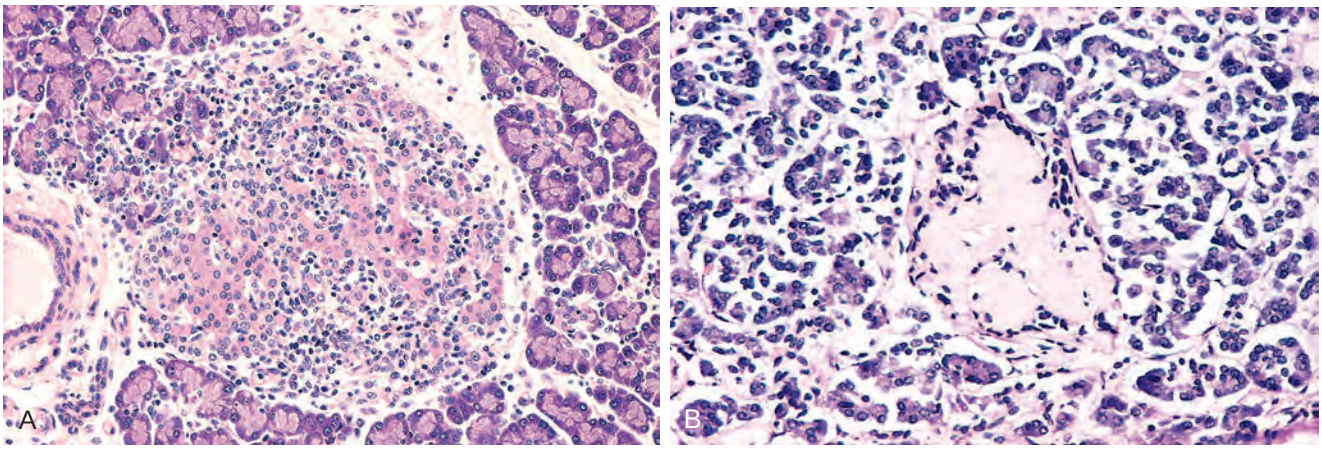

Figure 24-35 **A,** Insulitis**,** shown here from a rat (BB) model of autoimmune diabetes, also seen in type 1 human diabetes. **B,** Amyloidosis of a pancreatic islet in type 2 diabetes. (**A,** Courtesy Dr. Arthur Like, University of Massachusetts, Worchester, Mass.)

MORPHOLOGY

Pancreas

Lesions in the pancreas are inconstant and rarely of diagnostic value. Distinctive changes are more commonly associated with type 1 than with type 2 diabetes. One or more of the following alterations may be present:

- **Reduction in the number and size of islets.** This is most often seen in type 1 diabetes, particularly with rapidly advancing disease. Most of the islets are small and inconspicuous.
- **Leukocytic infiltrates in the islets** (insulitis) are principally composed of T lymphocytes, and are also seen in animal models of autoimmune diabetes (Fig. 24-35*A*). Lymphocytic infiltrates may be present in type 1 diabetics at the time of clinical presentation. The distribution of insulitis may be strikingly uneven in infants who fail to survive the immediate postnatal period.
- **In type 2 diabetes there may be a subtle reduction in islet cell mass,** demonstrated only by special morphometric studies.
- **Amyloid deposition within islets in type 2 diabetes** begins in and around capillaries and between cells. At advanced stages, the islets may be virtually obliterated (Fig. 24-35*B*); fibrosis may also be observed. Similar lesions may be found in older nondiabetics, apparently as part of normal aging.
- **An increase in the number and size of islets** is especially characteristic of nondiabetic newborns of diabetic mothers. Presumably, fetal islets undergo hyperplasia in response to the maternal hyperglycemia.

Diabetic Macrovascular Disease

Diabetes exacts a heavy toll on the vascular system. **Endothelial dysfunction** (Chapter 11), which predisposes to atherosclerosis and other cardiovascular morbidities, is widespread in diabetes, as a consequence of the deleterious effects of persistent hyperglycemia and insulin resistance on the vascular compartment. The hallmark of diabetic macrovascular disease is **accelerated atherosclerosis** involving the aorta and large- and medium-sized arteries. Except for its greater severity and earlier age at onset, atherosclerosis in diabetics is indistinguishable from that in nondiabetics (Chapter 11). **Myocardial infarction, caused by atherosclerosis of the coronary arteries, is the most common cause of death in diabetics. Gangrene of the lower extremities,** as a result of advanced vascular disease, is about 100 times more common in diabetics than in the general population. The larger renal arteries are also subject to severe atherosclerosis, but the most damaging effect of diabetes on the kidneys is exerted at the level of the glomeruli and the microcirculation. This is discussed later.

Hyaline arteriolosclerosis, the vascular lesion associated with hypertension (Chapters 11 and 20), is both more prevalent and more severe in diabetics than in nondiabetics, but it is not specific for diabetes and may be seen in older nondiabetics without hypertension. It takes the form of an amorphous, hyaline thickening of the wall of the arterioles, which causes narrowing of the lumen (Fig. 24-36). Not surprisingly, in diabetics it is related not only to the duration of the disease but also to the level of blood pressure.

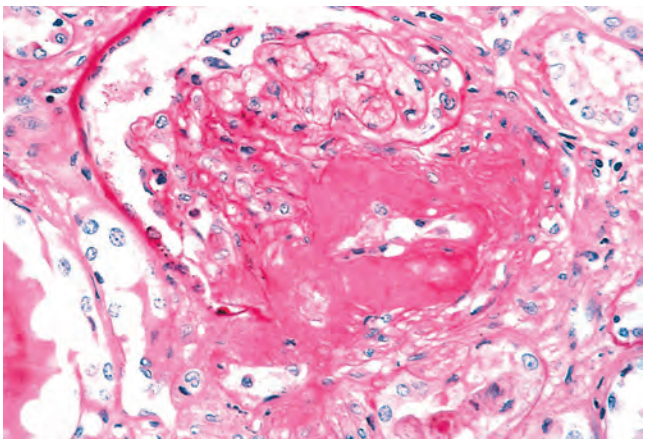

Figure 24-36 Severe renal hyaline arteriolosclerosis. Note a markedly thickened, tortuous afferent arteriole. The amorphous nature of the thickened vascular wall is evident. (PAS stain). (Courtesy M.A. Venkatachalam, MD, Department of Pathology, University of Texas Health Science Center at San Antonio, Texas.)