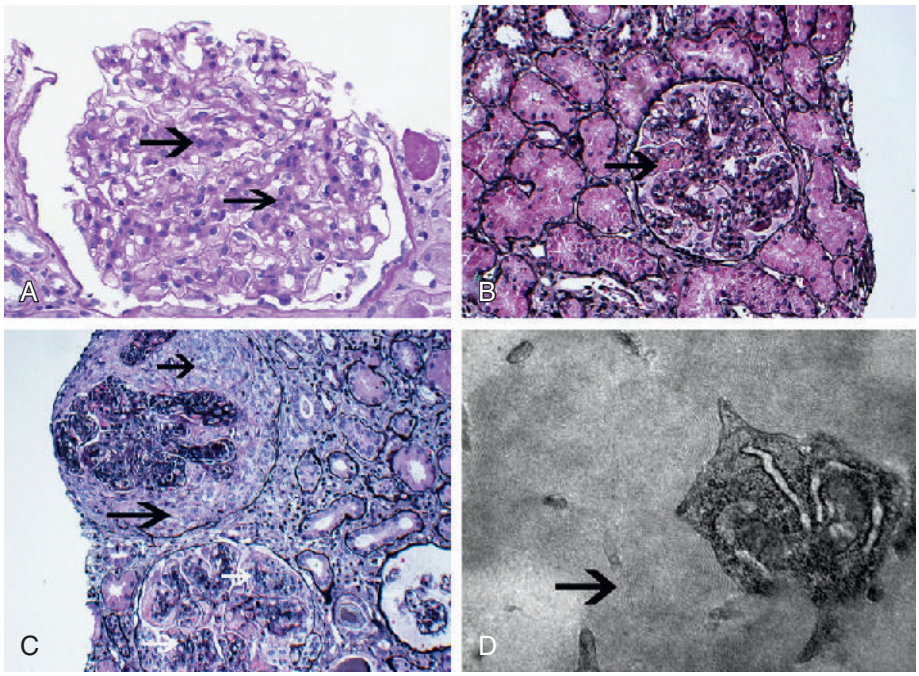

FIGURE 28-11 Light microscopy (**A** to **C**) and electron microscopy (**D**) are used to identify lupus nephritis. **A,** Mild mesangial proliferative glomerulonephritis (International Society of Nephrology/Renal Pathology Society [ISN/RPS] class II) has mesangial hypercellularity *(arrows)* (periodic acid–Schiff, ×40). **B,** Diffuse endocapillary proliferation with cryoglobulins in the glomerular capillaries, identified as pale, silver-negative material *(arrow)* (silver methenamine, ×20). **C,** In diffuse proliferative glomerulonephritis (ISN/RPS class IV), the glomerulus on top shows a large cellular crescent *(black arrows)*, and the glomerulus at the bottom shows diffuse endocapillary proliferation *(white arrows)* (silver methenamine, ×20). **D**, Electron-dense deposits have fingerprint substructures *(arrow)* (×46,000).

TABLE 28-5 CRYOGLOBULINS AND ASSOCIATED DISEASES

CRYOGLOBULINEMIA TYPE	IMMUNOGLOBULIN CLASS	ASSOCIATED DISEASES
I. Monoclonal immunoglobulins	M > G > A > BJP	Myeloma, Waldenström macroglobulinemia
II. Mixed cryoglobulins with monoclonal immunoglobulins	M/G ≫ G/G	Sjögren syndrome, Waldenström macroglobulinemia, lymphoma, essential cryoglobulinemia
III. Mixed polyclonal immunoglobulins	M/G	Infection, SLE, vasculitis, neoplasia, essential cryoglobulinemia

BJP, Bence Jones protein (κ light chain); SLE, systemic lupus erythematosus.

Treatment targets the underlying pathologic process to minimize or eliminate the associated cryoglobulinemia. Patients with active HCV infection, for example, should receive antiviral therapy when possible, and those with a monoclonal gammopathy should receive appropriate antimyeloma therapy. Immunosuppressive therapy (including the use of rituximab) with or without plasmapheresis should be considered for patients with a rapidly progressive, organ- or life-threatening course, regardless of the cause of the mixed cryoglobulinemia. Overall, the renal prognosis is usually good, with few patients progressing to ESRD. The long-term outcome reflects the underlying process.

GLOMERULAR DISEASES CAUSED BY PLASMA CELL DYSCRASIAS

Amyloidosis

Amyloidosis is characterized by systemic extracellular deposition of randomly arranged fibrils 8 to 12 nm in diameter that stain positive with Congo red (i.e., green birefringence with polarized light) or thioflavin T. Several processes, including malignancy, genetic mutations, and aging, can produce at least 24 amyloidogenic proteins. With renal deposition, amyloid in biopsy specimens appears as pale, amorphous, extracellular deposits that are periodic acid–Schiff (PAS) and methenamine silver stain negative (Fig. 28-12).

The affinity for kidney compared with other target organs varies according to the type of amyloid protein. Renal manifestations include proteinuria, nephrotic syndrome, and renal failure. Affected patients typically have large kidneys on ultrasound, but the diagnosis depends on demonstration of amyloid deposits. After amyloid is detected, typing should be performed when possible because treatments vary according to the protein involved. The most common approach to amyloid typing involves immunofluorescence or immunohistochemistry, but genetic testing and liquid chromatography mass spectrometry are also helpful for high-resolution amyloid typing.

Treatment of amyloidosis depends on the origin of the amyloidogenic protein. In patients with amyloid light chain (AL) amyloidosis, antimyeloma therapy with high-dose melphalan and autologous stem cell transplantation can be beneficial. In selected cases, bone marrow transplantation has led to resolution of the disease. Secondary amyloid A (AA) amyloidosis is most