

Placenta

Normal anatomy

Placental Membranes:

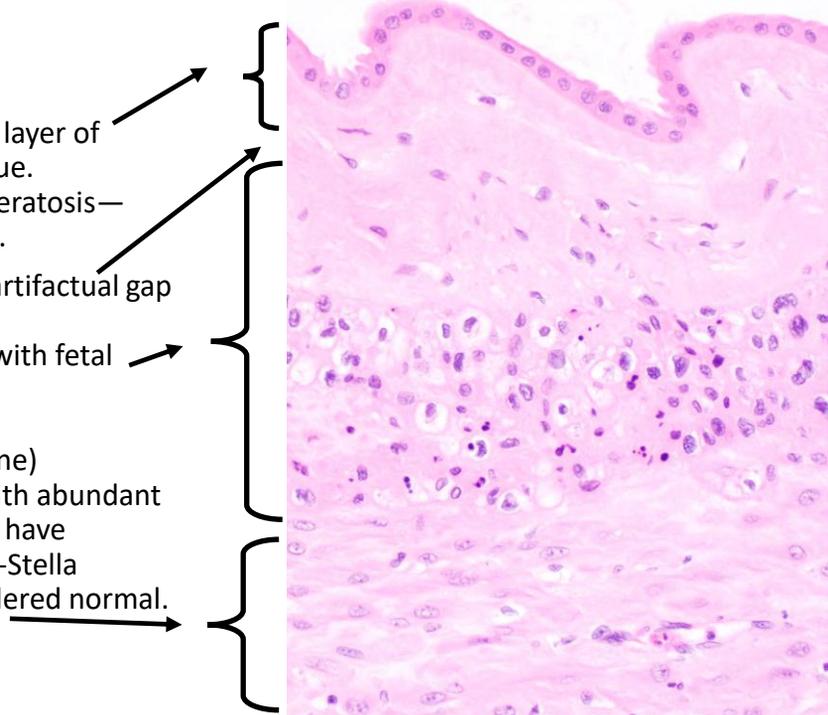
Amnion—innermost layer lined by a single layer of epithelium with underlying connective tissue.

Can see squamous metaplasia with hyperkeratosis—incidental finding associated with irritation.

Sometimes separated from chorion by an artifactual gap

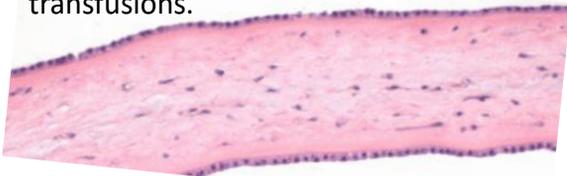
Chorion—Composed of connective tissue with fetal vasculature.

Decidua—Decidualized (due to progesterone) endometrial stroma with polygonal cells with abundant pink cytoplasm and large open nuclei. May have hypersecretory glandular epithelium (Arias-Stella reaction). Rare white blood cells are considered normal. Maternal blood vessels.

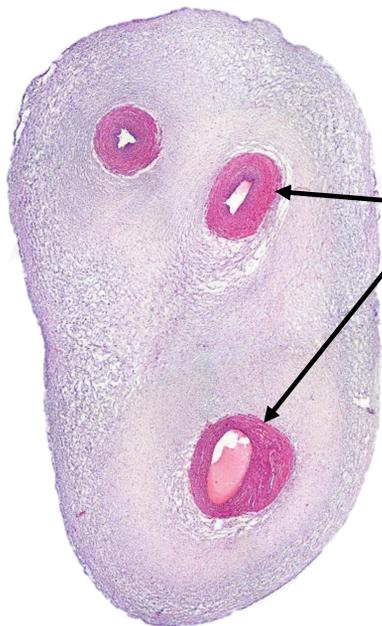
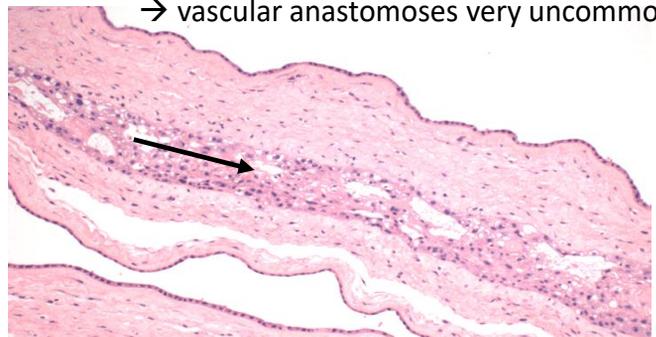


Twin Intervening Placental Membranes:

Diamniotic, Monochorionic (DiMo) Placenta
 → No intervening chorionic layer. More common.
 → Shared vascularity in disk → possible twin-twin transfusions.



