levels. C4 levels are usually normal or mildly decreased. Other nephrologic conditions associated with low complement are C3 glomerulopathy, lupus nephritis, cryoglobulinemic glomerulonephritis, and cholesterol emboli (Table 28-2).

Renal biopsy typically shows diffuse glomerular hypercellularity and infiltration of polymorphonuclear leukocytes, monocytes, or macrophages on light microscopy. Immunofluorescence shows granular deposition of IgG, C3, and occasionally immunoglobulin M (IgM). On electron microscopy, characteristic dome-shaped subepithelial deposits ("humps") can be seen along the GBM (Fig. 28-5).

Treatment is supportive and aims to minimize fluid overload, optimize blood pressure control, and eradicate ongoing infection. For children, the prognosis is excellent, with most patients recovering renal function in 1 to 2 months. Some patients have persistent microscopic hematuria, proteinuria, hypertension, and renal dysfunction and are said to have *atypical*, *persistent*, or *resolving* PSGN. Some of these patients have mutations or autoantibodies to proteins in the alternative complement cascade.

Immunoglobulin a Nephropathy

IgAN (i.e., Berger disease) is the most common form of a primary glomerulopathy. On light microscopy, mesangial proliferation is seen along with mesangial deposition of IgA on immunofluorescence and electron-dense deposits in the mesangial cells on electron microscopy (Fig. 28-6).

Patients may have episodes of macroscopic hematuria accompanying an intercurrent upper respiratory tract infection (synpharyngitic) or have asymptomatic hematuria, with or without proteinuria, detected on routine urinalysis. Proteinuria is common, but nephrotic syndrome occurs in less than 10% of cases and raises the possibility of a podocytopathy (e.g., MCD) superimposed on IgAN.

The pathogenesis of IgA nephropathy has been linked to galactose-deficient IgA1 (GD-IgA1) molecules and increased formation of anti–GD-IgA1 autoantibodies, with deposition of IgG or IgA anti–GD-IgA1 immune complexes in the mesangium, resulting in activation of complement and cytokine cascades. Secondary causes of IgAN include chronic liver disease, celiac disease, dermatitis herpetiformis, and ankylosing spondylitis.

In up to 60% of the patients, IgA nephropathy has a benign clinical course, and patients maintain proteinuria of less than 500 mg/24h and preserve renal function. However, progression to ESRD occurs in up to 40% of patients over 10 to 25 years. Clinical predictors of progression include proteinuria greater than 1 g/24h, hypertension, and impaired renal function at diagnosis. Any degree of proteinuria carries a worse prognosis for a patient with IgAN. IgAN frequently recurs after renal transplantation, but loss of the allograft from recurrent disease is uncommon.

The use of angiotensin II system blockade and high-dose corticosteroids has been beneficial in slowing or halting progression of renal disease. Henoch-Schönlein purpura is the systemic form of IgAN. The prognosis is generally good for children but varies for adults.

TABLE 28-2 GLOMERULAR DISEASES ASSOCIATED WITH HYPOCOMPLEMENTEMIA

Acute lupus nephritis
C3 glomerulopathy (C3 glomerulonephritis and dense deposit disease)
Cholesterol emboli
Cryoglobulinemic glomerulonephritis
Postinfectious glomerulonephritis

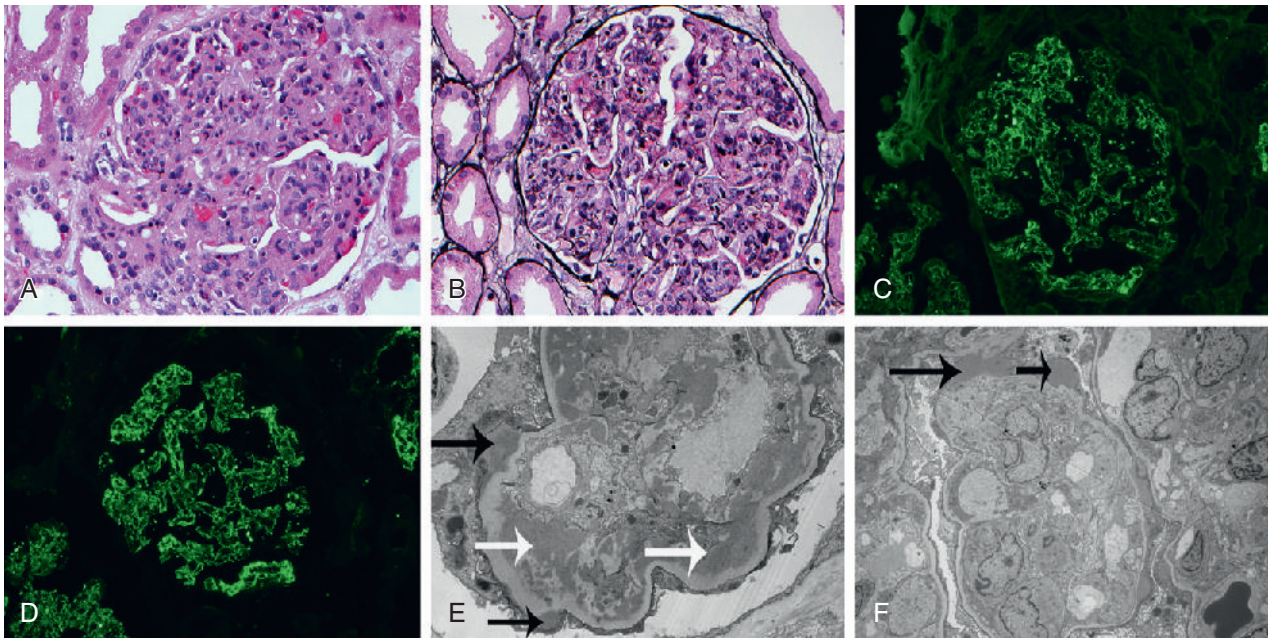

FIGURE 28-5 Postinfectious glomerulonephritis. **A** and **B,** Light microscopy shows diffuse endocapillary proliferative glomerulonephritis. Notice the prominent neutrophil infiltration in the glomerular capillaries (**A,** hematoxylin and eosin; **B,** silver methenamine; both ×40). **C** and **D,** Immunofluorescence studies show granular immunoglobulin G and C3 deposition along the capillary walls (both ×20). **E** and **F,** Electron microscopy shows subendothelial deposits *(white arrows)* and subepithelial humplike deposits *(black arrows)*. The subendothelial deposits likely result from circulating immune complexes that are deposited along the glomerular capillary walls and drive the inflammatory response (**E,** ×5800). The subepithelial deposits likely represent in situ immune complex formation (**F,** ×2850).