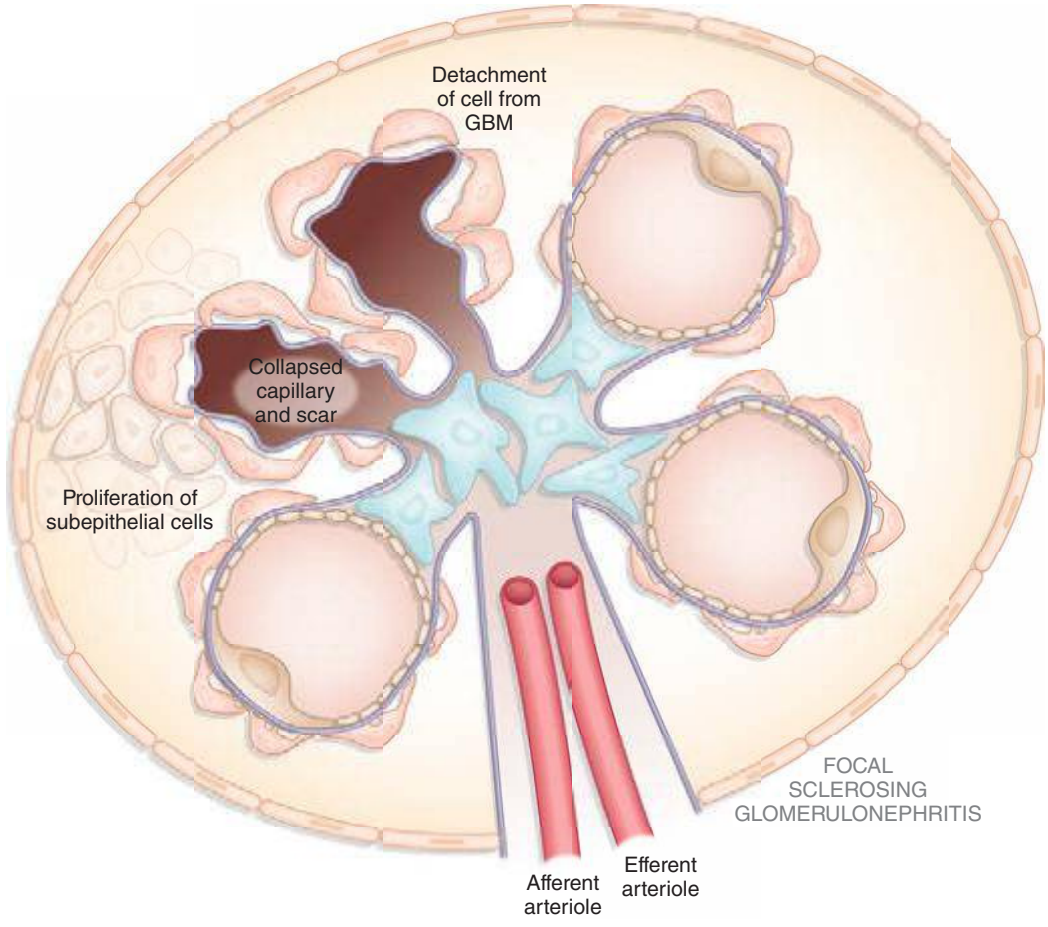
Glomerular schematic 5




after a longer course of therapy than patients with MCD. Proteinuria remits in only 20–45% of patients receiving a course of steroids over 6–9 months. Limited evidence suggests the use of cyclosporine in steroid-responsive patients helps ensure remissions. Relapse frequently occurs after cessation of cyclosporine therapy, and cyclosporine itself can lead to a deterioration of renal function due to its nephrotoxic effects. A role for other agents that suppress the immune system has not been established. Primary FSGS recurs in 25–40% of patients given allografts at end-stage disease, leading to graft loss in half of those cases. The treatment of *secondary FSGS* typically involves treating the underlying cause and controlling proteinuria. There is no role for steroids or other immunosuppressive agents in secondary FSGS.

## MEMBRANOUS GLOMERULONEPHRITIS

Membranous glomerulonephritis (MGN), or *membranous nephropathy* as it is sometimes called, accounts for approximately 30% of cases of nephrotic syndrome in adults, with a peak incidence between the ages of 30 and 50 years and a male to female ratio of 2:1. It is rare in childhood and the most common cause of nephrotic syndrome in the elderly. In 25–30% of cases, MGN is associated with a malignancy (solid tumors of the breast, lung, colon), infection (hepatitis B, malaria, schistosomiasis), or rheumatologic disorders like lupus or rarely rheumatoid arthritis (Table 338-6).

Uniform thickening of the basement membrane along the peripheral capillary loops is seen by light microscopy on renal biopsy (see Fig. 62e-7); this thickening needs to be distinguished from that seen in diabetes and amyloidosis. (See Glomerular Schematic 6.) Immunofluorescence demonstrates diffuse granular deposits of IgG and $C_3$, and electron microscopy typically reveals electron-dense subepithelial deposits. While different stages (I–V) of progressive membranous lesions have been described, some published analyses indicate the degree of tubular atrophy or interstitial fibrosis is more predictive of progression than is the stage of glomerular disease. The presence of subendothelial deposits or the presence of tubuloreticular inclusions strongly points to a diagnosis of membranous lupus nephritis, which may precede the extrarenal manifestations of lupus. Work in Heyman nephritis, an animal model of MGN, suggests that glomerular lesions result from in situ formation of immune complexes with megalin receptor–associated protein as the putative antigen. This antigen is not found in human podocytes. Human antibodies have been described against neutral endopeptidase expressed by podocytes in infants whose mothers lack this protein. In most adults, autoantibodies against the M-type phospholipase $A_2$ receptor ($PLA_2R$) circulate and bind to a conformational epitope present in the receptor on human podocytes, producing in situ deposits characteristic of idiopathic membranous nephropathy. Other renal diseases and secondary membranous nephropathy do not appear to involve such

**TABLE 338-6 MEMBRANOUS GLOMERULONEPHRITIS**

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| Primary/idiopathic membranous glomerulonephritis |
| Secondary membranous glomerulonephritis |
| Infection: Hepatitis B and C, syphilis, malaria, schistosomiasis, leprosy, filariasis |
| Cancer: Breast, colon, lung, stomach, kidney, esophagus, neuroblastoma |
| Drugs: Gold, mercury, penicillamine, nonsteroidal anti-inflammatory agents, probenecid |
| Autoimmune diseases: Systemic lupus erythematosus, rheumatoid arthritis, primary biliary cirrhosis, dermatitis herpetiformis, bullous pemphigoid, myasthenia gravis, Sjögren's syndrome, Hashimoto's thyroiditis |
| Other systemic diseases: Fanconi's syndrome, sickle cell anemia, diabetes, Crohn's disease, sarcoidosis, Guillain-Barré syndrome, Weber-Christian disease, angiofollicular lymph node hyperplasia |