18 Placenta

The gestational sac begins as a spherical structure, with the fetus surrounded by an *amnion*, a *chorion*, and placental *villi*. One surface of the gestational sac implants into the endometrium and becomes the placenta; the villi on the opposite surface degenerate. When you look at placental slides, you can see the layers of the amnion and chorion both in the membrane section (Figure 18.1) and on the fetal surface. In both locations, amnion is on the fetal side, chorion on the maternal side. The two membranes can be peeled apart grossly, because there is no tissue connection between the two.

The villi are fetal structures; they grow downward from the fetal surface in a branching architecture, like the roots of a tree. Vessels and cells inside the villi are fetal. There should not be any maternal vessels in the placenta itself. The spiral arteries of the decidua (endometrium), invaded by trophoblastic cells, spray maternal blood into the space between the villi.

Immature villi have an open and pale appearance (Figure 18.2); they are large compared with the terminal villi of the full-term placenta (when surface area is most required). They are lined by two cell layers, an outer syncytiotrophoblast and an inner cytotrophoblast layer. Very early villi may have a large intermediate trophoblastic proliferation on the surface, but it should be polar (only on one surface, like Don King's hair). Circumferential proliferation is suspicious for hydatidiform mole.

Mature villi acquire syncytial knots and perivillous fibrin (like hyaline membranes lining the villi). They become tiny—just large enough to hold a few capillaries (see Figure 18.2).

Twin placentas are divided into categories based on how many cell layers they share. Two separate eggs fertilized by two sperm will always form two separate placentas, although they may mash into each other. With two placentas you will see two chorionic plates and two complete sets of membranes (Figure 18.3); this is called diamnionic-dichorionic (di-di). An ovum that splits very early can also produce two entirely separate placentas, so a di-di placenta may be either monozygotic or dizygotic twins.

An ovum that splits a little later, after it has already formed a chorion, will produce two separate amnions and two fetuses; this is a diamnionic-monochorionic placenta (di-mo). An even later split produces two fetuses in the same amnionic sac, or monoamnionic-monochorionic (mo-mo). If the split occurs any later than this, conjoined twins will develop.

Approach to the Slides

In the *umbilical cord*, look at the vessels on low power (Figure 18.4). There should be two arteries (usually with constricted lumens) and a vein (open lumen, or the mouth on the surreal Mr. Bill faces that are found on the walls of most histology laboratories). The number of vessels is always noted on sign out, because a two-vessel cord often indicates a fetal abnormality.

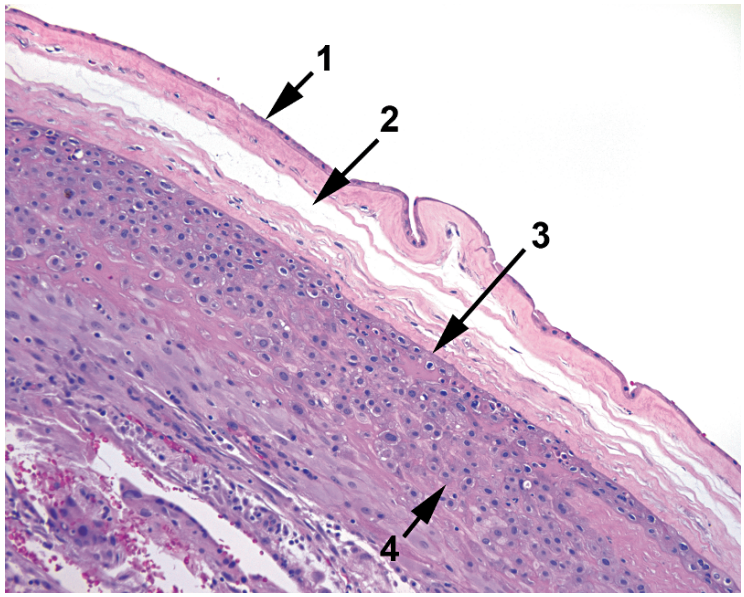

Figure 18.1. Placental membranes. In the membrane section, you can see amnion (1), an artifactual space (2) between amnion and chorion (3), and underlying decidua (4).

