



Figure 24-40 Nephrosclerosis in a patient with long-standing diabetes. The kidney has been bisected to demonstrate both diffuse granular transformation of the surface (*left*) and marked thinning of the cortical tissue (*right*). Additional features include some irregular depressions, the result of pyelonephritis, and an incidental cortical cyst (*far right*).

involved by nodular lesions, but even uninvolved lobules and glomeruli show striking diffuse mesangial sclerosis. As the disease advances, the individual nodules enlarge and may eventually compress and engulf capillaries, obliterating the glomerular tuft. These nodular lesions are frequently accompanied by prominent accumulations of hyaline material in capillary loops (“**fibrin caps**”) or adherent to Bowman capsules (“**capsular drops**”). Both afferent and efferent glomerular hilar arterioles show hyalinosis. As a consequence of the glomerular and arteriolar lesions, the kidney suffers from ischemia, develops tubular atrophy and interstitial fibrosis, and usually undergoes overall contraction in size (Fig. 24-40). Approximately 15% to 30% of individuals with long-term diabetes develop nodular glomerulosclerosis, and in most instances it is associated with renal failure.

Renal atherosclerosis and arteriosclerosis constitute part of the macrovascular disease in diabetics. The kidney is one of the most frequently and severely affected organs; however, the changes in the arteries and arterioles are similar to those found in other tissues. Hyaline arteriosclerosis affects not only the afferent but also the efferent arteriole. Such efferent arteriosclerosis is rarely, if ever, encountered in individuals who do not have diabetes.

Pyelonephritis is an acute or chronic inflammation of the kidneys that usually begins in the interstitial tissue and then spreads to affect the tubules. Both the acute and chronic forms of this disease are more common in diabetics than in the general population, and, once affected, diabetics tend to have more severe involvement. One special pattern of acute pyelonephritis, **necrotizing papillitis** (or papillary necrosis), is much more prevalent in diabetics than in nondiabetics.

Diabetic Ocular Complications

The eye is profoundly affected by diabetes mellitus. The architecture and microanatomy of the eye are discussed in Chapter 29.

Diabetes-induced hyperglycemia leads to acquired opacification of the lens, a condition known as *cataract*.

Long-standing diabetes is also associated with increased intraocular pressure (**glaucoma**) (see later), and resulting damage to the optic nerve.

The most profound histopathologic changes of diabetes are seen in the retina. The retinal vasculopathy of diabetes mellitus can be classified into *background* (*preproliferative*) *diabetic retinopathy* and *proliferative diabetic retinopathy* (Chapter 29).

Diabetic Neuropathy

The prevalence of peripheral neuropathy in individuals with diabetes depends on the duration of the disease; up to 50% of diabetics overall have peripheral neuropathy clinically, and up to 80% of those who have had the disease for more than 15 years. This is discussed further in Chapter 27.

Clinical Manifestations of Chronic Diabetes

Table 24-7 summarizes some of the pertinent clinical, genetic, and histopathologic features that distinguish type 1 and type 2 diabetes. **In both types it is the long-term effects of diabetes, more than the acute metabolic complications, that are responsible for the overwhelming majority of the morbidity and mortality.** In most instances these complications appear approximately 15 to 20 years after the onset of hyperglycemia. The severity of chronic complications is related to both the degree and the duration of hyperglycemia, as evidenced by the attenuation of end-organ damage by effective glycemic control in prospective studies.

- **Macrovascular complications such as myocardial infarction, renal vascular insufficiency, and cerebrovascular accidents are the most common causes of mortality in long-standing diabetes.** Diabetics have a two to four times greater incidence of coronary artery disease, and a fourfold higher risk of dying from cardiovascular complications than nondiabetics. An elevated risk for cardiovascular disease is even observed in prediabetics. Significantly, myocardial infarction is almost as common in diabetic women as in diabetic men. In contrast, myocardial infarction is uncommon in nondiabetic women of reproductive age. Diabetes is often accompanied by underlying conditions that favor the development of adverse cardiovascular events. For example, *hypertension* is found in approximately 75% of individuals with type 2 diabetes and potentiates the effects of hyperglycemia and insulin resistance on endothelial dysfunction and atherosclerosis. Another cardiovascular risk frequently seen in diabetics is *dyslipidemia*, which includes both increased triglycerides and LDL levels and decreased levels of the “protective” lipoprotein, high-density lipoprotein (Chapter 11). Insulin resistance is believed to contribute to “diabetic dyslipidemia” by favoring the hepatic production of atherogenic lipoproteins and by suppressing the uptake of circulating lipids in peripheral tissues. Finally, diabetics have elevated levels of PAI-1, which is an inhibitor of fibrinolysis and therefore acts as a procoagulant in the formation of atherosclerotic plaques.