Chapter 19

Miscellaneous Placental Lesions

Intervillous Thrombi

Pathogenesis

Intervillous thrombi are common lesions, occurring in approximately one fifth of term placentas. They are defined as localized clots in the intervillous space and were previously known as Kline's hemorrhages. Intervillous thrombi may occur secondary to *leakage from the fetal capillaries* and thus may be a manifestation of **fetomaternal hemorrhage**. If they are large or numerous, they may be an indication of significant hemorrhage (see Chap. 20). Immunohistochemistry for fetal hemoglobin has identified fetal red blood cells in intervillous thrombi, and in fact, a good correlation exists between the presence of fetal red blood cells in the maternal circulation and intervillous thrombi. It should also be mentioned that when the maternal and fetal bloods are compatible, clotting might not take place even in a significant fetal

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hemorrhage. However, in many cases, intervillous thrombi have no clinical impact on mother or infant.

On the other hand, intervillous thrombi may develop due to *increased thrombosis in the maternal circulation* in the setting of **maternal thrombophilias** or **preeclampsia**. When associated with the latter, they are often found in the maternal floor in relation to decidual vasculopathy. Intervillous thrombi are also seen in cases of **erythroblastosis fetalis** and in **hydatidiform moles**. In these situations, the edema so alters the intervillous blood flow as to cause local eddying and stasis, with thrombosis the end result. Fresh intervillous thrombi may also simply be the result of **local stasis of blood flow during labor**. Finally, small breaks may occur, perhaps from fetal movement, injuring the villi in some way. This may explain the frequency of fetal bleeding in otherwise normal placentas. It is not possible to differentiate the different etiologies on routine microscopic examination alone.

Pathologic Features

The maternal "jet" of blood enters in the center of the cotyledon. In this region, the villous tissue is usually composed of larger, more immature villi, which are separated by wide intervillous clefts. This is the most common site of intervillous thrombi. Gross examination of fresh intervillous thrombi reveals *red, shiny lesions with sharp, angular outlines* (Fig. 19.1). At times one can see that their triangular shape originates from vessels in the placental floor. They are *often laminated with light tan-gray and red alternating lines*. Older intervillous thrombi tend to be more white-tan (Fig. 19.2). They are sometimes confused with infarcts but can be differentiated from them grossly by the granular consistency and round contour in the latter.

Microscopically, intervillous thrombi *displace adjacent villous tissue* and form a clot in the intervillous space (Fig. 19.3). Older clots may contain macrophages that have engulfed red blood cells. *If intervillous thrombi become large, or if they are of longer duration, the compressed*

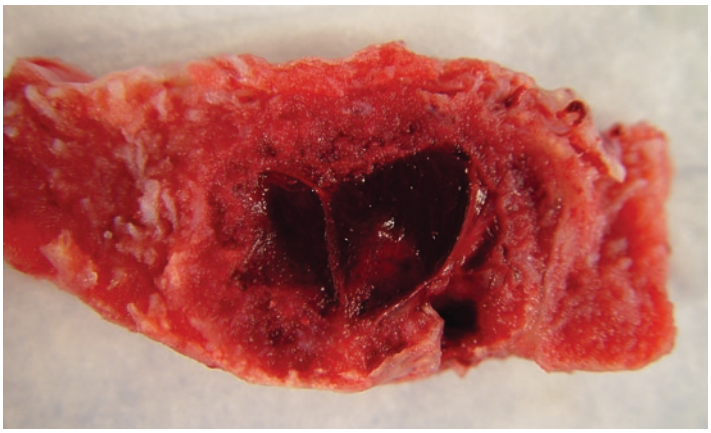

Figure 19.1. Intervillous thrombus in a term placenta shows recent clot with laminated fibrin.

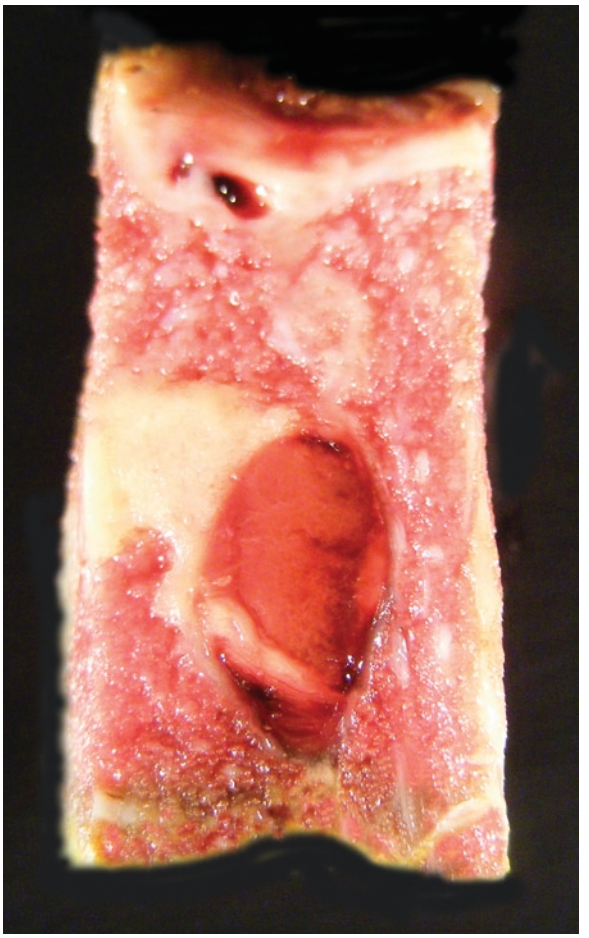

Figure 19.2. Layered fibrin is present in this older intervillous thrombus.

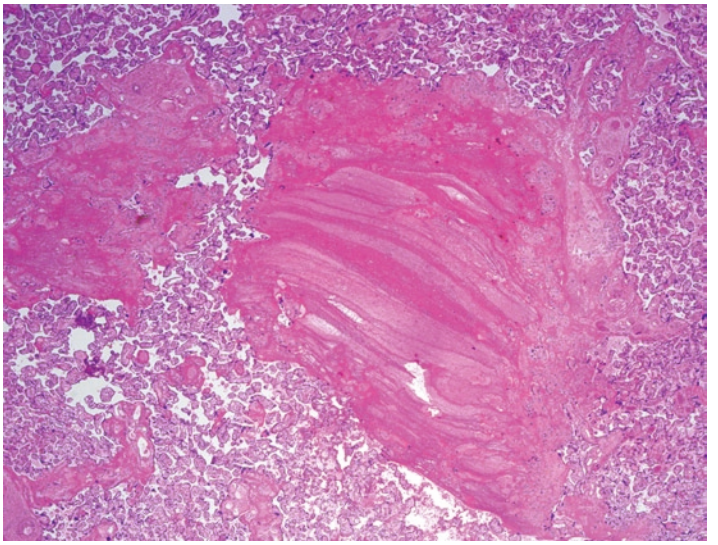

Figure 19.3. Layered fibrin with "lines of Zahn" in an intervillous thrombus H&E ×10.

adjacent villous tissue will become infarcted. Thus, older lesions may be difficult to differentiate from infarcts. They may also be found in the subchorionic region, forming because of eddying of the intervillous blood as it is reflected beneath the chorion and in this case would be better described as subchorionic thrombi or hematomas. This type of intervillous thrombus is common and increases with gestational age. It is of parenthetic interest here to note that intervillous thrombi *never undergo the repair process known to pathologists as "organization"* and so do not show the fibrous tissue ingrowth and neovascularization that occurs in other organs.

Suggestions for Examination and Report
(Intervillous thrombi)

Gross Examination: Description of the number and size of the intervillous thrombi is important in evaluating the clinical significance. Representative sections are recommended but in the case of multiple lesions, not all lesions need to be sampled.

