI	Advanced sclerosing lupus nephritis	Inactive urinary sediment Chronic renal failure

Modified from Weening JJ, D'Agati VD, Schwartz MM, et al: The classification of glomerulonephritis in systemic lupus erythematosus revisited, J Am Soc Nephrol 15:241–250, 2004.

influences the therapeutic decisions. The International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification of lupus nephritis recognizes six morphologic classes of renal involvement (Table 28-4). However, patients may migrate from one class to another spontaneously or after treatment.

Immunofluorescence typically shows glomerular deposition of IgG, IgM, IgA, C1q, and C3 (i.e., full-house pattern). On electron microscopy, tubuloreticular inclusions are common within glomerular and vascular endothelial cells. Electron-dense deposits sometimes show fingerprint-like substructures (Fig. 28-11). Histologic lesions correlate with the prognosis; classes III and IV have the worst prognosis (see Fig. 28-11). Other manifestations of SLE include acute and chronic tubulointerstitial nephritis and glomerular capillary thrombi in patients with antiphospholipid antibodies.

Three guidelines for the management of lupus nephritis have been published recently by the American College of Rheumatology, the Kidney Disease-Improving Global Outcomes (KDIGO) working group, and the Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA). For class I lupus nephritis, the prognosis is excellent, and no immunosuppression is required. Patients with class II lupus nephritis and proteinuria less than 1 g/24h should be treated as dictated by the extrarenal clinical manifestations of lupus. Patients with class II lupus nephritis and proteinuria greater than 3 g/24h should be treated with corticosteroids or calcineurin inhibitors.

Patients with class III or IV lupus nephritis should undergo induction therapy with corticosteroids plus cyclophosphamide or mycophenolate mofetil because both are considered equivalent. Pure class V (membranous) lupus nephritis usually has a benign prognosis, and initial therapy should be supportive. However, patients with progressive or persistent nephrotic-range proteinuria should be treated with corticosteroids plus an additional immunosuppressive agent (e.g., cyclosporine, mycophenolate mofetil). Patients with ESRD should be considered for renal transplantation because there is a low rate of recurrence in the transplanted kidney.

Cryoglobulinemic Glomerulonephritis

Cryoglobulins are immunoglobulins that precipitate at low temperatures and redissolve on rewarming. Cryoglobulinemia usually leads to a systemic inflammatory syndrome with weakness, arthralgias or arthritis, palpable purpura, peripheral neuropathy, and glomerulonephritis. Serum levels of C4 are typically low due to activation of complement by the classic pathway. The disease mainly involves small to medium-sized blood vessels and causes vasculitis due to cryoglobulin-containing immune complexes.

Cryoglobulinemia is classified as type I, II, or III on the basis of immunoglobulin composition. It can be idiopathic or occur in association with autoimmune diseases (see Fig. 26-11B), malignancy, or infection (Table 28-5). Cryoglobulinemia may be associated with chronic HCV infection.

Renal disease occurs in 20% to 60% of patients with cryoglobulinemia and manifests as proteinuria, microscopic hematuria, nephrotic syndrome, or renal impairment. Hypertension is common and may be severe, particularly in the setting of acute nephritic syndrome. The cryocrit values correlate poorly with disease activity. On light microscopy, renal biopsy specimens show an immune complex–mediated membranoproliferative pattern of injury, and on electron microscopy, diffuse, dense subendothelial deposits with a microtubular or crystalline appearance may be seen occluding the capillary loops.