formation of thrombi in arterioles and capillaries throughout the body, but particularly in the liver, kidneys, brain, and pituitary. Hypercoagulability is likely related to the reduced endothelial production of PGI_2, a potent antithrombotic factor, and increased release of procoagulant factors. Production of PGI_2 is stimulated by VEGF, and women with preeclampsia have decreased endothelial production of PGI_2, presumably due to antagonism of VEGF by sFlt1.

MORPHOLOGY

The **placenta** reveals various microscopic changes, most of which reflect malperfusion, ischemia, and vascular injury. These include (1) **infarcts**, which are larger and more numerous that those that may be seen in normal full-term placentas, (2) **exaggerated ischemic changes** in the chorionic villi and trophoblast, consisting of increased syncytial knots, (3) frequent **retroplacental hematomas** due to bleeding and instability of uteroplacental vessels, and (4) **abnormal decidual vessels**, which may show thrombi, lack of normal physiologic conversion (described earlier), fibrinoid necrosis, or intraintimal lipid deposition (acute atherosis) (Fig. 22-51).

The **liver** lesions, when present, take the form of irregular, focal, subcapsular, and intraparenchymal hemorrhages. On histologic examination there are fibrin thrombi in the portal capillaries and foci of hemorrhagic necrosis.

The **kidney** lesions are variable. The glomeruli show marked swelling of endothelial cells, amorphous dense deposits on the endothelial side of the basement membrane, and mesangial cell hyperplasia. Immunofluorescent studies show an abundance of fibrin in glomeruli. In advanced cases, fibrin thrombi are present in the glomeruli and capillaries of the cortex. If widespread and severe, these thrombi may produce complete destruction of the cortex in the pattern referred to as bilateral renal cortical necrosis (Chapter 20). The **brain** may have gross or microscopic foci of hemorrhage along with small-vessel thromboses. Similar changes are often found in the **heart** and the **anterior pituitary**.

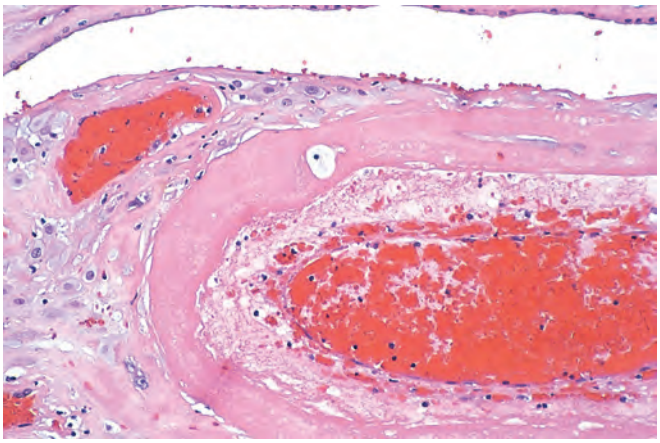

Figure 22-51 Acute atherosis of uterine vessels in eclampsia. Note fibrinoid necrosis of the vessel walls, subendothelial macrophages, and perivascular lymphocytic infiltrate. (Courtesy Dr. Drucilla J. Roberts, Massachusetts General Hospital, Boston, Mass.)

Clinical Features. *Preeclampsia* most commonly starts after 34 weeks of gestation but begins earlier in women with hydatidiform mole (discussed later) or preexisting kidney disease, hypertension, or coagulopathies. The onset is typically insidious, characterized by hypertension and edema, with proteinuria following within several days. Headaches and visual disturbances are serious events and are indicative of severe preeclampsia, often requiring delivery. *Eclampsia* is heralded by central nervous system involvement, including convulsions and eventual coma.

Management of preeclampsia differs depending on the gestational age and severity of disease. For term pregnancies, delivery is the treatment of choice regardless of disease severity. In preterm pregnancies, where delivery may not be in the best interest of the fetus, patients with mild disease can be managed expectantly by closely monitoring the mother and fetus. However, eclampsia, severe preeclampsia with maternal end-organ dysfunction, fetal compromise, or the HELLP syndrome are indications for delivery regardless of gestational age. Antihypertensive therapy does not affect the disease course or improve outcomes. Proteinuria and hypertension usually disappear within 1 to 2 weeks after delivery except when they predate the pregnancy. Although in most instances preeclampsia has no lasting sequelae, recent studies indicate that about 20% of affected women develop hypertension and microalbuminuria within 7 years of a pregnancy complicated by preeclampsia. There is also a twofold increase in the long-term risk of vascular diseases of the heart and the brain.

Gestational Trophoblastic Disease

Gestational trophoblastic disease encompasses a spectrum of tumors and tumor-like conditions characterized by proliferation of placental tissue, either villous or trophoblastic. The major disorders of this type are hydatidiform mole (complete and partial), invasive mole, choriocarcinoma, and placental site trophoblastic tumor (PSTT).

Hydatidiform Mole

Hydatidiform moles are important to recognize because they are associated with an increased risk of persistent trophoblastic disease (invasive mole) or choriocarcinoma. Moles are characterized histologically by cystic swelling of the chorionic villi, accompanied by variable trophoblastic proliferation. They are usually diagnosed during early pregnancy (average 9 weeks) by pelvic sonogram. Molar pregnancy can develop at any age, but the risk is higher at the two ends of reproductive life, in teenagers and between the ages of 40 and 50 years. For poorly explained reasons, the incidence varies considerably in different parts of the world. Hydatidiform mole occurs about once in every 1000 to 2000 pregnancies in the United States, but it is twice as common in Southeast Asia. Two types of benign, noninvasive moles—complete and partial—can be identified by cytogenetic and histologic studies.

Complete Mole

Complete mole results from fertilization of an egg that has lost its female chromosomes, and as a result the genetic material is completely paternally derived (Fig. 22-52*A, B*).