Diamniotic, Dichorionic (DiDi) Placenta
 → Intervening chorionic layer. Less common.
 → vascular anastomoses very uncommon



Umbilical Cord:

Covered by amniotic membrane. Underlying Wharton's jelly.

2 Umbilical arteries → carry deoxygenated blood from fetus to placenta

1 Umbilical vein → often larger → carries oxygenated blood from placenta to fetus

May see:

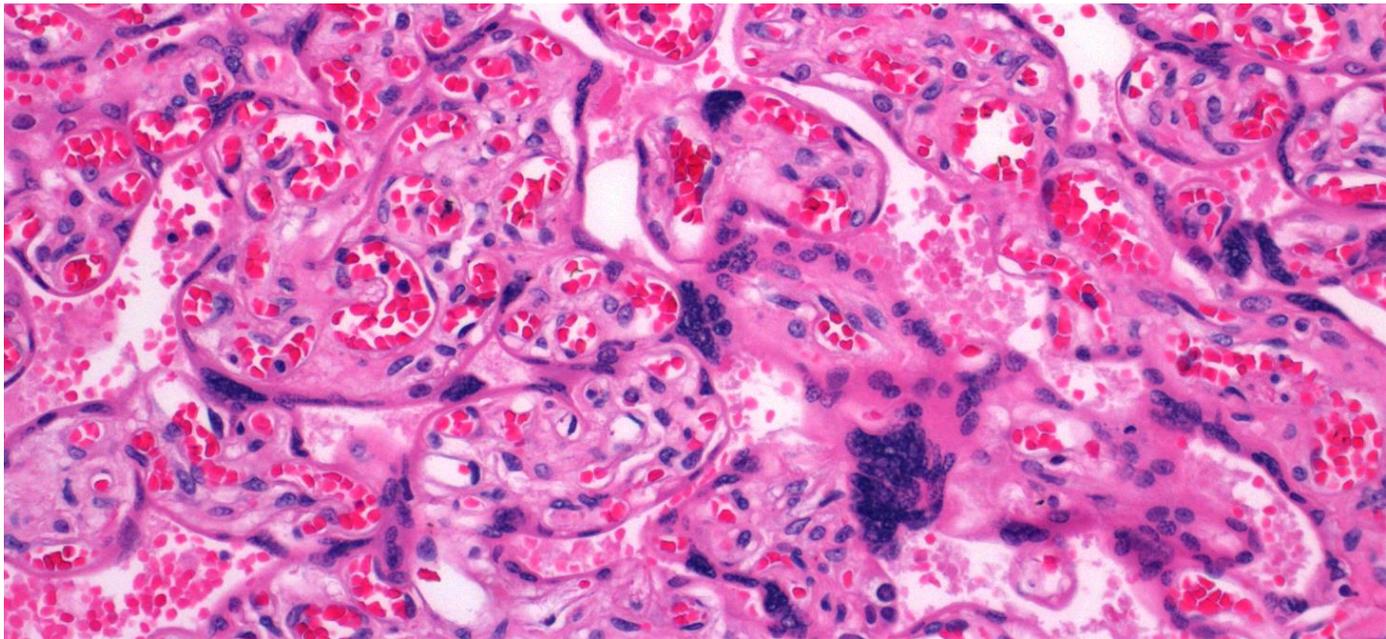
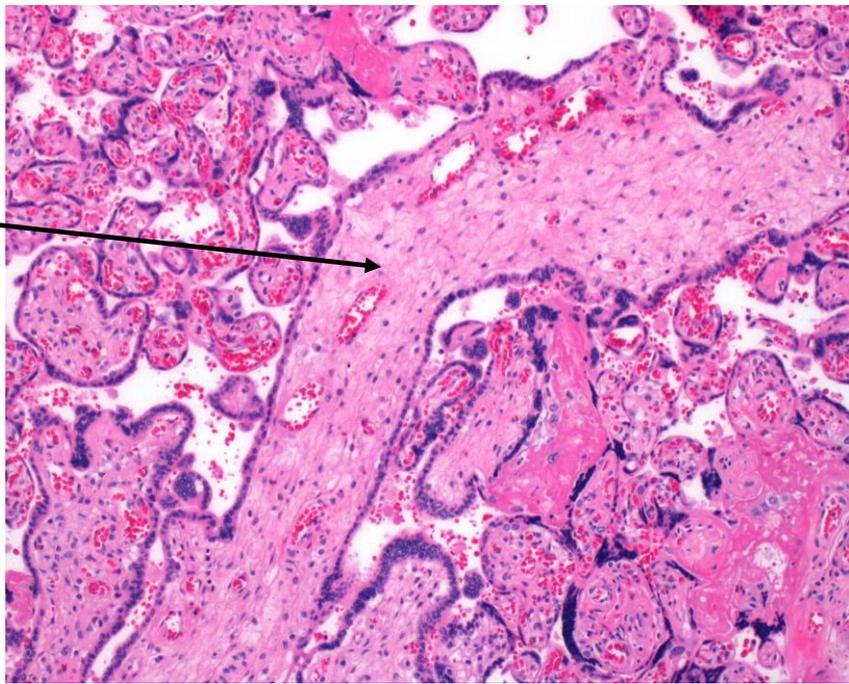
Persistent omphalomesenteric (vitelline) duct (derived from yolk sac)—small tubular structure lined by mucin-secreting epithelium.

