Thin Basement Membrane Lesion (Benign Familial Hematuria)

This is a fairly common hereditary entity manifested *clinically by familial asymptomatic hematuria*—usually uncovered on routine urinalysis—*and morphologically by diffuse thinning of the GBM* to widths between 150 and 225 nm (compared with 300 to 400 nm in healthy adults). Although mild or moderate proteinuria may also be present, renal function is normal and prognosis is excellent. The abnormality is estimated to affect 1% of the general population.

The disorder should be distinguished from IgA nephropathy, another common cause of hematuria, and X-linked Alport syndrome. In contrast to Alport syndrome, hearing loss, ocular abnormalities, and a family history of renal failure are absent.

The anomaly in thin basement membrane lesion has also been traced to mutations in genes encoding α_3 or α_4 chains of type IV collagen. The disease most often has an autosomal inheritance and most patients are heterozygous for the defective gene. The disorder in homozygotes resembles autosomal recessive Alport syndrome. Homozygotes or compound heterozygotes may progress to renal failure. Thus, these diseases illustrate a continuum of changes resulting from mutations in collagen type IV genes.

KEY CONCEPTS

Isolated Glomerular Abnormalities

- **IgA nephropathy,** characterized by mesangial deposits of IgA-containing immune complexes, is the most common cause of glomerulonephritis worldwide. It is a common cause of both a nephritic syndrome and of isolated and frequently recurrent hematuria; it commonly affects children and young adults and has a variable course.
- **Alport syndrome**, a form of **hereditary nephritis,** is caused by mutations in genes encoding GBM type IV collagen. It manifests as hematuria and slowly progressing proteinuria and declining renal function; glomeruli appear normal by light microscopy until late in the disease course.
- **Thin basement membrane lesion** has a benign clinical course and is also the result of mutations in genes coding for GBM type IV collagen and hence may be considered as part of a spectrum of diseases that includes hereditary nephritis.

Chronic Glomerulonephritis

Chronic glomerulonephritis refers to end-stage glomerular disease that may result from specific types of glomerulonephritis or may develop without antecedent history of any of the well-recognized forms of acute glomerulonephritis. Poststreptococcal glomerulonephritis is a rare antecedent of chronic glomerulonephritis, except in adults. Patients with crescentic glomerulonephritis, if they survive the acute episode, usually progress to chronic glomerulonephritis. Membranous nephropathy, MPGN, IgA nephropathy, and FSGS all may progress to chronic renal failure. Nevertheless, **in any series of individuals with chronic glomerulonephritis, a variable percentage of cases arise mysteriously with no antecedent history of acute glomerulonephritis.** These cases may represent the end result of relatively asymptomatic forms of glomerulonephritis, either known or still unrecognized, that progress to uremia. Predictably, the proportion of such unexplained cases depends on the availability of renal biopsy material from patients early in their disease.

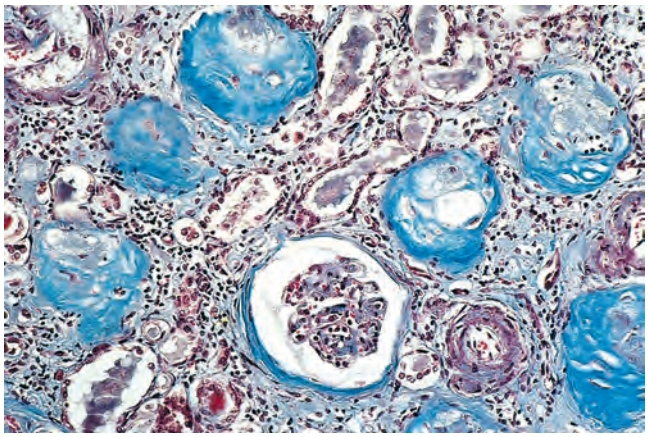

Figure 20-21 Chronic glomerulonephritis. A Masson trichrome preparation shows complete replacement of virtually all glomeruli by blue-staining collagen. (Courtesy Dr. M.A. Venkatachalam, Department of Pathology, University of Texas Health Sciences Center, San Antonio, Tex.)

MORPHOLOGY

The kidneys are symmetrically contracted and have diffusely granular cortical surfaces. On section, **the cortex is thinned,** and there is an increase in peripelvic fat. The glomerular histology depends on the stage of the disease. In early cases, the glomeruli may still show evidence of the primary disease (e.g., membranous nephropathy or MPGN). However, there eventually ensues **obliteration of glomeruli,** transforming them into acellular eosinophilic masses, representing a combination of trapped plasma proteins, increased mesangial matrix, basement membrane-like material, and collagen (Fig. 20-21). Because hypertension is an accompaniment of chronic glomerulonephritis, **arterial and arteriolar sclerosis may be conspicuous.** Marked atrophy of associated tubules, irregular interstitial fibrosis, and mononuclear leukocytic infiltration of the interstitium also occur.

Clinical Course. In most individuals, chronic glomerulonephritis develops insidiously and slowly progresses to renal insufficiency or death from uremia during a span of years or possibly decades (see the discussion of chronic renal failure). Not infrequently, patients present with such nonspecific complaints as loss of appetite, anemia, vomiting, or weakness. In some, the renal disease is suspected with the discovery of proteinuria, hypertension, or azotemia on routine medical examination. In others, the underlying renal disorder is discovered in the course of investigation of edema. Most patients are hypertensive, and sometimes the dominant clinical manifestations relate to cerebral or cardiovascular disease. In all, the disease is relentlessly progressive, though at widely varying rates. In nephrotic patients, as glomeruli become obliterated and therefore the GFR decreases, the protein loss in the urine diminishes. If patients with chronic glomerulonephritis do not receive dialysis or if they do not receive a renal transplant, they invariably succumb to their disease.