Comment: If intervillous thrombi are large or numerous, the possibility of a fetomaternal hemorrhage should be raised and a Kleihauer–Betke test recommended (see Chap. 20). This is particularly important in the case of a fetal demise or if there is evidence of fetal anemia. The latter may be given in the clinical history or indirect evidence of fetal anemia may be concluded from the presence of pale villous tissue (see Chap. 20).

Intravillous Hemorrhage

Intravillous hemorrhage is most commonly due to sudden placental ischemia with disruption of the capillaries and therefore by nature is an acute process. Trauma to the placenta, particularly abruptios resulting from motor vehicle accidents, leads to this type of "bruising" of the villous tissue. Histologically, it consists simply of extravasation of red blood cells from the villous capillaries into the stroma without associated alternation of the villous structure (Fig. 19.4). As this is an acute change, it precedes evidence of the early ischemic change of the villi following an abruption or an infarction, e.g., collapse of the intervillous space.

Suggestions for Examination and Report
(Intravillous hemorrhage)

Gross Examination: This lesion is not usually visible grossly.

Comment: Intravillous hemorrhage is seen in conditions of early ischemia, trauma or acute hypoxia.

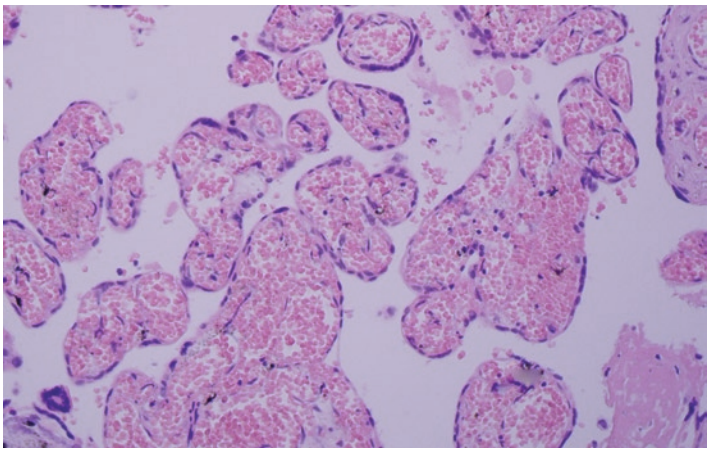

Figure 19.4. Intravillous hemorrhage in an immature placenta 14 h after an automobile accident. H&E, *left* ×40, *right* ×160.

Retroplacental Hematoma and Abruptio Placentae

Pathogenesis

An **abruptio placentae** is defined as the *detachment of the placenta from its decidual seat*. There are many causes of abruptio, including *maternal vascular disease, trauma from accidents, amniocentesis, uterine anomalies, placenta previa, folic acid deficiency, grand multiparity, and rarely pheochromocytoma*. Most abruptios are the result of either *maternal vascular disease or trauma*, with preeclampsia being the cause in 13% and eclampsia in 35%. Thus, hypertensive disease in pregnancy is the most common cause of abruptios. Automobile accidents are the commonest cause of *traumatic* placental hemorrhages and abruptios.

Clinical Features and Implications

The frequency of abruptio placentae is estimated to be between 0.96 and 3.75% of all deliveries. With a total abruptio, or with a large acute abruptio, there may be pain due to sudden stretching of the uterine peritoneal covering, sometimes accompanied by vaginal bleeding or backache. More often, abruptio is partial and is often painless. If the separation and thus the bleeding are not in close proximity to the cervical os, no vaginal bleeding may be present, and this is referred to as a "concealed abruption." Since not all abruptios bleed externally or produce the classical clinical signs of a painful, rigid abdomen, the diagnosis is bound to be missed clinically in some cases. Clinical "abruptio" may also mimicked by *active peripheral bleeding that ultimately leads to circumvallation and by marginal hemorrhage associated with severe ascending infection*. Therefore, placental examination is essential in these cases to determine the cause of the symptomatology.

When pregnant women are involved *in car accidents with blunt trauma to the abdomen, fetal loss occurs in 25%*, with 50% of these due to maternal death. When one-half or more of the placenta detaches suddenly, the fetus usually dies. If placental detachment takes place over a long period, in stages and with infarcts ensuing, then the fetus may survive but will suffer from deficient transplacental oxygen and nutrient supply. This may result in *hypoxia, growth restriction, or neurologic injury*. In some cases, if the placenta itself is also torn by trauma, *severe fetal hemorrhage and anemia* may develop, and transplacental hemorrhage may also accompany the trauma. *Vaginal bleeding, uterine rupture, fetal brain damage, and skull fractures* also have been reported in motor vehicle accidents. Delayed abruptio has been reported to occur up to 5 days after an automobile accident, but careful examination of the placenta will reveal damage that is coincident with the trauma. If extension of the abruption occurs over time, fetal death may be the result, but this usually occurs within 48 h.

Pathologic Features

Premature placental separation, or abruptio, is diagnosed pathologically by the presence of a **retroplacental hematoma**. Abruptio placentae and retroplacental hematoma are very similar, but not equivalent diagnoses. A retroplacental hematoma is the pathologic lesion that results from the clinical condition of abruptio. Alternatively, retroplacental hematomas by their nature will lead to separation of the placenta from the uterus or an abruption. Grossly, fresh retroplacental hematomas, those less than an hour or so old, may not be distinguishable from the normally present postpartum maternal blood clot that is loosely adherent. *After several hours, however, the retroplacental clot will become adherent to the maternal surface* and identifiable on gross examination. These clots are most commonly present at the margin of the placenta. *Compression of the underlying villous tissue then follows* (Fig. 19.5; see also Fig. 18.13 in Chap. 18) in a few hours. With time, the blood dries, becomes firmer and stringy, and then changes color to brown and eventually may become greenish. The placental tissue underneath the clot becomes compressed and will ultimately become infarcted (Figs. 19.6 and 19.7). Over time, *the blood cells begin to degenerate and there is laminated fibrin present. Hemosiderin-laden macrophages will be present after approximately 4–5 days*. The decidua basalis becomes degenerated and necrotic and is often replaced by the hematoma. Depression of the villous tissue disappears as the overlying placenta becomes infarcted and then atrophies.

Since most abruptios are the result of maternal vascular disease or trauma, assessment of the decidual spiral arterioles is desirable. In the locale of the abruption, this may be impossible as the vessels here are often destroyed by the process or have remained behind during the delivery of the placenta. One must therefore look in adjacent portions of decidua and, especially, in the decidua capsularis. *Atherosis and thrombosis* are often well displayed in these vessels. In some cases, it may be impossible to rule out vascular changes as the cause of abruption, and thus the etiology remains obscure.

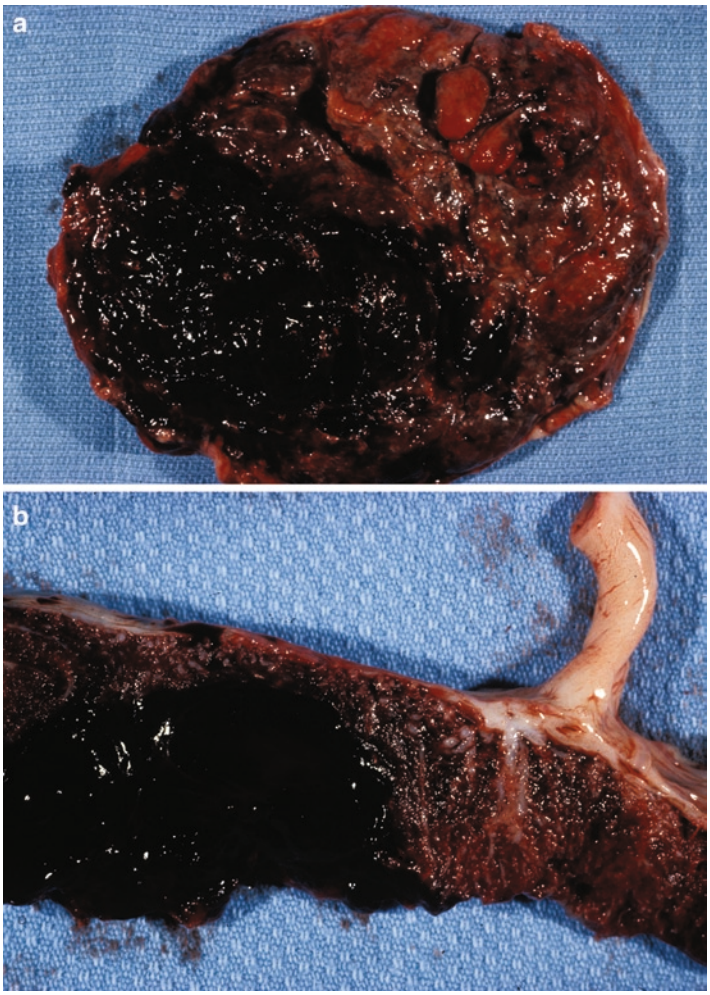

Figure 19.5. (**a**) Maternal surface of the placenta with a retroplacental hematoma showing recent adherent blood clot. (**b**) Cross section of the placenta shows that the recent blood clot compresses the underlying villous tissue, which shows no alteration.