Persistent allantoic duct (derived from allantois, attaches to urachus)—small tube with epithelium resembling urothelium located between arteries.

Placental Disk:

Stem Villi—transport blood from chorionic vessels to smaller villi. Trophoblastic covering collagenous stroma and large fetal vessels.
→ Hierarchical branching to smaller villi to allow nutrient/waste exchange

Terminal Villi—appearance (“maturity”) changes dramatically with gestational age to facilitate more O₂ exchange (see later discussion). Covered by syncytiotrophoblasts and cytotrophoblasts.
Later gestational age placentas show more peripheral vasculature.



Normal Disk Findings in Term Placentas:

- Scattered coarse calcifications within or adjacent to villi (Abnormal if very dramatic or in premature birth)
- Small infarcts (Abnormal in premature births or if >3cm)
- Moderate amounts of perivillous fibrin (< 25% is ok)
- Fresh retroplacental blood clot that is easily detached and does not associated with infarct or placenta compression.

The Stanford Placenta Helper

Pro Tip: Use the easy Stanford Placenta Helper Plus to calculate expected weight for gestational age and populate your reports!

<https://pathologists.stanford.edu/ap/placenta/>

Amniotic Fluid Infection Sequence

Usually results from **ascending infection** after premature rupture of membranes (before labor).

Common pathogens: *Ureaplasma*, *Fusobacterium*, *Bacteriodes*, Mixed Gram-positive anaerobes, *E. coli*, *Group B streptococcus*, *S. pneumoniae*.

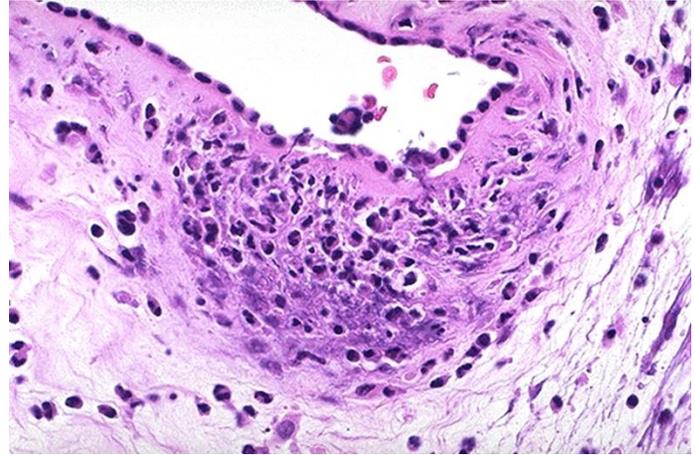
Amniotic fluid infection associated with extreme preterm delivery in mid-gestation raises concern for cervical incompetence

Chorioamnionitis

Acute inflammation in the chorion or chorioamnion.

Maternal response to infection.
Usually occurs before fetal response.

Scattered neutrophils are a non-specific finding in the decidua. However, a dense infiltrate of neutrophils in the decidua = subchorionitis (the earliest stage of maternal inflammatory response)



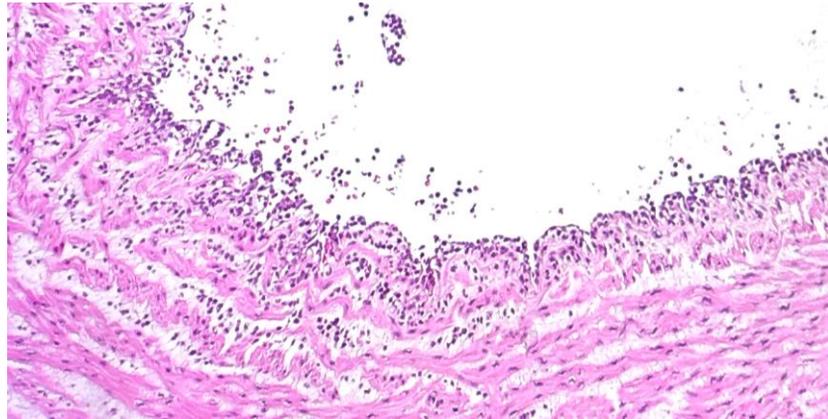
Funisitis

Acute inflammation of the umbilical cord and umbilical vessels.