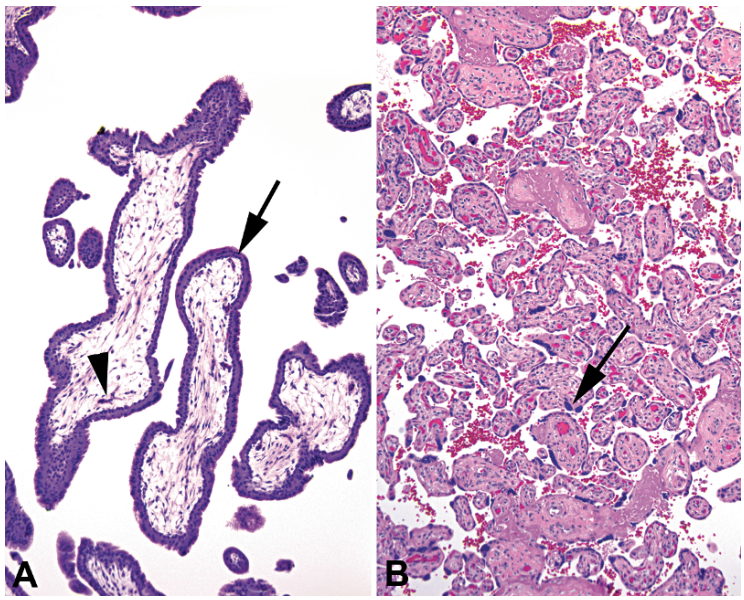

Figure 18.2. Immature villi versus terminal villi. **(A)** Villi at around 8–10 weeks are large in diameter and have a double layer of cells lining the surface (arrow). Tiny fetal capillaries have nucleated red blood cells inside (arrowhead). **(B)** Taken at the same magnification as A, this shows mature villi at approximately 38 weeks. The villi are much smaller, the fetal capillaries are more prominent, and the cytotrophoblasts have pulled away from the gas-exchange surface into syncytial knots (arrow). Maternal blood and fibrin are visible between villi.

Study the muscular wall of each vessel to look for neutrophils. Umbilical phlebitis, or neutrophils migrating into the vein wall, is an indicator of early funisitis (a fetal inflammatory response). More advanced funisitis involves the arteries (arteritis), and the most severe cases show neutrophils in the Wharton's jelly (Figure 18.5).

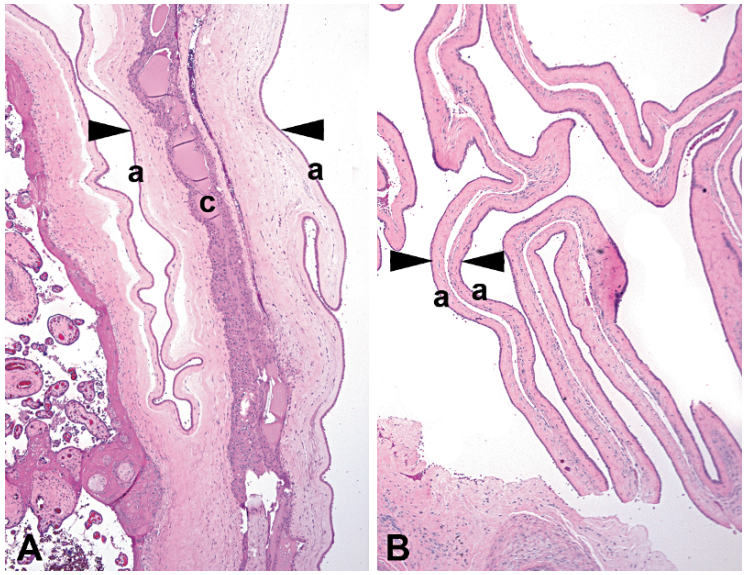

FIGURE 18.3. Twin placentas. **(A)** In a diamnionic, dichorionic placenta, the dividing membrane is captured here between the arrowheads. Amnion is seen on both surfaces (a), and a double layer of chorion is sandwiched in the middle (c). **(B)** In a diamnionic, monochorionic placenta, no chorion is present between the layers (arrowheads) of amnion (a).