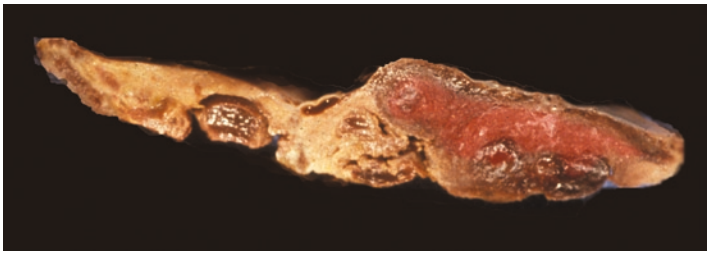

Figure 19.6. Several retroplacental hematomas are seen in this cut section of a placenta from a woman with severe preeclampsia. The fetal surface is at the *top* of the figure and maternal surface at the *bottom*. The hematoma on the *left* is old with infarction of the underlying villous tissue presenting as white, firm tissue. A more recent hematoma is seen on the *right* with mild discoloration of the underlying villous tissue consistent with a more recent infarct.

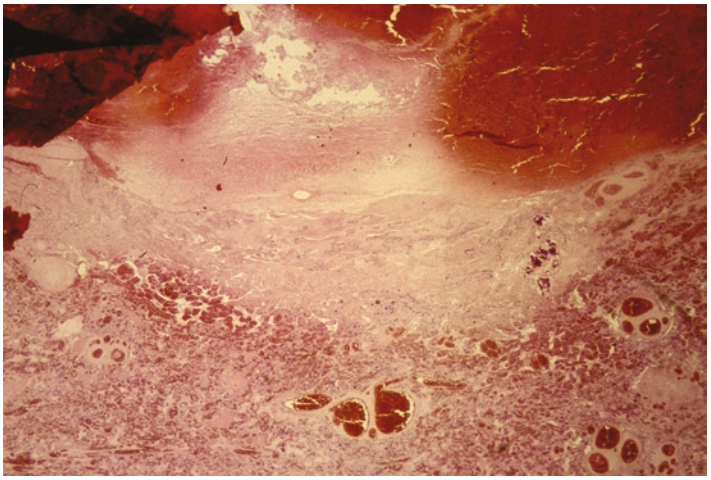

Figure 19.7. Histologic picture of a retroplacental hematoma from a recent abruption. The maternal surface is at the *top* and shows a recent clot with some compression of the villous tissue but no obvious infarction. H&E ×20.

Suggestions for Examination and Report
(Retroplacental hematoma)

Gross Examination: Identification of the retroplacental hematoma, the percentage of the placenta involved and the age of the hematoma is essential. Representative sections of the clot and underlying villous tissue should be taken. If parts of the hematoma appear grossly older, it recommended that the oldest and most recent clot both be submitted.

Comment: The presence of the retroplacental hematoma, percentage of the surface involved and the findings of maternal vascular disease or other associated lesions should be included in the report as well as the acuteness of the lesion.

Chorangiosis and Chorangiomatosis

Chorangiosis, chorangiomas, and chorangiomatosis are related lesions and can be generally defined as follows:

- **Chorangiosis** – a diffuse increase in the number of villous capillaries
- **Chorangioma** – a benign neoplastic proliferation of capillaries and stroma within a villus forming an expansile nodular lesion
- **Chorangiomatosis** – a multifocal lesion characterized by an increase in villous capillaries that tends to permeate the normal villous structures and commonly involves stem villi

Chorangiosis and chorangiomatosis are discussed in the following sections while chorangiomas are discussed with other neoplasms in Chap. 22.

Chorangiosis

Pathologic Features

Chorangiosis is diagnosed principally by low-power lens inspection of histological sections. It has been specifically defined as *ten or more capillaries in each of ten villi in ten fields inspected with a 10× objective in three different, noninfarcted areas of the placenta* (Fig. 19.8). Three or more areas are best interpreted in separate sections from three different areas of the placenta. A grading system has been developed but is seldom used. Meeting the full criteria requires counting a total of 3,000 capillaries and thus may not be practical or even necessary in every case. With experience, counting a number of fields in different areas and confirming that the process is diffuse throughout the placenta is often sufficient for the diagnosis. Furthermore, if the criteria is not completely met but a significant number of villi contain 15 or 20 or more vessels, this is also evidence of increased capillary proliferation and therefore may be diagnosed as chorangiosis with a comment for the basis of the diagnosis. At times "focal chorangiosis" is sometimes diagnoses based on the focality of the changes. Normally three to five capillaries are present in normal terminal villi and when there are more than five but less than 10, the term "borderline chorangiosis" has been used. Neither of these terms has been well studied, and so their clinical significance is not known precisely.

The increase in capillary lumen cross sections seen in this lesion comes about through endothelial proliferation. It thus takes *weeks to develop full-blown chorangiosis*. Villous congestion should not be misinterpreted as chorangiosis (Fig. 19.9). Congestion of the terminal villi may occur when the cord has been clamped soon after delivery of the neonate, from cord compression, knots, torsion, cord entanglements, and the like.

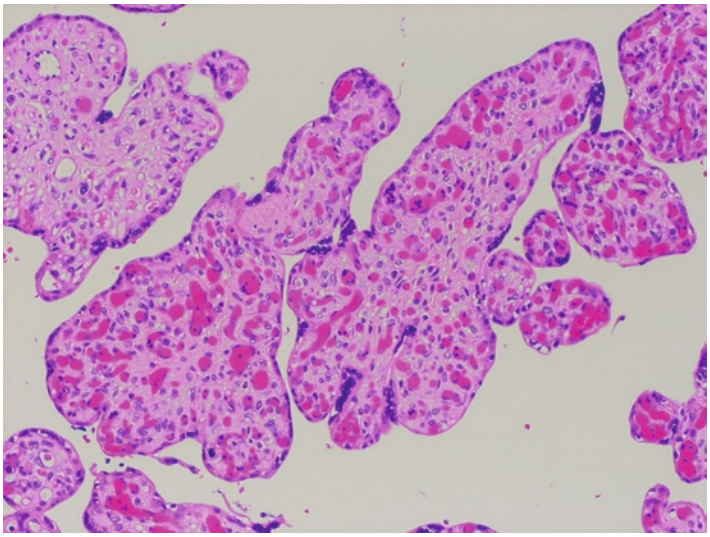

Figure 19.8. Chorangiosis showing a marked increased in the number of villous capillaries. H&E ×200.

