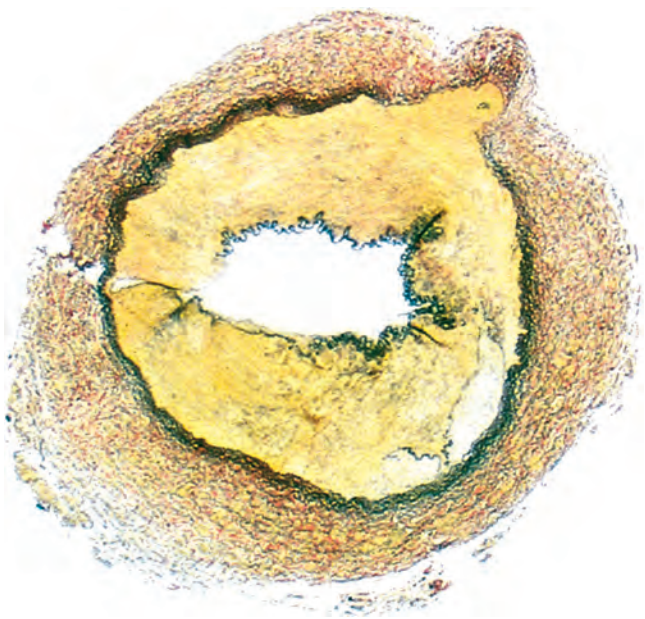

Figure 20-39 Fibromuscular dysplasia of the renal artery, medial type (elastic tissue stain). The media shows marked fibrous thickening, and the lumen is stenotic. (Courtesy Dr. Seymour Rosen, Beth Israel Hospital, Boston, Mass.)

The plaque is usually concentrically placed, and superimposed thrombosis often occurs.

The second most frequent cause of stenosis is **fibromuscular dysplasia** of the renal artery. This heterogeneous entity is characterized by fibrous or fibromuscular thickening that may involve the intima, the media, or the adventitia of the artery (Fig. 20-39). The stenoses, as a whole, are more common in women and tend to occur in younger age groups (i.e., in the third and fourth decades).

The ischemic kidney is reduced in size and shows signs of **diffuse ischemic atrophy**, with crowded glomeruli, atrophic tubules, interstitial fibrosis, and focal inflammatory infiltrates. The arterioles in the ischemic kidney are usually protected from the effects of high pressure, thus showing only mild arteriolosclerosis. In contrast, the contralateral nonischemic kidney may show more severe arteriolosclerosis, depending on the severity of the hypertension.

Clinical Course. Few distinctive features suggest the presence of renal artery stenosis, and in general, these patients resemble those with essential hypertension. On occasion, a bruit can be heard on auscultation of the affected kidneys. Elevated plasma or renal vein renin, response to angiotensin-converting enzyme inhibitor, renal scans, and intravenous pyelography may aid with diagnosis, but arteriography is required to localize the stenotic lesion. The cure rate after surgery is 70% to 80% in well-selected cases.

Thrombotic Microangiopathies

The term *thrombotic microangiopathy* encompasses a spectrum of clinical syndromes that includes thrombotic thrombocytopenic purpura (TTP) and hemolytic-uremic syndrome (HUS). As already discussed in Chapter 14, **HUS and TTP are caused by diverse insults that lead to the excessive activation of platelets, which deposit as thrombi in capillaries and arterioles in various tissue beds, including those of the kidney** (Fig. 20-40). Widespread "consumption" of platelets leads to thrombocytopenia, and the resulting thrombi create flow abnormalities that shear red cells, producing a microangiopathic hemolytic anemia. Of even greater importance, the thrombi produce microvascular occlusions that cause tissue ischemia and organ dysfunction.

This group of disorders is now classified according to the current understanding of their causes or associations, as follows:

- *Typical HUS (synonyms: epidemic, classic, diarrhea-positive)*, most frequently associated with consumption of food contaminated by bacteria producing Shiga-like toxins
- *Atypical HUS (synonyms: non-epidemic, diarrhea-negative)*, associated with:
  - Inherited mutations of complement-regulatory proteins
  - Diverse acquired causes of endothelial injury, including: antiphospholipid antibodies; complications of pregnancy and oral contraceptives; vascular renal diseases such as scleroderma and hypertension; chemotherapeutic and immunosuppressive drugs; and radiation
- *TTP*, which is often associated with inherited or acquired deficiencies of ADAMTS13, a plasma metalloprotease that regulates the function of von Willebrand factor (vWF)

Pathogenesis. Within the thrombotic microangiopathies, two pathogenetic triggers dominate: (1) *endothelial injury*, and (2) *excessive platelet activation and aggregation*. As will be discussed, endothelial injury appears to be the primary cause of HUS, whereas platelet activation may be the inciting event in TTP.

Endothelial injury. In typical (epidemic, classic, diarrhea-positive) HUS, the trigger for endothelial injury and activation is usually a Shiga-like toxin, while for inherited forms of atypical HUS the cause of the endothelial injury appears to be excessive, inappropriate activation of complement. Many other exposures and conditions can occasionally precipitate a HUS-like picture, presumably also by injuring the endothelium. The endothelial injury in

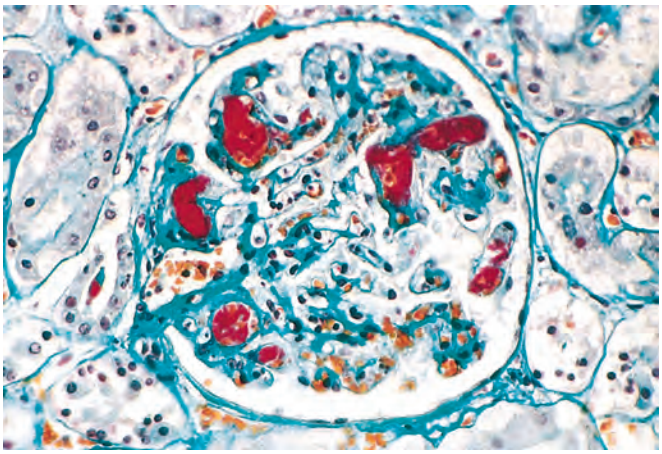

Figure 20-40 Fibrin stain showing platelet-fibrin thrombi (*red*) in the glomerular capillaries, characteristic of thrombotic microangiopathic disorders.