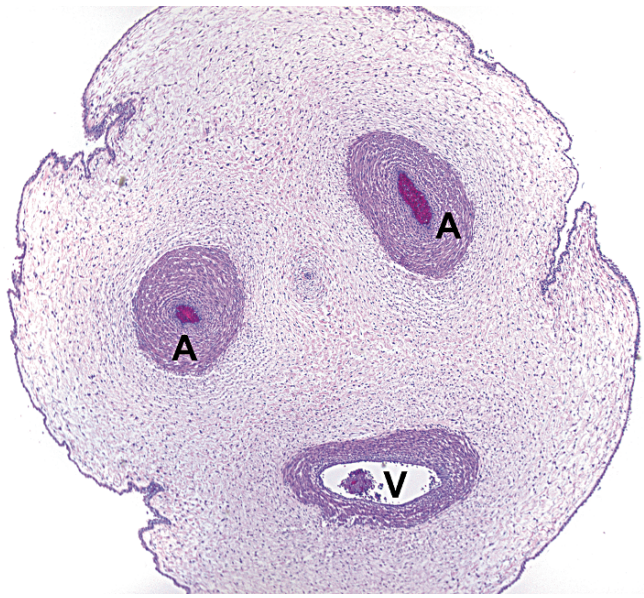

FIGURE 18.4. An umbilical cord in cross section, showing two arteries (A) and one vein (V).

The *membrane roll* is evaluated for the following:

- Chorionitis and chorioamnionitis: Look for neutrophils invading the chorion and/or amnion. Neutrophils in the decidua (below the chorion) are okay (Figure 18.6). Table 18.1 summarizes staging and grading of chorioamnionitis. Inflammation may result in a very reactive (tall, papillary) amnion. Unlike funisitis, this is a maternal response.
- Meconium staining: If, on low power, the amnion has a flat and autolyzed look, with edema separating amnion from chorion, look closely for meconiophages (Figure 18.7). These are histiocytes eating meconium (baby bile) pigment, and they appear granular and brown-gold.

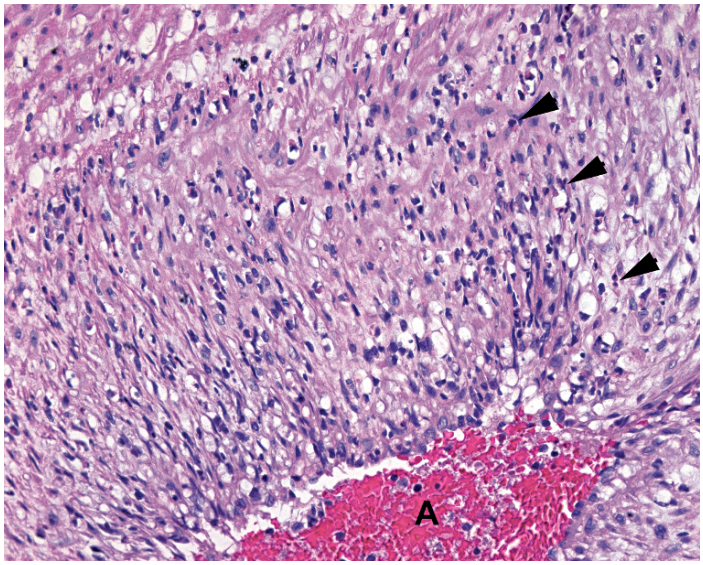

Figure 18.5. Funisitis. Neutrophils (arrowheads) can be seen squeezing through the muscular layer of an umbilical artery (A). This migration is a fetal response to infection.