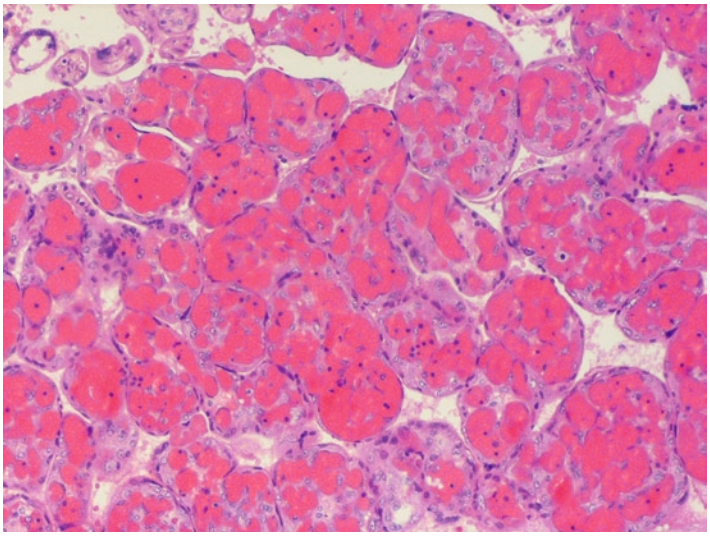

Figure 19.9. Villous congestion. Contrast this appearance with that of chorangiosis in Fig. 19.8. Here the capillaries are enlarged and distended with blood but their number is not increased. H&E ×200.

Pathogenesis

At term, the terminal villi comprise nearly 40% of the villous volume and about 60% of villous cross sections. These figures explain why a remarkable reduction of terminal villi, as in terminal villus deficiency (see Chap. 18), may lead to fetal hypoxia. *There is a clear-cut inverse relation between the area of villous vasculosyncytial membranes and fetal hypoxia*. Conversely, the proliferation of villous capillaries seen in chorangiosis is an adaptation to chronic oxygen deficiency. This is supported by the fact that chorangiosis occurs in placentas of women *at very high altitude, in preeclampsia*, and in *severely anemic mothers*. It is also seen in mothers who *smoke, are exposed to heavy pollutants, and in mothers who have chronic hypoxia to heart disease or other conditions*. Further support comes from experiments in guinea pigs in which an increase in capillaries can be demonstrated when they are chronically (45 days) deprived of oxygen. Thus, *an altered capillary/villus ratio is characteristic of hypoxic placentas*.

Clinical Features and Implications

Chorangiosis is presently underrated as an indicator of *chronic prenatal hypoxia*. In an unselected population, chorangiosis is relatively rare but it is found with increasing frequency in the placentas of infants admitted to neonatal intensive care units. It is strongly correlated with *perinatal mortality*, and a wide variety of pregnancy and placental disorders, including *perinatal circumstances that suggest long-standing hypoxia*. It is more commonly observed in the placentas of babies who develop *cerebral palsy* and in infants with *cord problems* of one kind or another. Its presence betrays a deleterious intrauterine environment for the fetus and a manifestation of an attempt (teleologically speaking) of the placenta to enlarge its diffusional surface.

Suggestions for Examination and Report
(Chorangiosis)

Gross Examination: Chorangiosis is not diagnosed grossly.

Comment: Chorangiosis is associated with conditions of chronic hypoxia and is strongly correlated with perinatal morbidity and mortality.

Chorangiomatosis

Like chorangiosis, **chorangiomatosis** is characterized by an increase the villous capillaries. However, chorangiosis involves terminal villi, while in chorangiomatosis, the process involves immature intermediate or stem villi and the terminal villi are generally spared. In chorangiosis, the capillaries are surrounded by basement membranes only, while in chorangiomatosis the vessels are surrounded by loose bundles of reticular fibers that blend into the surrounding stroma. Chorangiomatosis also has many features in common with chorangiomas, namely the presence of *perivascular cells around vessels, increased cellularity, and stromal collagen*. Chorangiomas are also thought to arise from immature intermediate or stem villi.

Chorangiomatosis may be divided histologically into two main patterns, **localized (focal or segmental)** and **diffuse multifocal**. **Focal** and **segmental chorangiomatosis** involve focal areas of contiguous villi, with segmental chorangiomatosis involving greater than five villi and focal chorangiomatosis involving five or less. Microscopically, small-clustered groups of *stem villi or immature stem villi show increased cellularity of the stroma as well as increased vessels*. Perivascular cells are present but are not easily identified on routine tissue stains. **Diffuse, multifocal chorangiomatosis** involves multiple independent areas of the placenta. Although it is not considered a gross lesion, occasionally it may be identified as multiple nodules within the villous parenchyma (Fig. 19.10). In this pattern, *there are multiple nodules of expanded chorionic villi, which contain numerous small capillaries* (Fig. 19.11). While localized chorangiomatosis is associated with prematurity, preeclampsia, and multiple gestation, diffuse multifocal chorangiomatosis is associated

Suggestions for Examination and Report
(Chorangiomatosis)

Gross Examination: If nodules are identified grossly, generous sampling of the villous tissue is recommended. Lesions may be difficult to identify on gross examination if small.

Comment: A comment on the clinical associations may be made, i.e., preeclampsia, prematurity and multiple births for localized chorangiomatosis and IUGR, extreme prematurity, preeclampsia, placentomegaly and congenital anomalies for diffuse multifocal chorangiomatosis.

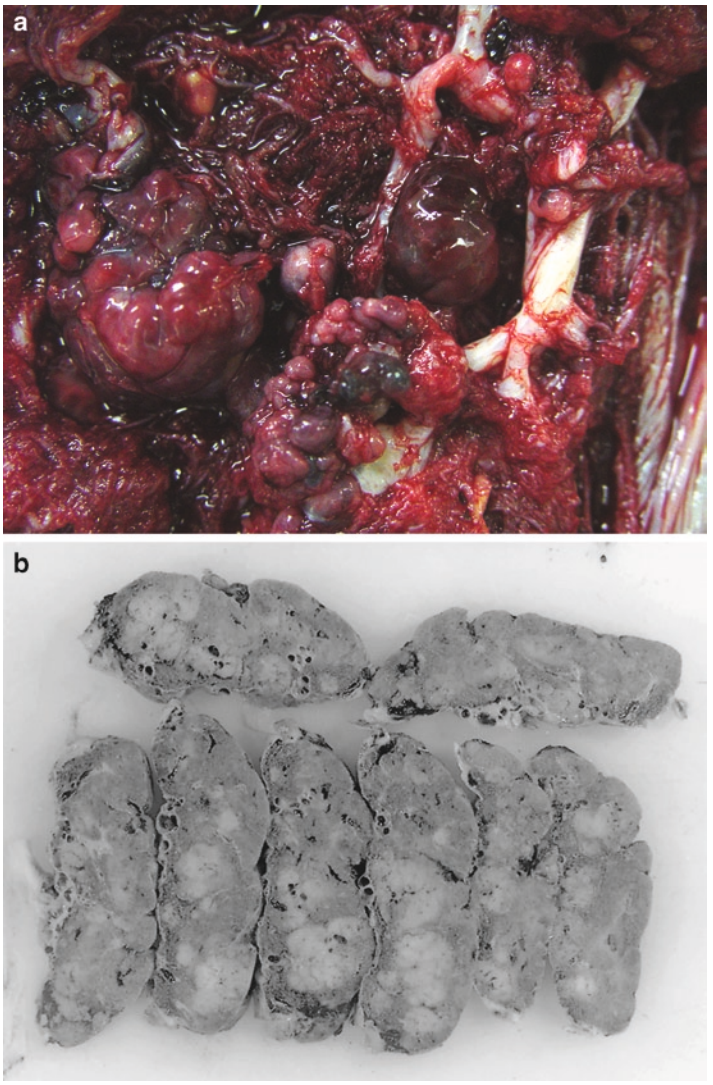

Figure 19.10. (**a**) Multifocal chorangiomatosis may be visible grossly as nodular areas in the placenta. (**b**) Cross sections of villous tissue may show nodular pale lesions as well.

with extreme prematurity, preeclampsia, intrauterine growth restriction (IUGR), placentomegaly, and congenital anomalies. It has been suggested that the diffuse multifocal form of chorangiomatosis may be a developmental abnormality of the villi.

