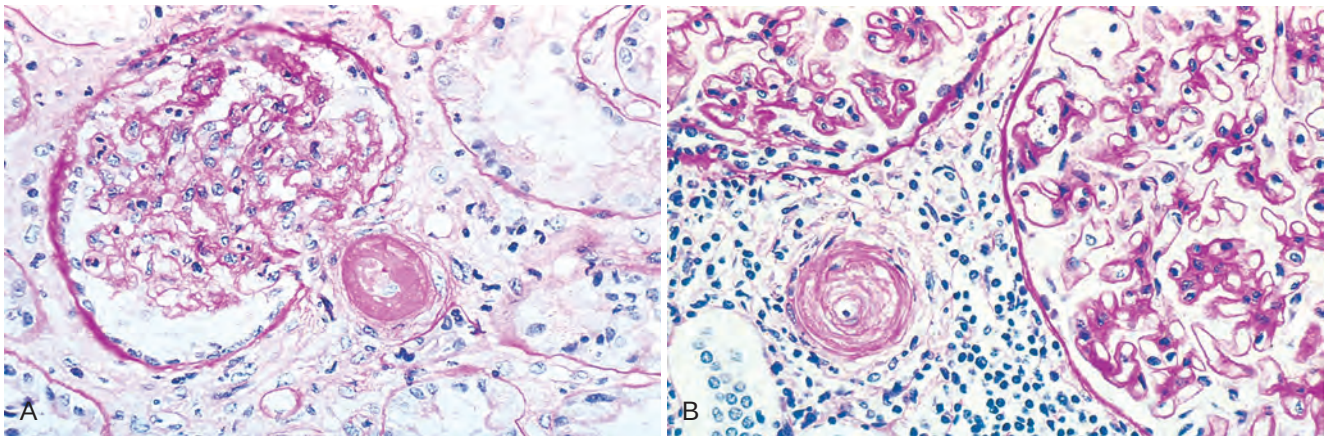

Figure 20-38 Accelerated hypertension. **A,** Fibrinoid necrosis of afferent arteriole (PAS stain). **B,** Hyperplastic arteriolitis (onion-skin lesion). (Courtesy Dr. H. Rennke, Brigham and Women's Hospital, Boston, Mass.)

- In the interlobular arteries and arterioles, there is intimal thickening caused by a proliferation of elongated, concentrically arranged smooth muscle cells, together with fine concentric layering of collagen and accumulation of pale-staining material that probably represents deposition of proteoglycans and plasma proteins. This alteration has been referred to as **onion-skinning** because of its concentric appearance. The lesion, also called **hyperplastic arteriolitis**, correlates with renal failure. There may be superimposed intraluminal thrombosis. The arteriolar and arterial lesions result in considerable narrowing of all vascular lumens, ischemic atrophy and, at times, infarction distal to the abnormal vessels.

Clinical Features. The full-blown syndrome of malignant hypertension is characterized by systolic pressures greater than 200 mm Hg and diastolic pressures greater than 120 mm Hg, papilledema, retinal hemorrhages, encephalopathy, cardiovascular abnormalities, and renal failure. Most often, the early symptoms are related to increased intracranial pressure and include headaches, nausea, vomiting, and visual impairments, particularly scotomas or spots before the eyes. "Hypertensive crises" are sometimes encountered, characterized by loss of consciousness or even convulsions. At the onset, there may only be marked proteinuria and microscopic or macroscopic hematuria, but renal failure soon ensues. The syndrome is a medical emergency requiring aggressive and prompt antihypertensive therapy to prevent irreversible renal injury. Before the development of current antihypertensive drugs, malignant hypertension was associated with a 50% mortality rate within 3 months of onset, progressing to 90% within a year. At present, however, about 75% of patients survive 5 years, and 50% survive with restoration of pre-crisis renal function.

KEY CONCEPTS

Nephrosclerosis

- Nephrosclerosis, which is commonly associated with hypertension, is defined by the presence of varying degrees of glomerulosclerosis, interstitial fibrosis and tubular atrophy, arteriosclerosis, and arteriolosclerosis.
- Luminal reduction of the renal vasculature (arteries and arterioles) contributes to glomerulosclerosis (both global and segmental), which can subsequently cause interstitial fibrosis and tubular atrophy.
- Malignant nephrosclerosis is associated with malignant hypertension. The renal lesions manifest as fibrinoid necrosis of arterioles and hyperplastic arteriolosclerosis. The latter lesion affects interlobular arteries and arterioles and is characterized by proliferation of smooth muscle cells of the arterial wall that are arranged concentrically.

Renal Artery Stenosis

Unilateral renal artery stenosis is responsible for 2% to 5% of hypertension cases, and is important to recognize because it is potentially curable by surgery. Furthermore, important insights into renal mechanisms of hypertension came from studies of experimental and human renal artery stenosis.

Pathogenesis. **Hypertension secondary to renal artery stenosis is caused by increased production of renin from the ischemic kidney.** The classic experiments of Goldblatt and colleagues showed that constriction of one renal artery in dogs results in hypertension and that the magnitude of the effect is proportional to the amount of narrowing. Elevation in blood pressure, at least initially, is due to stimulation of renin secretion by the juxtaglomerular apparatus and the subsequent production of the vasoconstrictor angiotensin II. A large proportion of individuals with renovascular hypertension have elevated renin levels, and almost all show a reduction of blood pressure when given drugs that block angiotensin II activity. Other factors, however, may contribute to the maintenance of renovascular hypertension after the renin-angiotensin system has initiated it, including *sodium retention*.

MORPHOLOGY

The most common cause of renal artery stenosis (70% of cases) is narrowing at the origin of the renal artery by an atheromatous plaque. This occurs more frequently in men, and the incidence increases with advancing age and diabetes mellitus.