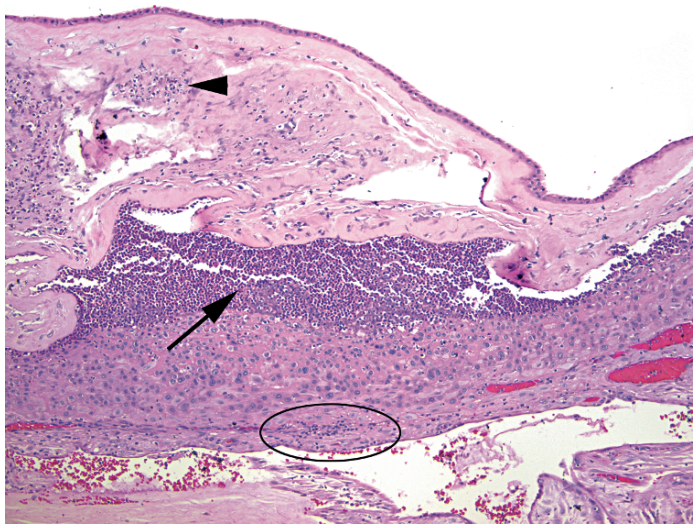

Figure 18.6. Chorioamnionitis. A collection of neutrophils (pus) has formed between the amnion and chorion (arrow). Neutrophils can also be seen beneath the amnion (arrowhead). Inflammation in the decidua (oval) may be physiologic and is not sufficient to diagnose chorioamnionitis. This is a maternal response to infection.

Table 18.1. Criteria for staging of acute chorioamnionitis and funisitis.

Stage	Maternal response	Fetal response (funisitis)
1	Subchorionitis and chorionitis: *maternal neutrophils* line up beneath the chorionic surface of either the chorionic plate or membranes	Chorionic plate vasculitis and umbilical phlebitis: *fetal neutrophils* marginate through the vessel wall
2	Chorioamnionitis: neutrophils cross the basement membrane into the connective tissue between chorion and amnion	Umbilical arteritis: neutrophils in the arterial wall
3	Necrotizing chorioamnionitis: sheets of neutrophils below the amnion, reactive or necrotic amnion, thickened amnionic basement membrane	Umbilical perivasculitis: neutrophils spread out from the vessels in a wave

Grade 1 = focal disease; grade 2 = extensive disease.

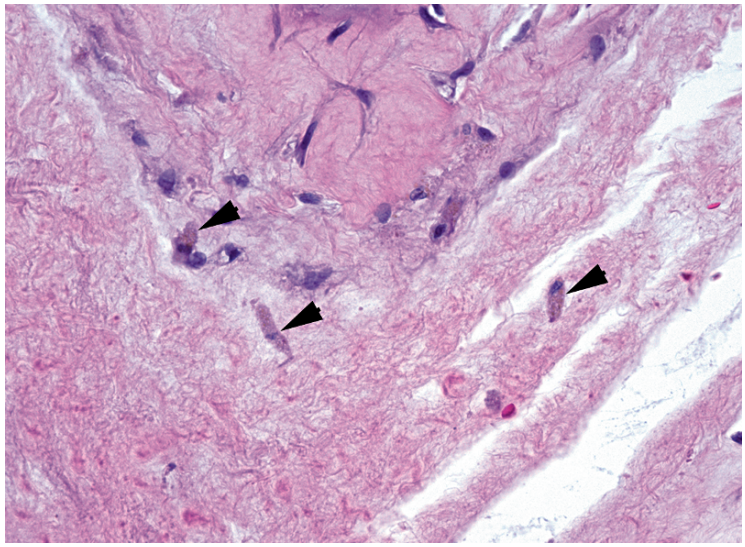

FIGURE 18.7. Meconiophages between the amnion and chorion, with deposits of brown pigment (arrowheads).