Fetal response to infection.

Inflammation on surface is associated with candida infection → get PASd .

Can see toxoplasmosis organisms in Wharton's jelly.



Staging and Grading of the Maternal and Fetal Inflammatory Responses in Ascending Intrauterine Infection

Maternal Inflammatory Response

Stage 1—acute subchorionitis or chorionitis
Stage 2—acute chorioamnionitis: polymorphonuclear leukocytes extend into fibrous chorion and/or amnion
Stage 3—necrotizing chorioamnionitis: karyorrhexis of polymorphonuclear leukocytes, amniocyte necrosis, and/or amnion basement membrane hypereosinophilia

Grade 1—not severe as defined
Grade 2—severe: confluent polymorphonuclear leukocytes or with subchorionic microabscesses

Fetal Inflammatory Response

Stage 1—chorionic vasculitis or umbilical phlebitis
Stage 2—involvement of the umbilical vein and one or more umbilical arteries
Stage 3—necrotizing funisitis

Grade 1—not severe as defined
Grade 2—severe: near-confluent intramural polymorphonuclear leukocytes with attenuation of vascular smooth muscle

Uteroplacental Underperfusion

Also called "Maternal Vascular Malperfusion"

Changes associated with **chronic suboptimal uterine-to-placental blood flow**.

Caused by maternal conditions including preeclampsia, hypertension, diabetes, autoimmune disease (e.g., systemic lupus erythematosus and antiphospholipid syndrome), abnormal uterine anatomy, etc...

Gross findings: small placenta, infarction, retroplacental hemorrhage.

Often associated with fetal growth restriction and preterm labor. Can recur in subsequent pregnancies.

Villous Maturity

Increased villous maturation ("hypermaturation" or "accelerated villous maturation") is seen with chronic placental ischemia.

Evaluate closer to maternal surface.

Immature Terminal Villi (less good at O₂ exchange)
Larger, cellular, edematous. Central capillaries.
Evenly distributed trophoblast covering.

Mature Terminal Villi (Better at O₂ exchange)
Smaller, less cellular. Peripheral fetal capillaries.
Condensed syncytiotrophoblasts covering with prominent syncytial knots

Maturity Timeline:

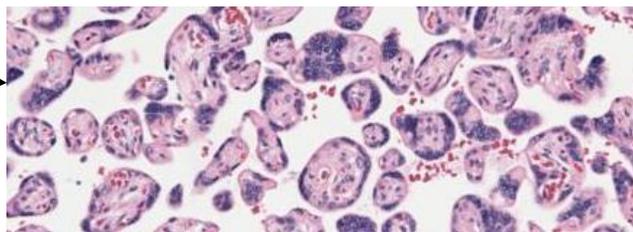
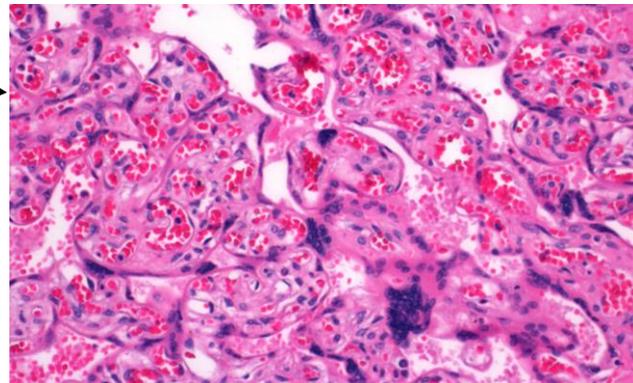
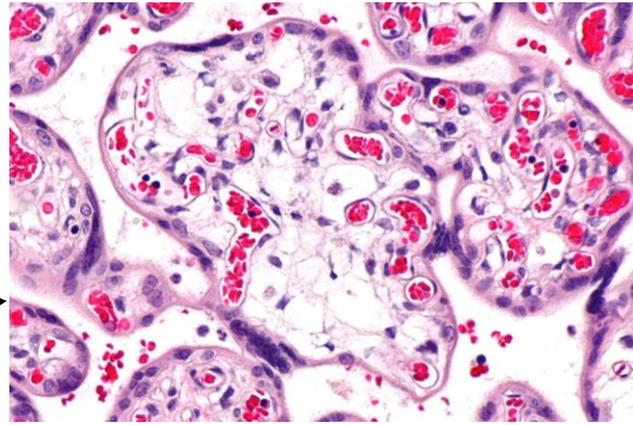
20-25 wks → 25% immature

