

### Diabetic Microangiopathy

One of the most consistent morphologic features of diabetes is **diffuse thickening of basement membranes**. The thickening is most evident in the capillaries of the skin, skeletal muscle, retina, renal glomeruli, and renal medulla. However, it may also be seen in such nonvascular structures as renal tubules, the Bowman capsule, peripheral nerves, and placenta. It should be noted that despite the increase in the thickness of basement membranes, **diabetic capillaries are more leaky than normal to plasma proteins. The microangiopathy underlies the development of diabetic nephropathy, retinopathy, and some forms of neuropathy.** An indistinguishable microangiopathy can be found in aged nondiabetic patients but rarely to the extent seen in patients with long-standing diabetes.

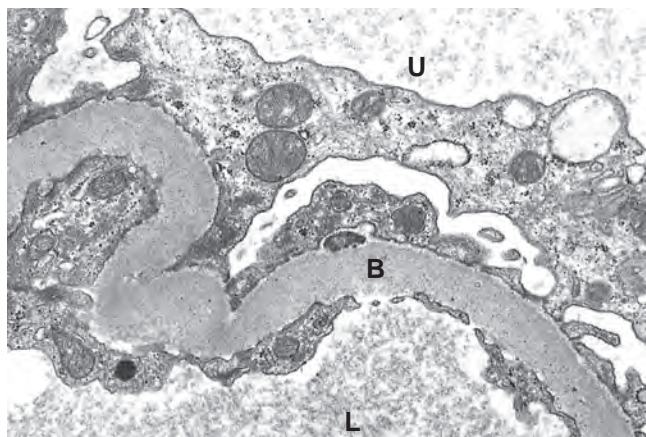
### Diabetic Nephropathy

The kidneys are prime targets of diabetes. Renal failure is second only to myocardial infarction as a cause of death from this disease. **Three lesions are encountered: (1) glomerular lesions; (2) renal vascular lesions, principally arteriosclerosis; and (3) pyelonephritis, including necrotizing papillitis.**

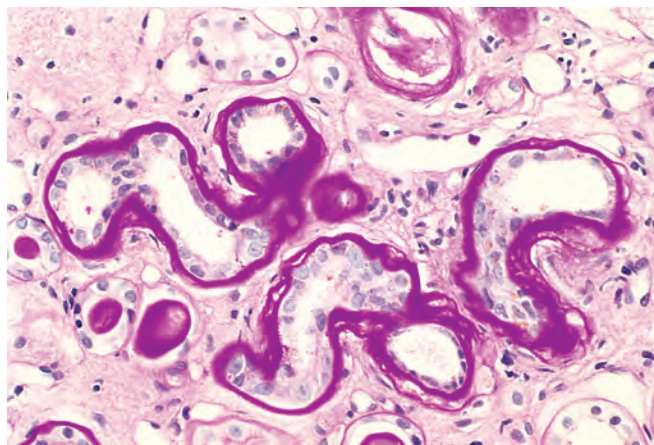
The most important glomerular lesions are capillary basement membrane thickening, diffuse mesangial sclerosis, and nodular glomerulosclerosis.

**Capillary Basement Membrane Thickening. Widespread thickening of the glomerular capillary basement membrane (GBM)** occurs in virtually all cases of diabetic nephropathy and is part and parcel of the diabetic microangiopathy. Pure capillary basement membrane thickening can be detected only by electron microscopy (Fig. 24-37). Careful morphometric studies demonstrate that this thickening begins as early as 2 years after the onset of type 1 diabetes and by 5 years amounts to about a 30% increase. The thickening continues progressively and usually concurrently with mesangial widening. Simultaneously, there is thickening of the tubular basement membranes (Fig. 24-38).

**Diffuse Mesangial Sclerosis.** This lesion consists of **diffuse increase in mesangial matrix**. There can be mild proliferation



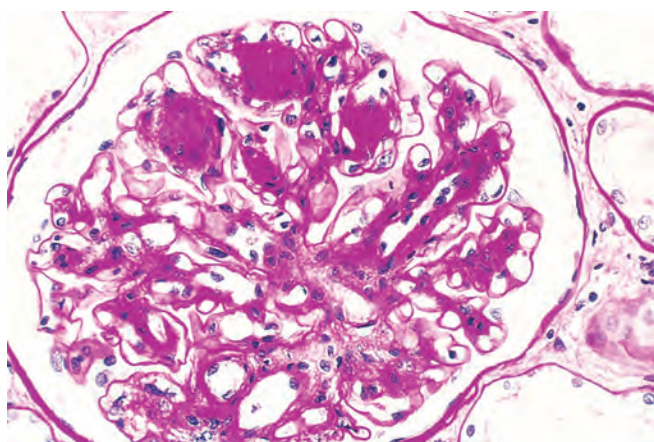
**Figure 24-37** Electron micrograph of a renal glomerulus showing markedly thickened glomerular basement membrane (B) in a diabetic. L, glomerular capillary lumen; U, urinary space. (Courtesy Dr. Michael Kashgarian, Department of Pathology, Yale University School of Medicine, New Haven, Conn.)



**Figure 24-38** Renal cortex showing thickening of tubular basement membranes in a diabetic patient (PAS stain).

of mesangial cells early in the disease process, but cell proliferation is not a prominent part of this injury. The mesangial increase is typically associated with the overall thickening of the GBM. The matrix depositions are PAS-positive (Fig. 24-39). As the disease progresses, the expansion of mesangial areas can extend to nodular configurations. The progressive expansion of the mesangium has been shown to correlate well with measures of deteriorating renal function such as increasing proteinuria.

**Nodular Glomerulosclerosis.** This is also known as **intercapillary glomerulosclerosis or Kimmelstiel-Wilson disease**. The glomerular lesions take the form of ovoid or spherical, often laminated, nodules of matrix situated in the periphery of the glomerulus. The nodules are PAS-positive. They lie within the mesangial core of the glomerular lobules and can be surrounded by patent peripheral capillary loops (Fig. 24-39) or loops that are markedly dilated. The nodules often show features of mesangiolysis with fraying of the mesangial/capillary lumen interface and disruption of sites at which the capillaries are anchored into the mesangial stalks. The latter may produce capillary microaneurysms as the untethered capillaries distend outward due to force imparted by intracapillary blood pressure and flow. Usually, not all the lobules in individual glomeruli are



**Figure 24-39** Diffuse and nodular diabetic glomerulosclerosis (PAS stain). Note the diffuse increase in mesangial matrix and characteristic acellular PAS-positive nodules.