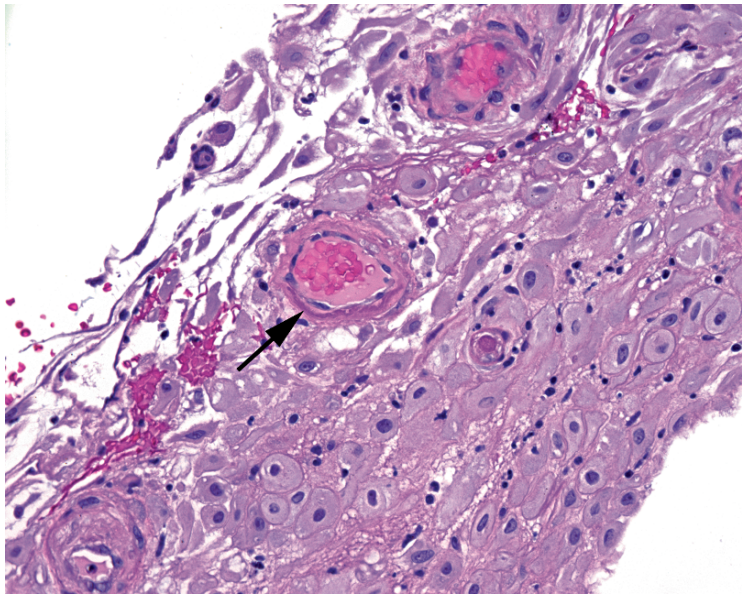

FIGURE 18.8. Fibrinoid necrosis. The dark pink condensation of the wall of this small artery (arrow) is an early sign of fibrinoid necrosis, which may be seen in preeclampsia.

The attenuated look of the amnion is due to the caustic nature of the meconium, just as gallbladders look when they have been sitting around for a day or so.

- Decidual vasculopathy: The membrane roll usually shows a nice lining of decidua, which is where you will find maternal vessels. Evaluate these for fibrinoid necrosis, a common finding in preeclampsia (Figure 18.8).

On the *fetal surface*, look for the following:

- Subchorionitis: Subchorionitis is the earliest manifestation of chorioamnionitis (maternal response). Neutrophils line up in the fibrin layer below the chorionic plate (see Table 18.1 for staging and grading chorionitis).

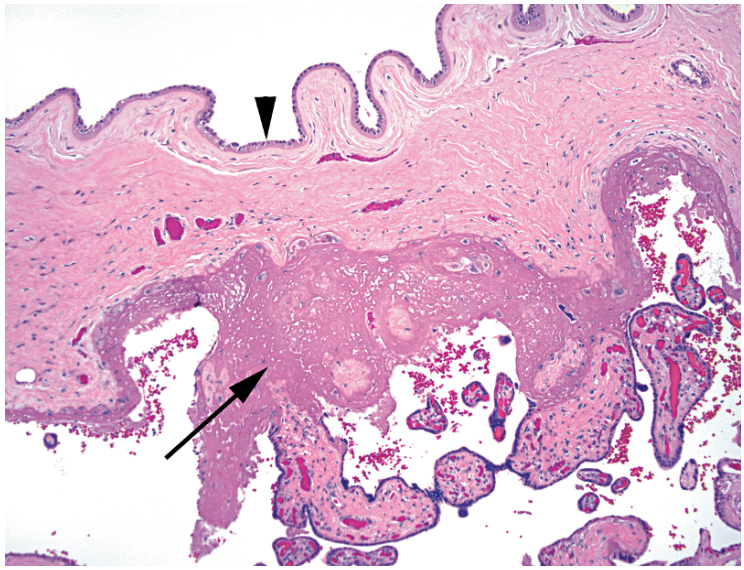

Figure 18.9. Fibrin, subchorionic. Subchorionic deposits of fibrin (arrow) are normal in a term placenta and should not be mistaken for infarct. The amnion lies atop the fetal surface (arrowhead).