26-32 wks → 10% immature

33-36 wks → 5% immature

≥ 37 wks → 1% immature

Syncytial knots on more than 1/3 of villi in term placenta = increased



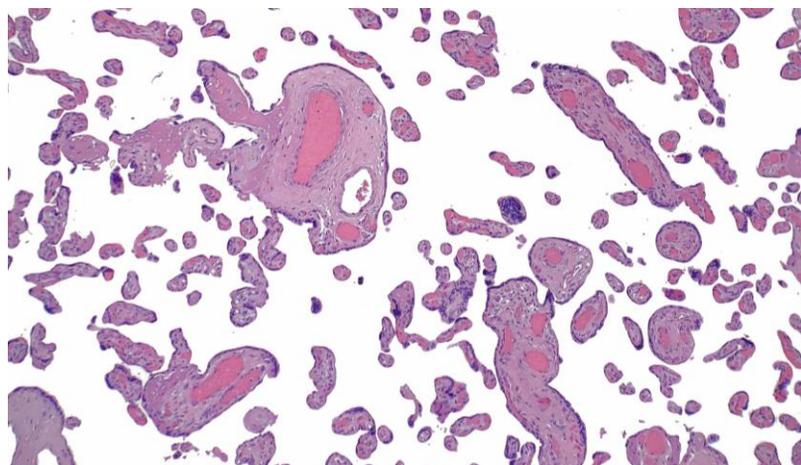
Distal Villous Hypoplasia

Paucity of terminal villi in relation to the number of stem villi.

Villi are pencil-shaped (long and thin).
Increased syncytial knots.

More commonly seen with underperfusion early in pregnancy.

Evaluate lower in placental disk toward maternal surface.



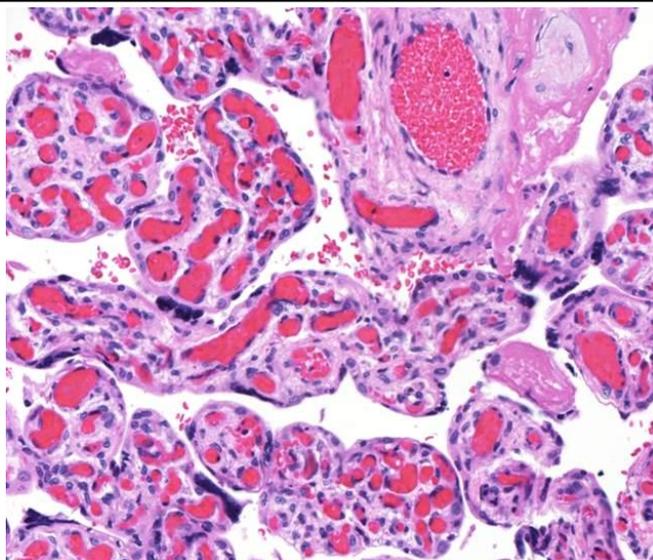
Chorangiosis

Fetal capillary proliferation defined by “rule of 10’s”

More than 10 capillary cross sections present in more than 10 contiguous villi, in at least four placental regions.

Localized response to hypoxia → Due to low oxygen tension in maternal blood.

See with high-altitude, diabetes, and pre-eclampsia.



Infarcts

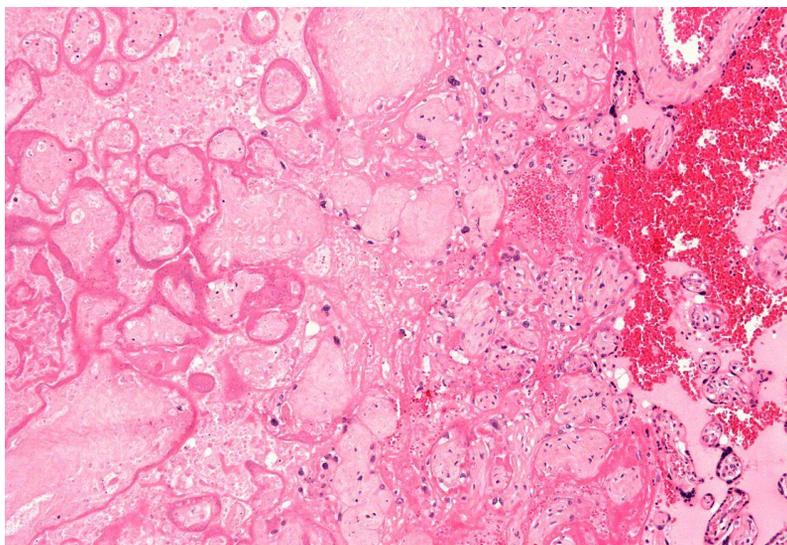
Estimate % size grossly

Early infarcts:

Crowded and congested villi (collapse of intervillous space from localized cessation of maternal blood flow), which may be hemorrhagic, with early loss of nuclear staining.

Remote infarcts:

Ischemic necrosis with pyknosis and karyorrhexis, loss of nuclear staining, and eventually ghost villi.