Fibrinoid Deposition

Normal Perivillous Fibrinoid

Perivillous fibrin or fibrinoid deposition is a normal feature of term placentas. It likely develops secondary to damage of the syncytiotrophoblast with subsequent clotting in the intervillous space and closure

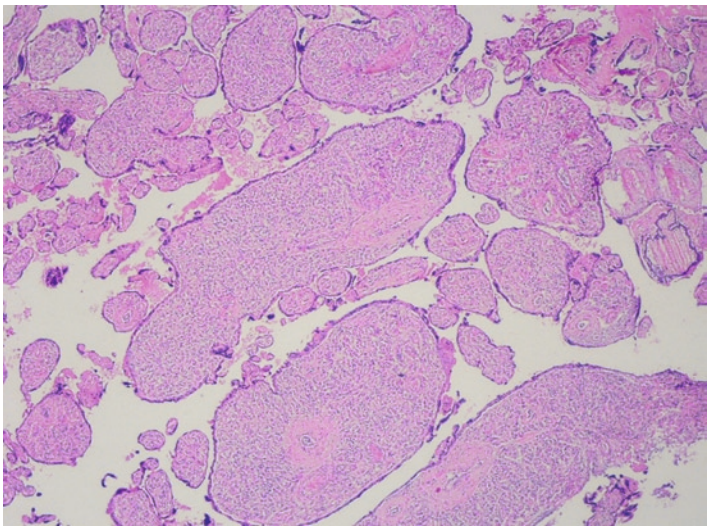

Figure 19.11. Diffuse, multifocal chorangiomatosis. Note the multiple, nodular foci of villi with increased capillaries. H&E ×100.

of the trophoblastic defect by a fibrinoid plug. It is particularly prominent in stem villi, whose trophoblastic surface is largely replaced by fibrinoid at term. One normally finds some increase in fibrinoid encasing larger groups of villi below the chorionic plate (*subchorionic laminated fibrin or fibrinoid*), and in the *marginal zone*. The amount of fibrinoid increases with advancing pregnancy. Although modest amounts are considered normal, a diffuse increase may be interpreted as reflecting *chronic intervillous perfusional problems* as it is seen in *preeclampsia and abnormal maternal coagulation*. If the perivillous fibrinoid is excessive, it is referred to as **maternal floor infarction** or **massive perivillous fibrin deposition** (see below). In foci of more significant fibrinoid deposition, *shiny, white irregular deposits* may be grossly visible in the villous tissue. Microscopically fibrinoid is *pink and lamellar in structure*. Perivillous fibrinoid either *fills gaps in the syncytiotrophoblastic cover of villi, or encases villi or small groups of villi* (Fig. 19.12). The syncytiotrophoblast of these villi is often degenerated and may be absent.

Maternal Floor Infarction and Massive Perivillous Fibrin Deposition

Pathogenesis

Maternal floor infarction (MFI) is a placental lesion with specific pathologic features and clinical associations. The incidence has been reported to be as high as one in 200 placentas, but that figure is much higher than is our experience. The cause is unknown but suggested etiologies have included *congenital infection, immune mediated rejection, and abnormal extravillous trophoblastic proliferation*. It appears to be a specific entity, in part because of its frequently recurrent nature. It may be related to an *abnormal host/placental interaction*, but the interaction may not necessarily be an immunological one. Some investigators have differentiated cases in which the maternal floor was primarily involved from those

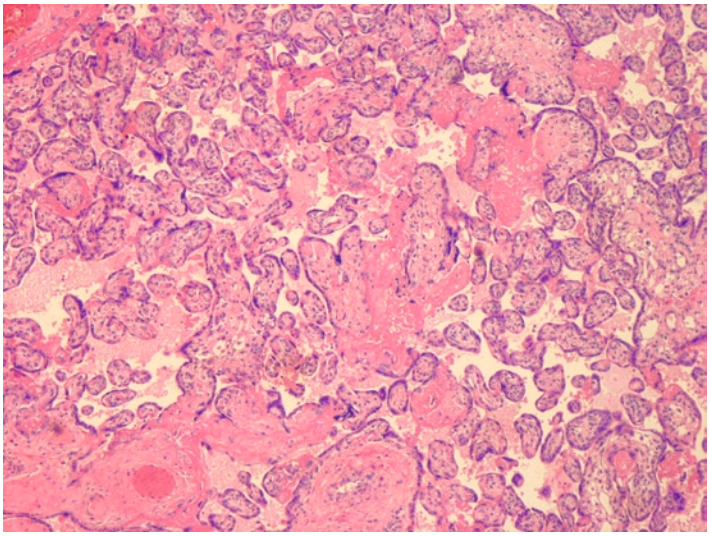

Figure 19.12. Mature placenta with typical amount of perivillous fibrinoid. H&E ×40.

with diffuse fibrinoid deposition; hence the designation of "**massive perivillous fibrin deposition**." At this time, there is no convincing evidence that these are two different entities. However, since in many cases, the fibrin deposition is not primarily in the maternal floor and the infarction of villous tissue that occurs is not primary but secondary, massive perivillous fibrin deposition may be a more appropriate term.

Pathologic Features

Excessive fibrinoid deposition is the main diagnostic feature of **MFI**. In this condition, the decidual floor is heavily infiltrated by fibrinoid, which also disseminates throughout the villous tissue. This infiltration is visible and even palpable on gross examination. The maternal surface loses its normal cotyledonary development and shows a corrugated appearance. The *floor of the placenta is thick, stiffened, and often yellow* (Fig. 19.13). On cut section, the villous tissue is diffusely penetrated with gray fibrinoid (Figs. 19.14 and 19.15), even though the process is not always completely expressed. Thus, in some placentas, the characteristic fibrinoid deposition does not involve the entire floor or portions of the villous tissue are inexplicably spared.

Microscopically, *fibrinoid encases villi in a net-like pattern* while intervening villi are normal. Initially the encased villi appear viable (Fig. 19.16). Over time, the syncytiotrophoblast degenerates and eventually disappears completely. A thickened trophoblastic basal lamina then surrounds the fibrotic villous stroma. In some cases, chronic villitis may be associated with the lesion. The fetal vessels sometimes remain intact, but ultimately become obliterated. The villi are literally strangled by the fibrinoid. Therefore, older lesions appear quite similar to true villous infarcts. However, the *diffuse pattern of fibrinoid infiltration, the lack of confluence of infarcted villi, and the fact that the process is*

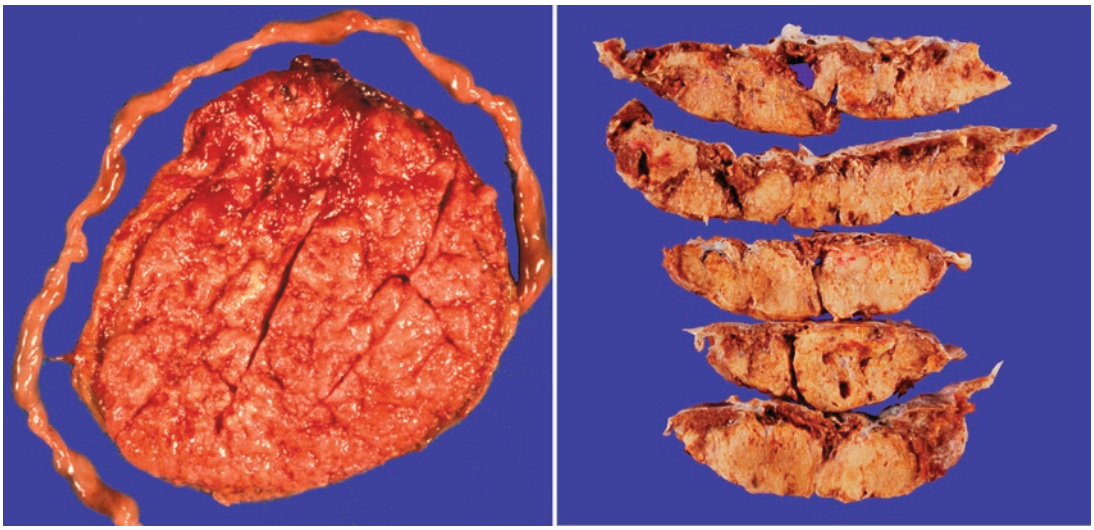

Figure 19.13. Maternal floor infarction. On the *left*, the maternal surface of the placenta shows loss of normal cotyledonary structure with yellow discoloration of the surface. On the *right*, cross sections of the placenta demonstrate the typical "net-like" deposition of fibrinoid material throughout the parenchyma.