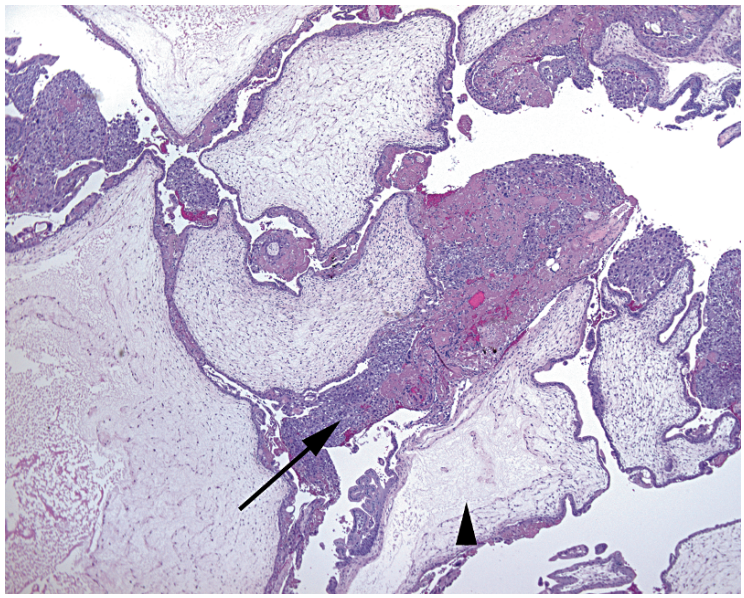

Figure 18.10. Molar villi. The villi are markedly enlarged, some with central cavities or cisterns (arrowhead). Dense trophoblastic proliferation is visible (arrow); on higher power, the cells may be very pleomorphic. This is a complete mole, so there are no fetal capillaries within the villi.

- Fetal vasculitis: The vessels that coalesce to become the umbilical vessels arborize on the fetal surface, sandwiched between the amnion and chorion. This is another place to look for a fetal phlebitis or arteritis.
- Subchorionic fibrin: Subchorionic fibrin is normal, and you may see large deposits in full-term placentas (Figure 18.9). Do not call it an infarct.

Below the fetal surface and above the maternal surface you will find the villi, the massive gas- and nutrient-exchange surface area of the placenta. In very early villi, such as in spontaneous or elective abortion, look for changes suggestive of a *hydatidiform mole* (Figure 18.10).

These changes include large swollen villi with no internal fetal vessels, circumferential and atypical trophoblast proliferation, and lack of fetal parts (in a complete mole). A complete mole is diploid with two paternal genomes and by definition has no fetus. A partial mole is triploid, one maternal and two paternal copies, and has a fetus, as well as two distinct populations of villi: normal and hydropic (edematous). An incidentally discovered early partial mole can be very subtle.

In a more mature placenta, such as an obstetric specimen, evaluate the villi for the following:

- Villous maturity: A full-term placenta should have a dense network of tiny terminal villi, each full of capillaries and lined with syncytial knots. A preterm placenta (<32 weeks or so) should have more immature villi, with larger contours, few syncytial knots, and myxoid stroma. A mismatch in gestational age and maturity is called hyper- or hypomaturity. Hypermaturity may indicate ischemia.
- Fibrin: Perivillous fibrin, which looks like hyaline membranes outlining the villi, increases with maturity, especially around the larger stem villi. Massive deposition may look like an infarct.
- Villitis: An increase in chronic inflammation within the villi may indicate a cytomegalovirus or syphilis infection. Often no organism can be found, in which case it is *villitis of uncertain etiology*.
- Infarct: Usually visible grossly as dense white patches, a true infarct has the look of coagulative necrosis (loss of nuclei and cell structure) with the mummified villi touching each other (Figure 18.11). Do not confuse this with perivillous fibrin deposition, in which fibrin encases a wide area of villi (encased villi should still show nuclear detail and be separated by abundant surrounding fibrin).
- Hematoma: A large acellular mass of fibrin, complete with lines of Zahn, is evidence of a prior hemorrhage. The hematoma may be subchorionic, intraplacental, or retroplacental (clinical abruption).
- Fetal capillaries: After prolonged death in utero, these capillaries collapse and the villi become fibrotic. Also look for nucleated red blood cells, which are abnormal in third trimester placentas.