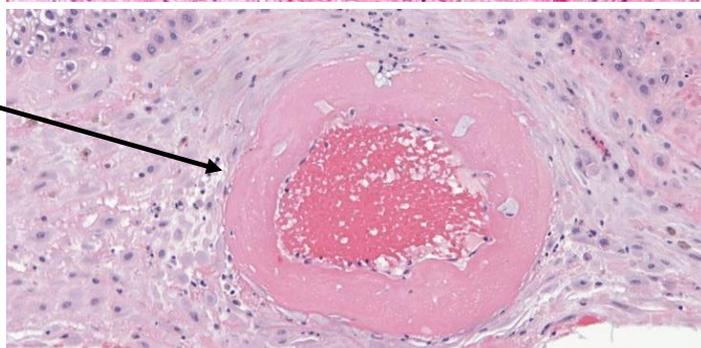
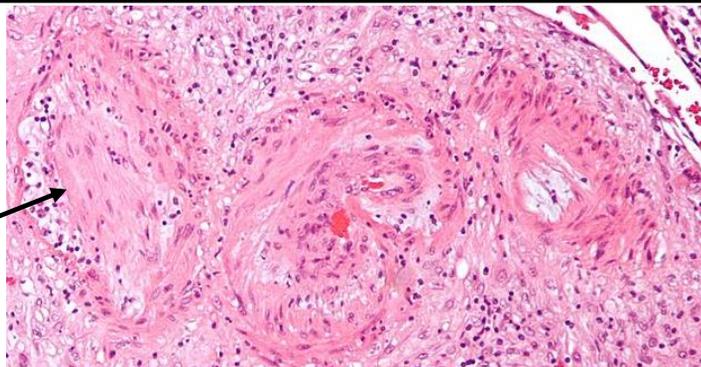
Decidual Arteriopathy

Occurs with failed normal conversion of maternal spiral arterioles into amuscular low-resistance vessels.

Mild decidual arteriopathy → retention of smooth muscle in arterial walls

Severe decidual arteriopathy → fibrinoid necrosis of spiral arterioles (deposition of eosinophilic material in wall). Can be associated foamy macrophages (atherosis) and lymphocytes.

Associated with maternal hypertension, autoimmune diseases, and pre-eclampsia.



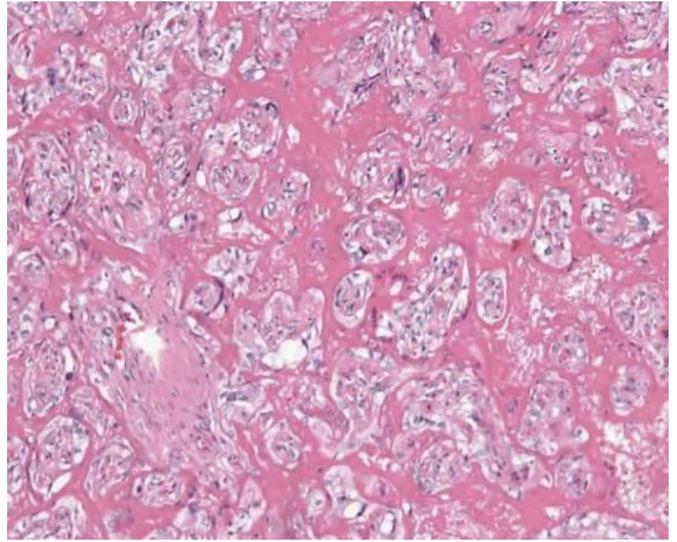
Perivillous Fibrin

Deposition of fibrin between villi

(Homogeneous pink material with intact villous nuclear basophilia, as opposed to in an infarct where everything is homogenously pink with coagulative necrosis)

Normal finding in term placenta if < 25% of volume. Can be intervillous or nodular.

If >25% = “Massive perivillous fibrin” deposition
→ potentially compromises fetal perfusion
→ associated with worse outcomes



Maternal Floor Infarct

Grossly visible white rind on maternal surface → extensive fibrin deposition in the decidua/intervillous space. Similar to “Massive perivillous fibrin” deposition, associated with worse outcomes.