Figure 19.14. Another placenta showing grossly identifiable fibrinoid deposition consistent with a maternal floor infarction.

often confined to the placental floor favors the diagnosis of maternal floor infarction (Fig. 19.17). In addition, in true infarcts, the villi are collapsed and only a thin layer of fibrinoid encases the villi. *Proliferation of extravillous trophoblast* is occasionally associated with this lesion, and in some cases the proliferation may be quite striking (Fig. 19.18). In most cases, extravillous trophoblastic cells are present in *strings or as single cells deep within the fibrinoid*.

Clinical Features and Implications

In maternal floor infarction, the excessive fibrinoid deposits reduce blood flow in the intervillous space, obstructing maternofetal exchange.

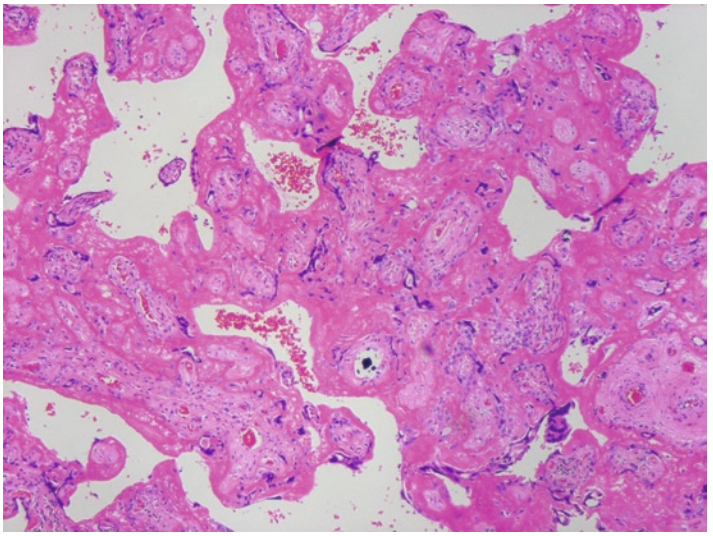

Figure 19.15. Maternal floor infarction with villi encased in fibrinoid material. Here, the villi are still viable and have begun to show only minimal degenerative change. H&E ×100.

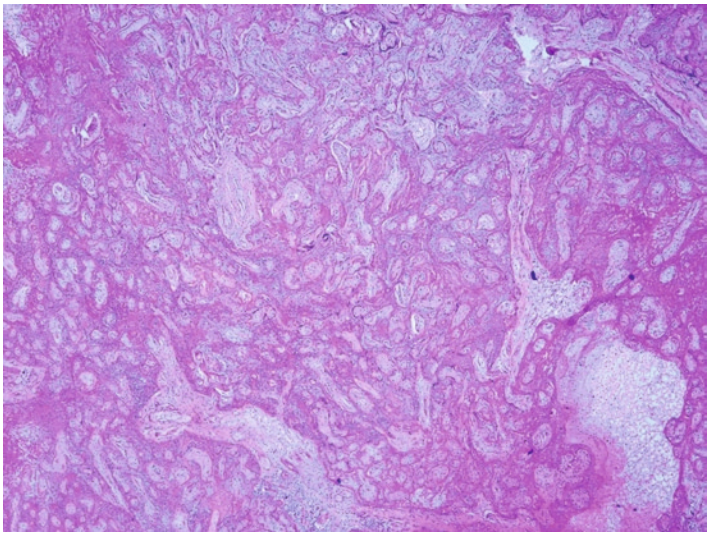

Figure 19.16. More advanced maternal floor infarction with almost complete infarction of villous tissue. The vague net-like pattern can still be appreciated and strands of fibrinoid are still present. H&E ×20.

If a large enough area is involved, fetal growth and survival may be endangered. Typically, the pregnant patient who develops maternal floor infarction is clinically normal and drop-off of fetal growth or decreased fetal movements in the late second or third trimesters is the only indication of problems. Some reports have shown an association with MFI and *maternal thrombophilias.* Oligohydramnios may be associated with the

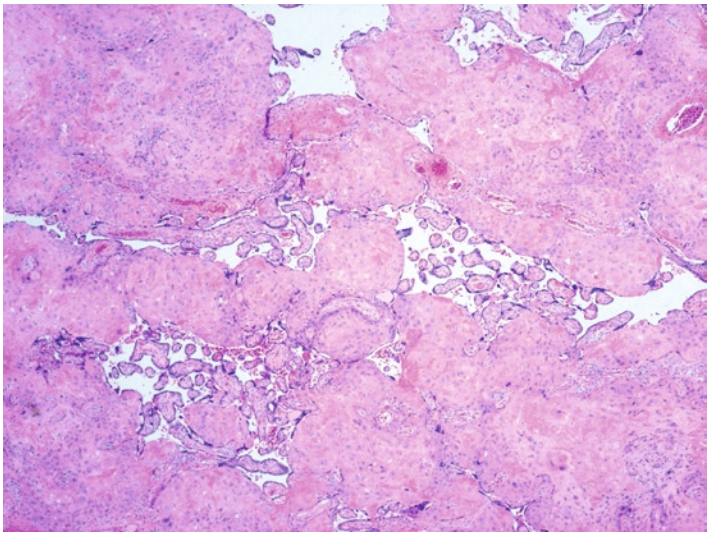

Figure 19.17. Maternal floor infarction with excessive fibrinoid associated with a more prominent proliferation of extravillous trophoblast. H&E ×20.

lesion, particularly when growth restriction is present. MFI *strongly correlates with IUGR, intrauterine fetal demise (IUFD), and neurologic impairment*. *Microcephaly* has also been described. Importantly, the condition recurs frequently in subsequent pregnancies at rates of 30% or more. One patient had nine consecutive losses due to maternal floor infarction. With other patients in whom the lesion had previously occurred, the anticipation of its recurrence has led to intense fetal monitoring and improvement outcome. *Elevations in maternal serum alpha-fetoprotein*, likely due to disruption of the maternal–fetal interface, may be detected from the second trimester on. Major basic protein (MBP) levels in maternal serum are also significantly elevated in some patients with maternal floor infarction. Ultrasonographic criteria for the diagnosis of maternal floor infarction have been established and are useful in anticipating the disease.

Suggestions for Examination and Report
(Maternal floor infarction)

Gross Examination: Recognition and description of the gross pathologic features is essential. These include firmness and discoloration of the maternal surface and deposition of fibrinoid in the placental parenchyma. An estimate of the percentage of involvement of the placental tissue by fibrinoid is also important. Sections should be taken of any grossly "normal" tissue as well as additional section of abnormal tissue.

Comment: Maternal floor infarction has been associated with IUGR, IUFD and poor neurologic outcome as well as recurrence in subsequent pregnancies.