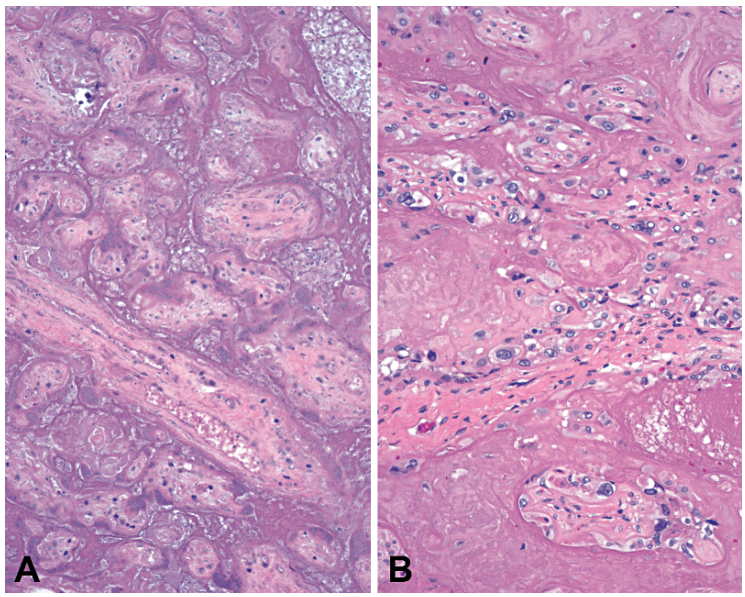

Figure 18.11. Infarct versus perivillous fibrin. **(A)** In an infarct, there is loss of basophilia and cellular detail with residual apoptotic bodies, as in coagulative necrosis elsewhere. **(B)** In a mass of perivillous fibrin, while the low power impression is a sheet of consolidated pink, on high power you can see the villi remain viable, with good nuclear detail.

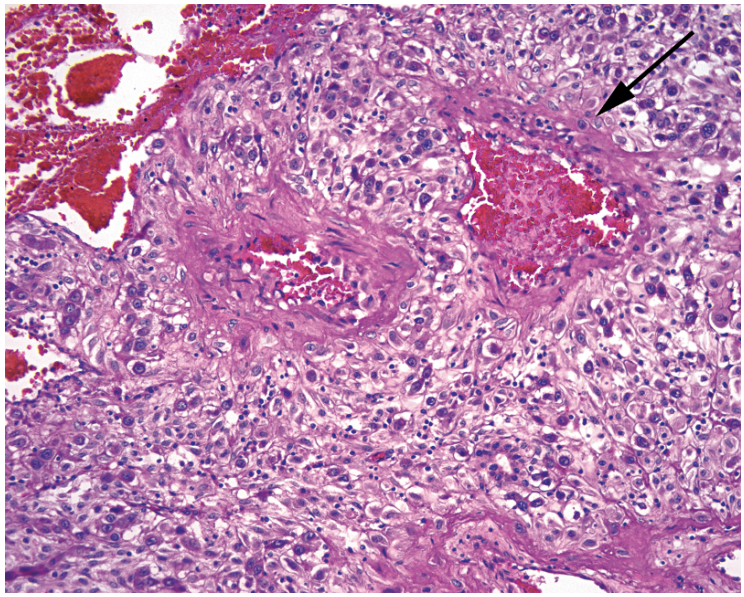

Figure 18.12. Trophoblasts in vessels. Intermediate trophoblasts (arrow) invading the wall of the maternal arteries. This is a normal process, opening fire hoses of blood to supply the placenta.

- Intervillous inflammation: Neutrophils or abscesses in the intervillous space are unusual but indicate maternal sepsis, such as from *Listeria*.

The *maternal surface* shows a layer of decidua, with implantation site changes. Trophoblasts invade the maternal muscular arteries, dissolving their muscular wall to create wide-open pipes (Figure 18.12). This invasive but normal process leaves behind a fibrinous layer—do not mistake this for fibrinoid necrosis or vasculopathy. True fibrinoid necrosis is best seen on the small maternal vessels in the membrane roll and also has an inflammatory component. However, in the maternal floor, the persistence of muscular arteries *is* a form of maternal vasculopathy, because it means the trophoblasts did not do their job, and the placenta may be ischemic. This is another component of preeclampsia.

A *maternal floor infarct* is not really a true infarct but a dense rind of fibrin encasing all of the villi along the maternal surface. *Placenta accreta* is the implantation of trophoblastic cells directly into myometrium. Histologically you may see placental villi very close to smooth muscle, with no intervening decidua. Accreta is a cause of postpartum hemorrhage.

The features of preeclampsia are the following:

- Decidual vasculopathy, also called acute atherosis: fibrinoid necrosis of decidual vessels, with accumulation of fibrin and foamy macrophages in the lumen and destruction of the arterial wall
- Hypertrophic vasculopathy (retained muscular wall) of the maternal floor vessels
- Increased perivillous fibrin, syncytial knots, and villous maturity