Fetal Vascular Malperfusion

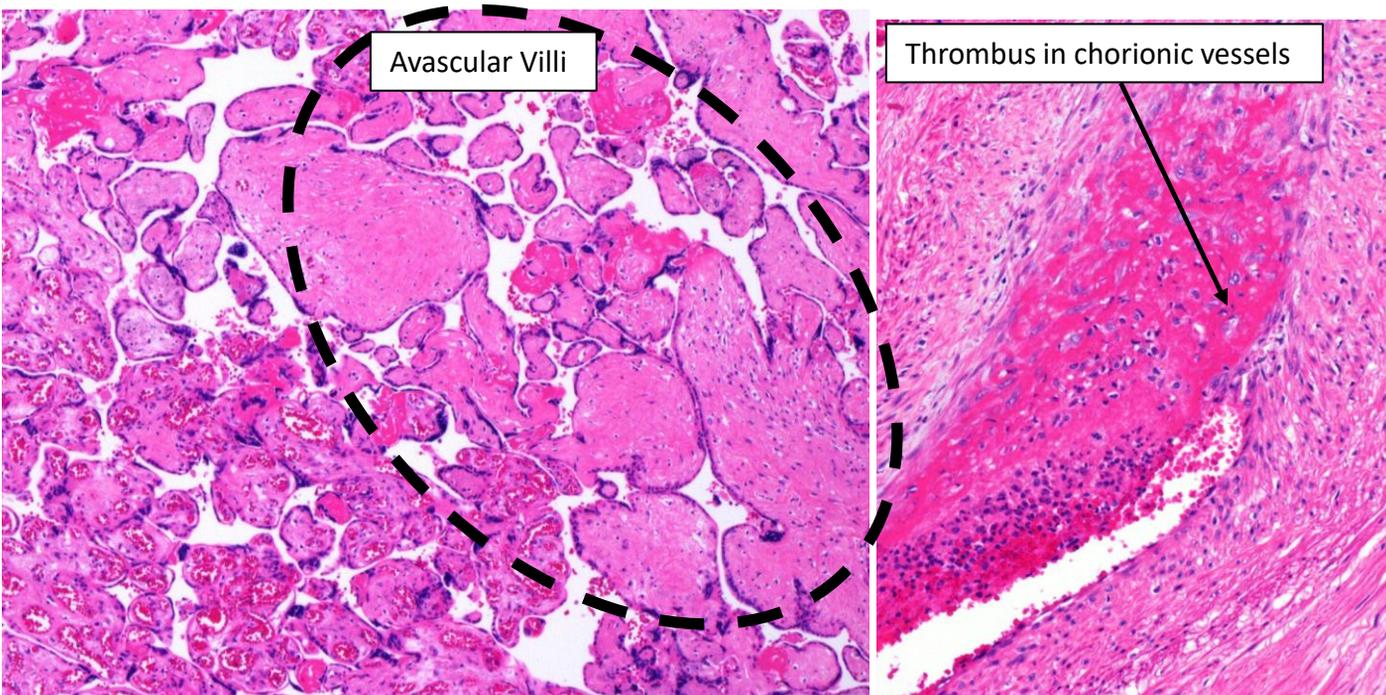
Old name: Fetal Thrombotic Vasculopathy

Seen secondary to obstruction of fetal blood flow. Can be antemortem or post-mortem process.

Common findings: **Thrombosis, avascular villi, vascular obliteration, and villous karyorrhexis.**

Antemortem changes are focal or multifocal—can result from umbilical cord lesions, hypercoagulability, maternal diabetes, and fetal cardiac dysfunction. Can result in IUGR.

Postmortem changes are **global**—diffuse loss of vascularity is seen with the passive involutional changes seen after fetal death.

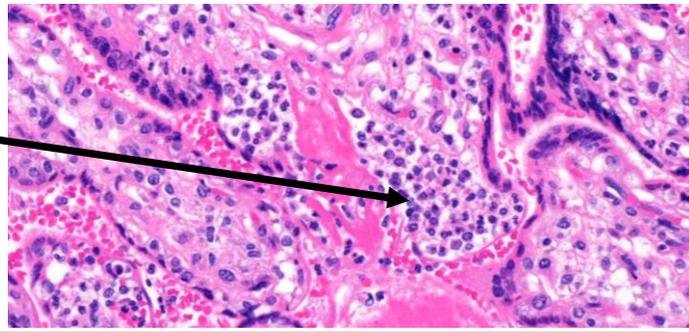


Villitis

Acute Villitis

Neutrophils in villi and intervillous space.
Can form microabscesses.
Strongly associated with maternal bacteremia.

Common pathogens: Listeria, Group B Strep., Syphilis.
Do Gram and Silver Stains!



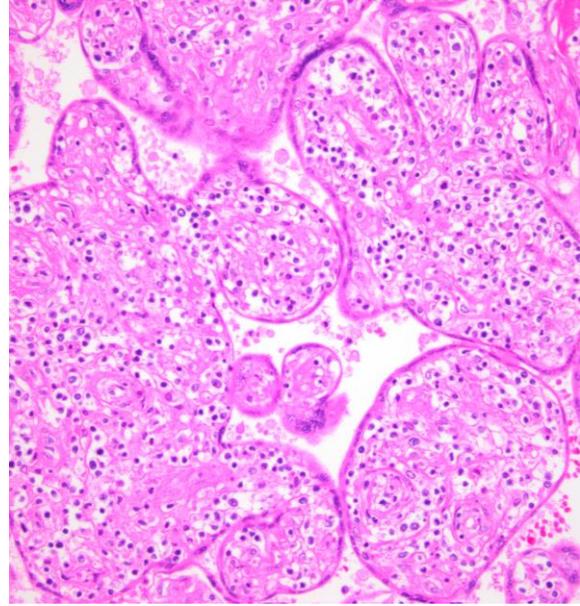
Chronic Villitis

Mostly histiocytes with scattered lymphocytes in villi.

