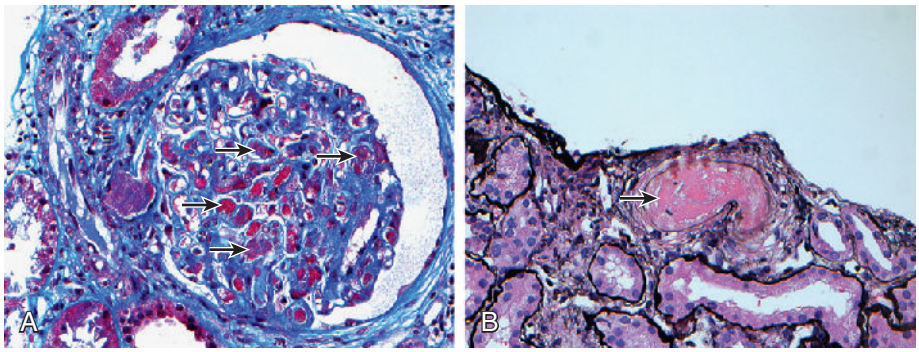

FIGURE 28-14 Thrombotic microangiopathy. **A,** Light microscopy shows multiple, small thrombi *(arrows)* in glomerular capillaries in the setting of hemolytic uremic syndrome (Masson trichrome, ×40). **B,** Light microscopy shows a thrombus *(arrow)* in a small artery in the setting of scleroderma (silver methenamine, ×20).

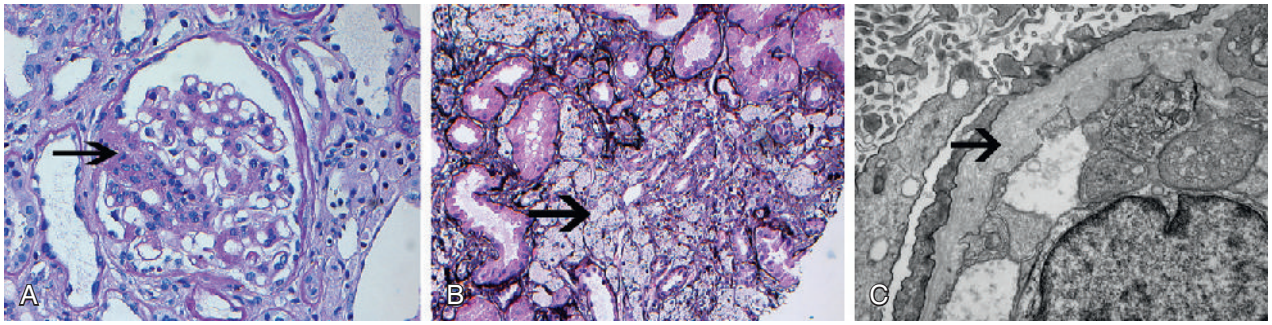

FIGURE 28-15 Alport syndrome. **A,** Light microscopy shows focal segmental glomerulosclerosis *(arrow)* (periodic acid–Schiff, ×40). **B,** Light microscopy shows numerous foam cells *(arrow)* in the interstitium (silver methenamine, ×40). **C,** Electron microscopy shows thickening of the glomerular capillary walls with multiple lamellations of basement membrane material *(arrow)* and formation of the classic basket-weave appearance (×212,000).

children with D+ HUS and severe central nervous system involvement such as seizures, stroke, or coma.

Thrombotic Thrombocytopenic Purpura

TTP results from mutations in the von Willebrand factor (vWF)–cleaving protease (ADAMTS13) or development of an autoantibody against ADAMTS13. ADAMTS13 cleaves large multimers of vWF, and abnormalities or deficiency of ADAMTS13 activity affects vWF function. Patients can have acute or chronic (i.e., relapsing) TTP. Microthrombi rich in large vWF multimers develop in the arterioles and capillaries of the brain and other organs.

Genetic or acquired forms of ADAMSTS13 deficiency can be treated by plasma infusion or exchange to supply functional protease. Plasma exchange should be initiated promptly, based on findings of microangiopathic hemolytic anemia and thrombocytopenia without evidence of other causes of thrombotic microangiopathy (e.g., scleroderma, malignancy, antiphospholipid syndrome). Treatment should not await test results for the levels or activity of ADAMTS13.

DISEASES WITH GLOMERULAR BASEMENT MEMBRANE ABNORMALITIES

Alport Syndrome

Alport syndrome is an inherited disorder of basement membranes. In more than one half of patients, the disease results from a mutation in the *COL4A5* gene that codes for the α5 chain of type IV collagen (α5[IV]). The mutation in *COL4A5* disables a developmental switch in the GBM collagen that retains its embryonic phenotype and results in a friable GBM.

Alport syndrome is frequently associated with sensorineural hearing loss and ocular abnormalities (e.g., lenticonus of the anterior lens capsule). Patients characteristically have persistent or intermittent hematuria and usually have mild proteinuria, which progresses with age and may reach nephrotic range in up to 30%. The disease is X-linked in approximately 85% of patients, but autosomal recessive and autosomal dominant patterns of inheritance have been described.

In virtually all male patients, the syndrome progresses to ESRD, often before the age of 30 years. The disease is usually mild in heterozygous women, but some develop ESRD, usually after the age of 50 years. The rate of progression to ESRD is fairly constant among affected men within individual families, but it varies markedly from family to family. The degree of deafness correlates with the rate of progression to ESRD.

On light microscopy, the glomerular changes are nonspecific. Diagnostic features are usually seen on electron microscopy. At an early stage, thinning of the GBM may be the only visible abnormality and may suggest thin basement membrane disease. With time, the GBM thickens, and the lamina densa splits into several irregular layers that may branch and rejoin, producing a characteristic basket-weave appearance (Fig. 28-15).