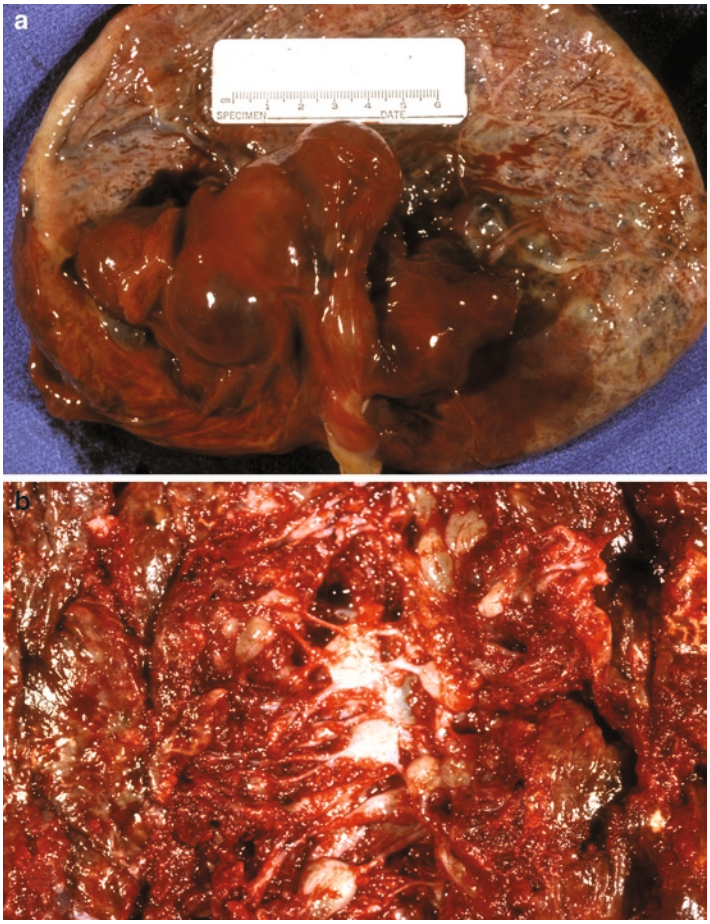

Figure 19.18. (**a**) Fetal surface of a placenta with mesenchymal dysplasia demonstrating large, dilated and tortuous vessels surrounded by gelatinous material and blood. (**b**) Maternal surface of the same placenta with dilated chorionic villi similar to those seen in a partial mole. The remaining villous tissue appears grossly normal.

Placental Mesenchymal Dysplasia

Clinical Features and Implications

Mesenchymal dysplasia is a rare condition of unknown etiology with specific gross and microscopic placental abnormalities. Over 80 cases have been reported at present, and 20% of these have been associated with Beckwith–Wiedemann syndrome. Approximately half of the remaining cases have been associated with IUGR. Fetal or neonatal demise occurs in 43%. Mesenchymal dysplasia has also been associated with *preeclampsia, maternal hypertension, polyhydramnios, macrosomia, omphalocele, and kidney abnormalities*. In addition, some cases have reported *congenital hemangiomas, vascular hamartomas, and hepatic mesenchymal hamartomas* in the fetus in these cases. Most commonly, the fetus has a 46, XX karyotype, and 82% of the cases that have been reported

are in female fetuses. Clinically, mesenchymal dysplasia may be misdiagnosed as a partial hydatidiform mole since it has a similar appearance on prenatal ultrasound examination. Imaging may also reveal large vascular areas with features consistent with both arterial and venous signals under the chorionic plate. There are also gross and microscopic features that may be confused with a partial mole as well (see below).

Pathogenesis

The pathogenesis of this disorder is unknown; however, there is much recent work on the possible etiology or etiologies. The thrombosis noted in many fetal vessels has led some authors to suggest the possibility of maternal thrombophilia as an etiologic factor, but this has not been well studied. Another theory is that chronic hypoxia develops due to fetal thrombotic vasculopathy and decreased gas exchange in the dysplastic villi. This is supported by the often-associated finding of chorangiosis and the association with IUGR. A few cases have shown genetic mosaicism in the placenta with a mixture of androgenetic cells and biparental cells in amnion, chorion, and mesenchyme but not in the trophoblast, and it is suggested that this leads to the abnormal develop of the mesenchymal tissue in the placenta. This is supported by the congenital hamartomas reported in some fetuses. These findings, the association with Beckwith–Wiedemann, and the female preponderance all suggest that imprinting may have an important role in the etiology.

Pathologic Features

Grossly, there is significant *placentomegaly* with an increase in both placental size and weight. This is usually true even in cases that are not associated with Beckwith–Wiedemann syndrome. Abnormalities of the umbilical cord have been seen in a number of cases including excessively long or twisted cords, single umbilical artery, and abnormal insertions. The *surface chorionic vessels are markedly dilated and somewhat tortuous, and gelatinous material may be visible around the vessels* (Fig. 19.19a). Thrombosis in these vessels is common, which can be visible on gross inspection. *Grossly enlarged and cystic villi* may also be visible (Fig. 19.19b). These changes are usually focal, with more grossly normal areas intervening, but may involve up to 80% of the placental parenchyma.

Histologically, the *stem villi are enlarged and contain loose connective tissue and cistern-like formations* (Fig. 19.20). Some stem villi may measure up to 1.5 cm in diameter. The enlargement and hydropic change of the villi is the basis for confusion with partial moles. However, there is no trophoblastic proliferation, and *the hydropic villi are well vascularized*. They may contain *cisterns*, but, unlike moles, there is often a concentration of vessels under the trophoblastic cover. *These smaller vessels tend to be abnormally small and thick walled* but may show *thrombosis or aneurysmal dilatation*. Occasionally, *some villi have a more fibromatous stroma with a myxoid core*. Overall, there appears to be an increase in the amount of villous stromal tissue leading some authors to suggest the term "placental mesenchymal hyperplasia" rather than dysplasia for this entity. The grossly normal areas usually show immature appearing

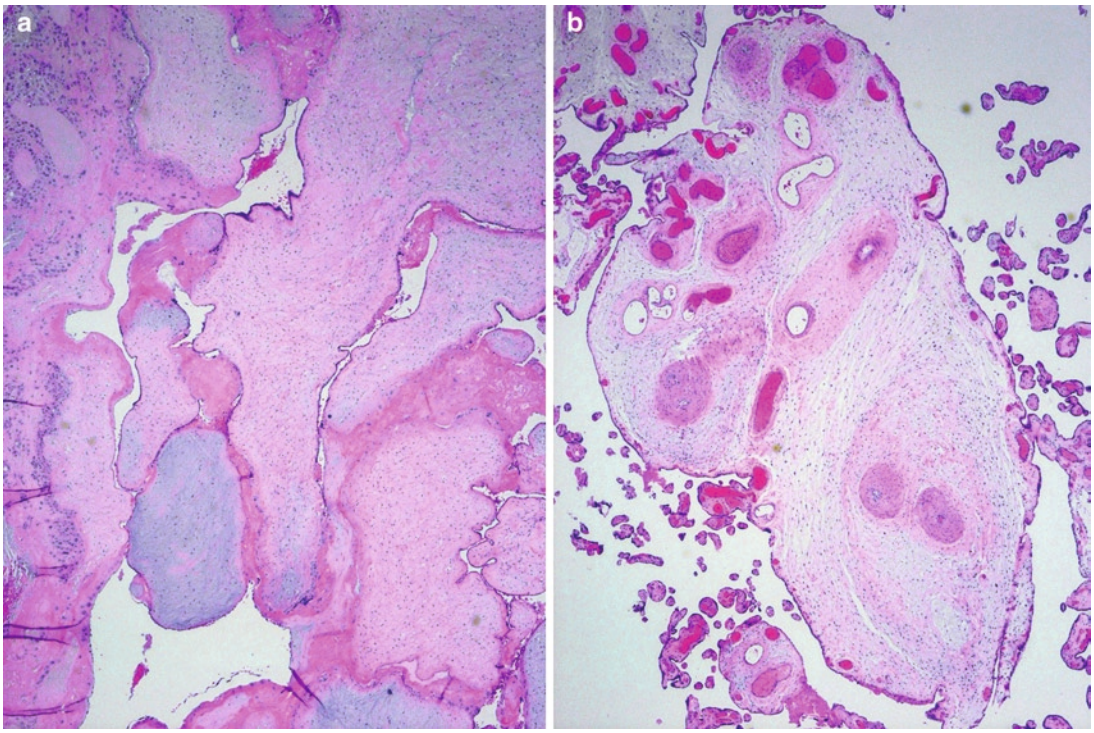

Figure 19.19. (**a**) Mesenchymal dysplasia showing dilated and hydropic villi underneath the chorionic plate. In contrast to moles, there is no trophoblastic proliferation. Myxoid stroma is present in some villi. H&E ×20. (**b**) Mesenchymal dysplasia showing an enlarged villus with persistence of fetal vessels which appear thick walled and abnormal. Normal villi are seen in the vicinity. H&E ×20.

