In all patients, treatment with an ACEI or ARB, alone or in combination, may substantially reduce proteinuria and prolong renal survival. Patients who have a non–nephrotic-range proteinuria have the best renal survival (>80% at 10 years). In patients who continue to have a high degree of proteinuria (>10 g/day), end-stage renal disease (ESRD) typically develops over 5 to 20 years. Idiopathic FSGS may recur in a transplanted kidney.

HIV-Associated Nephropathy

Patients with HIV infection can have many forms of kidney injury due to sepsis, co-infection with hepatitis B or C virus (HBV or HCV), nephrotoxic drugs, and use of antiretroviral agents. HIV-associated nephropathy (HIVAN) is a clinicopathologic entity characterized by nephrotic-range proteinuria and a collapsing form of FSGS, often with microcystic tubular dilation. On electron microscopy, tubuloreticular inclusions (i.e., interferon fingerprints) may be seen within the glomerular and vascular endothelial cells.

HIVAN occurs almost exclusively in patients of African descent when CD4 levels are low. It is thought to be caused by infection and subsequent expression of HIV viral genes in podocytes. The onset of proteinuria is typically acute. Proteinuria can be greater than 10 g/day, and renal insufficiency can progress rapidly.

Membranous Nephropathy

Membranous nephropathy is the leading cause of nephrotic syndrome in whites. It occurs in persons of all ages and races but is most often diagnosed in middle age, with the incidence peaking during the fourth and fifth decades of life. The male-to-female ratio is about 2 : 1.

Autoantibodies against the phospholipase A_2 receptor in podocytes are found in about 70% of patients with the primary form of the disease. Most patients have nephrotic syndrome, normal renal function, and no hypertension. Microscopic hematuria may be detected in about one third of patients. Secondary membranous nephropathy is caused by autoimmune diseases (e.g., SLE, autoimmune thyroiditis), infection (e.g., HBV, HCV), drugs (e.g., penicillamine, NSAIDs), and solid malignancies (e.g., colon cancer, lung cancer).

On light microscopy, capillary walls may appear thickened, and methenamine silver stain shows subepithelial projections ("spikes") along the capillary walls. Immunofluorescence microscopy shows marked granular deposition of IgG and C3 along the capillary walls, and subepithelial deposits are seen on electron microscopy (Fig. 28-4).

Up to one third of the patients with membranous nephropathy undergo spontaneous remission, and another one third of patients undergo partial remission. Initial therapy should include angiotensin II receptor blockade, a low-salt diet (<4 g/day), a low-protein diet (0.8 to 1 g/kg/day), and lipid control. If spontaneous remission occurs, it usually does so within the first 12 to 24 months.

Patients who remain nephrotic or those with declining renal function are candidates for immunosuppressive therapy, including a combination of corticosteroids and cytotoxic agents or calcineurin inhibitor monotherapy. Rituximab has recently garnered attention as a potential breakthrough in the treatment of membranous nephropathy, and studies are being conducted. The probability of renal survival is more than 80% at 5 years and about 60% at 15 years. Patients with an accelerated course should be evaluated for superimposed anti-GBM disease, acute interstitial nephritis, or renal vein thrombosis.

GLOMERULAR DISEASES MANIFESTING WITH NEPHRITIC SYNDROME

Infection-Associated Glomerulonephritis

Poststreptococcal glomerulonephritis (PSGN) is a classic form of acute glomerulonephritis that develops 1 to 4 weeks after a pharyngitis or skin infection with specific (nephritogenic) strains of group A β-hemolytic streptococci. It typically occurs in children and usually has a benign course. More recently, however, infection-associated glomerulonephritis has been recognized to have a broader spectrum, including affecting elderly and immunocompromised patients and being associated with different bacteria, particularly staphylococci. Unlike classic PSGN, the variant occurs when the infection is still active and has an unfavorable prognosis.

Infection-associated glomerulonephritis manifests clinically with the abrupt onset of nephritic syndrome. In patients with PSGN, cultures are usually negative, but elevated titers of antistreptolysin O (ASO), antistreptokinase, antihyaluronidase, and anti-deoxyribonuclease (anti-DNAse B) antibodies may provide evidence of recent streptococcal infection. Activation of the alternative complement pathway is reflected by low C3 complement

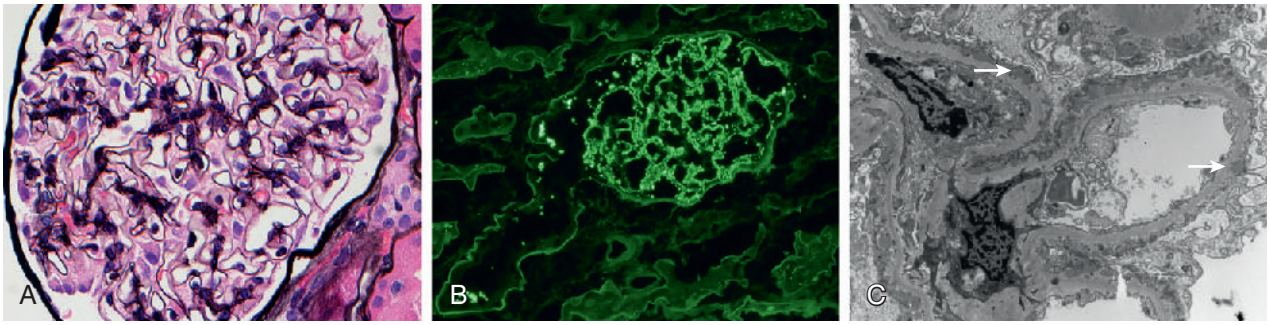

FIGURE 28-4 Membranous nephropathy. **A,** Light microscopy shows thickened glomerular basement membranes (×60). **B,** Immunofluorescence study shows granular immunoglobulin G deposition along the capillary walls (×20). **C,** Electron microscopy shows subepithelial electron-dense deposits *(arrows)* (×15,000).