diagnosis is MCD until proved otherwise, and treatment with high-dose corticosteroid therapy can be started, often without the need of a renal biopsy.

More than 90% of children achieve complete remission after 4 to 8 weeks of treatment. Children who do not respond to corticosteroid therapy should undergo a renal biopsy. Adolescents and adults also respond to high-dose corticosteroids (>80%), but the response is slower, and treatment for 16 weeks or more may be required to achieve remission. Therapy usually is continued for 4 to 8 weeks after remission.

Among patients who have a response to corticosteroids, about 25% have a long-term remission. However, up to 25% of the patients have frequent relapses, and up to 30% become steroid dependent. For these patients, alternative therapies aiming to minimize corticosteroid toxicity include the use of alkylating agents, antimetabolites, and calcineurin inhibitors. Although these agents may allow a lower corticosteroid dose, some patients respond poorly or not all, and use of an agent may be complicated by development of significant side effects. Noncompliance is always a concern, especially in young patients. Rituximab is a chimeric human-murine monoclonal antibody that targets the CD20 antigen expressed on B cells. It has been efficacious in a number of autoimmune diseases and has promise in the treatment of MCD.

Focal Segmental Glomerulosclerosis

Focal segmental glomerulosclerosis (FSGS) is a clinicopathologic syndrome, and the common pathophysiologic element is podocyte injury and depletion leading to glomerular scarring (Fig. 28-3). FSGS accounts for less than 15% of cases of idiopathic nephrotic syndrome in children and up to 25% in adults. FSGS is thought to be the most common form of idiopathic nephrotic syndrome in African Americans; it most likely represents a different disease from FSGS in Caucasians. Hypertension is found in 30% to 50% of patients with FSGS, and microscopic hematuria occurs in 25% to 75% of cases. Up to 30% of those with FSGS have impaired renal function.

The pathogenesis of idiopathic or primary FSGS is unknown. A circulating permeability factor has been demonstrated in some patients. More recently, the soluble urokinase-type plasminogen activator receptor (suPAR) has been identified as a potential marker because levels are elevated in two thirds of cases of primary FSGS and levels are higher in renal transplant recipients with recurrent FSGS. However, suPAR levels do not distinguish primary from secondary FSGS, and serum levels increase with reductions in the glomerular filtration rate. Further research is needed to define the role of serum suPAR in idiopathic FSGS.

Secondary causes of FSGS include genetic mutations in podocyte genes, human immunodeficiency virus (HIV) infection, sickle cell disease, vesicoureteral reflux, obesity, unilateral renal agenesis, remnant kidneys, and aging (Table 28-1). Four histologic variants of FSGS have been described. The cellular or collapsing variant, which has the worst prognosis, is more common in African Americans and patients with HIV infection.

Spontaneous remission of proteinuria is uncommon (<5% of cases). Treatment of the primary forms consists of prolonged (>4 months), high-dose corticosteroid therapy (prednisone, 1 mg/kg/day), but there is no study comparing this approach with other forms of therapy. If patients are going to respond to corticosteroids, proteinuria starts to decrease soon after the start of treatment, and those who show no reduction in proteinuria after 2 to 3 months of prednisone at 1 mg/kg/day are unlikely to respond. For patients who respond to corticosteroids but undergo relapse, alternative therapy includes the use of cytotoxic drugs alone or in combination with corticosteroids, calcineurin inhibitors, and possibly rituximab. For patients with secondary forms of FSGS, treatment should target the cause.

TABLE 28-1 CAUSES OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS

PRIMARY (IDIOPATHIC) FSGS
• Attributed to a circulating permeability factor
SECONDARY FSGS
• Genetic mutations in podocyte genes • Viral: HIV-associated nephropathy, parvovirus B19, simian virus 40, cytomegalovirus • Drug induced: heroin, interferon (α, β, γ), pamidronate, sirolimus, calcineurin inhibitors • Adaptive: reduced nephron mass or glomerular adaptation, unilateral renal agenesis, obesity-related glomerulopathy, basement membrane defects healing phase of focal proliferative glomerulonephritis, body building, sickle cell anemia, hypertensive nephrosclerosis, thrombotic microangiopathy, aging kidney • Other causes: hemophagocytic syndrome

FSGS, Focal segmental glomerulosclerosis; HIV, human immunodeficiency virus.

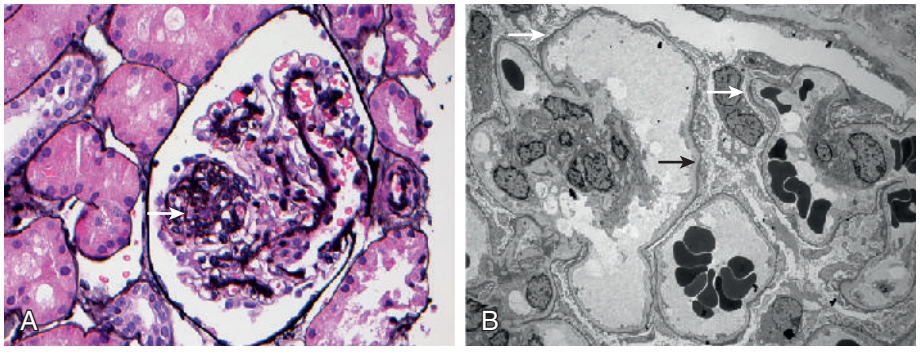

FIGURE 28-3 Focal segmental glomerulosclerosis. **A,** Light microscopy shows segmental sclerosis *(arrow)* with segmental consolidation of the glomerular capillary tufts and visceral epithelial cell hypertrophy over the segmentally sclerosed tufts (silver methenamine, ×40). **B,** Electron microscopy shows diffuse foot process effacement *(arrows)* of the visceral epithelial cells (×1850). Immunofluorescence studies were negative for immune deposits.