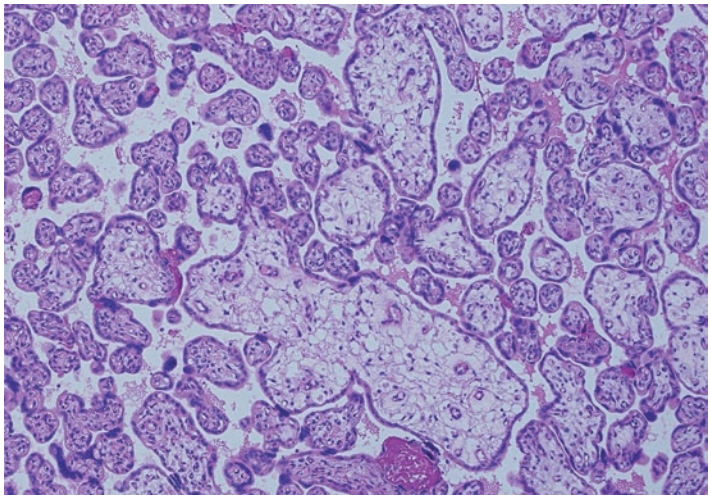

Figure 19.20. Villous immaturity or dysmaturity in a term placenta. The villi are larger than would be expected in a term placenta, with well-defined trophoblastic cover rather than the rarified trophoblast seen normally. In addition, the vessels are more centrally located and thus there are decreased vasculosyncytial membranes with a resultant decrease in diffusional capacity. H&E ×100.

villi, which are occasionally hydropic. *Villous chorangiosis* is also a relatively common finding in the remaining "normal" villi. These changes are less prominent in earlier gestations.

Suggestions for Examination and Report
(Mesenchymal dysplasia)

Gross Examination: Additional sections of the abnormal vessels and cystically dilated villi should be submitted with a full description of all the changes.

Comment: Mesenchymal dysplasia is a disorder of unknown etiology, which may be associated with fetal anomalies and adverse perinatal outcome. Correlation with clinical history, if given, is suggested.

Villous Edema and Villous Immaturity

Villous edema, when severe and diffuse, is associated with **fetal hydrops** and is often referred to as **placental hydrops**. The placenta is usually markedly enlarged and pale on gross examination, corresponding to severe, widespread edema of terminal villi. (Fetal hydrops is discussed in further detail in Chap. 20.) On occasion, focal severe villous edema is seen in term or near-term placentas not associated with fetal hydrops or severe fetal anemia. This is a relatively nonspecific finding and of unclear etiology. However, it has been seen with increased frequency in infants who develop neurologic impairment and cerebral palsy.

Villous immaturity, also called **distal villous immaturity** or **villous dysmaturity**, is an interesting maturation defect of the terminal villi. Microscopically, the terminal villi are *enlarged with increased numbers of capillaries, macrophages, and fluid within the villi*. They are often considered to have *increased vasculosyncytial membranes* and thus there is often a greater distance between the villous capillaries and the syncytiotrophoblastic basement membrane. This in turn is thought to decrease the efficiency or maternal–fetal exchange. This finding is most often associated with *maternal diabetes* (see Chap. 17) and has also been seen in infants with *Beckwith–Wiedemann syndrome*. Infants with this finding are at an increased risk of *IUFD*, but at this time this finding requires further study and characterization (Fig. 19.21).

Suggestions for Examination and Report
(Villous edema and villous immaturity)

Gross Examination: These lesions are not visible on gross examination.

Comment: Severe villous edema, when focal and not associated with hydrops, should be diagnosed but no comment is recommended. If villous immaturity is present in the setting of a fetal demise, then a comment about the association with this outcome can be made with the proviso that the etiology of this change is still unclear.

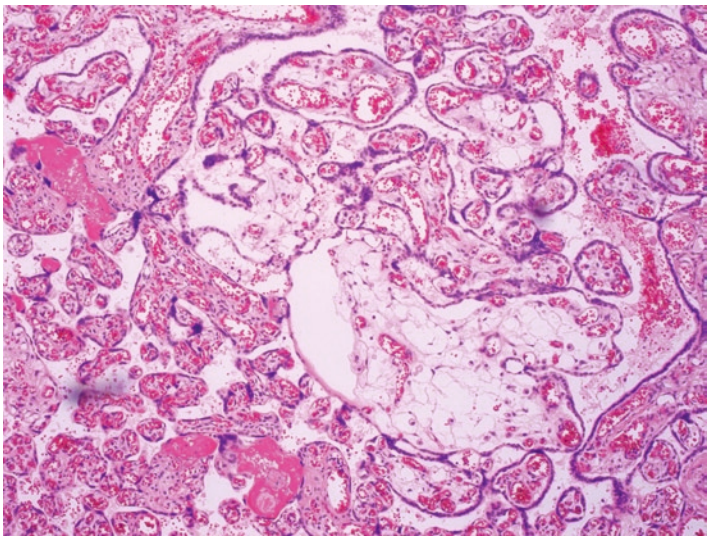

Figure 19.21. Focal villous edema. In contrast to Fig. 19.20, the changes are focal. A few villi in the central portion of the figure are larger and swollen with identifiable edema of the stroma. Fluid spaces are easily identifiable but peripherally located capillaries are still present.

Selected References

PHP5, pages 565–567 (Intervillous Thrombus), 480, 615–620 (Retroplacental Hematoma/Abruptio Placentae), 871–873 (Chorangiosis and Chorangiomatosis), 226–233 (Fibrinoid), 281–284 (Maternal Floor Infarction), 873 (Placental Mesenchymal Dysplasia).

Adams-Chapman I, Vaucher YE, Bejar RF, et al. Maternal floor infarction of the placenta. Association with central nervous system injury and adverse neurodevelopmental outcome. J Perinatol 2002;22:236–241.

Altshuler G. Chorangiosis: an important placental sign of neonatal morbidity and mortality. Arch Pathol Lab Med 1984;108:71–74.

Benirschke K, Gille J. Placental pathology and asphyxia. In: L Gluck (ed) Intrauterine asphyxia and the developing fetal brain. Chicago: Year Book Medical Publishers, 1977.

Fox H. Perivillous fibrin deposition in the human placenta. Am J Obstet Gynecol 1967;98:245–251.

Khong TY. Chorangioma with trophoblastic proliferation. Virchows Arch 2000;436:167–171.

Ogino S, Redline RW. Villous capillary lesions of the placenta: distinctions between chorangioma, chorangiomatosis and chorangiosis. Hum Pathol 2000;31:945–954.

Parveen Z, Tongson-Ignacio JE, Fraser CR, Killeen JL, Thompson KS. Placental mesenchymal dysplasia. Arch Pathol Lab Med 2007;131:131–137.

Pham T, Steele J, Stayboldt C, Chan L, Benirschke K. Placental mesenchymal dysplasia is associated with high rates of intrauterine growth restriction and fetal demise. Am J Clin Pathol 2006;126:67–78.

Reshetnikova OS, Burton GJ, Milovanov AP. Effects of hypobaric hypoxia on the fetoplacental unit: The morphometric diffusing capacity of the villous membrane at high altitude. Am J Obstet Gynecol 1994;171:1560–1565.
Vernof KK, Benirschke K, Kephart GM, et al. Maternal floor infarction: Relationship to X cells, major basic protein, and adverse perinatal outcome. Am J Obstet Gynecol 1992;167:1355–1963.