90% due to an **abnormal immune** reaction of maternal T-lymphocytes to fetal antigens, termed "**villitis of unknown etiology**" (VUE). This can recur with subsequent pregnancies and lead to IUGR or even fetal demise if severe.

10% due to **TORCH infections** → most often CMV
→ **Get CMV, PAS, Gram, AFB and Syphilis stains!**

If lots of multinucleated giant cells → "Granulomatous villitis"
Despite name, true granulomas are often not present. Can be caused by infection or possibly very exuberant VUE.



Villous Edema

Chronic Villous Edema (Hydrops):

Villi are diffusely enlarged with clear, watery, hypocellular stroma.

Associated with fetal hydrops.

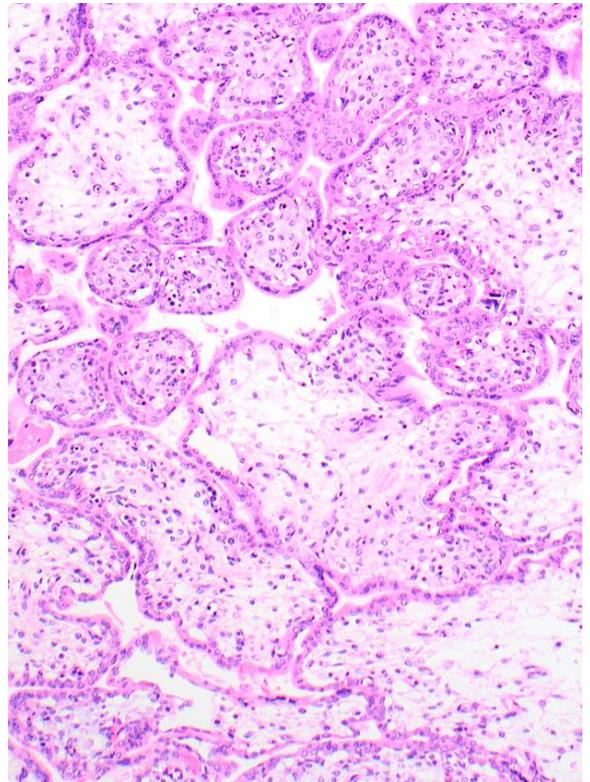
Common causes: Fetal cardiovascular disease, Fetal aneuploidy, Fetal thoracic anomalies, Severe fetal anemia, and complications from twinning.

Less common now: Immune-mediated hydrops from maternal antibodies destroying fetal RBCs (e.g., Rh-mediated).

Acute Villous Edema:

Patchy villi with round loculations of watery fluid.

Commonly accompanies chorioamnionitis, but can be seen in many settings.



Other Findings

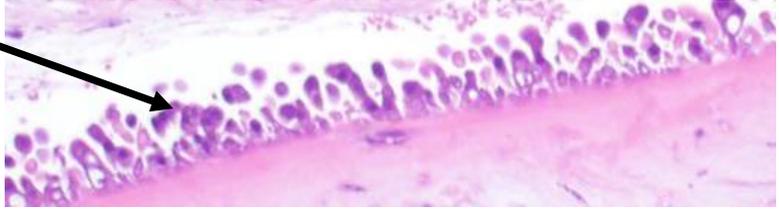
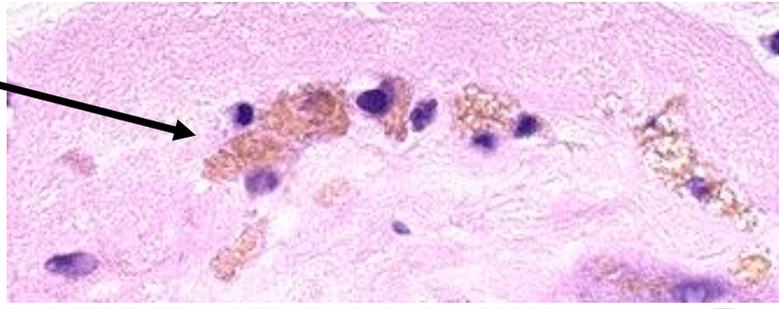
Meconium

Orange-brown non-refractile pigment in macrophages → derived from first infant stool if voided in utero

- potential sign of fetal distress → can cause meconium aspiration syndrome.
- Can cause chorionic vascular necrosis

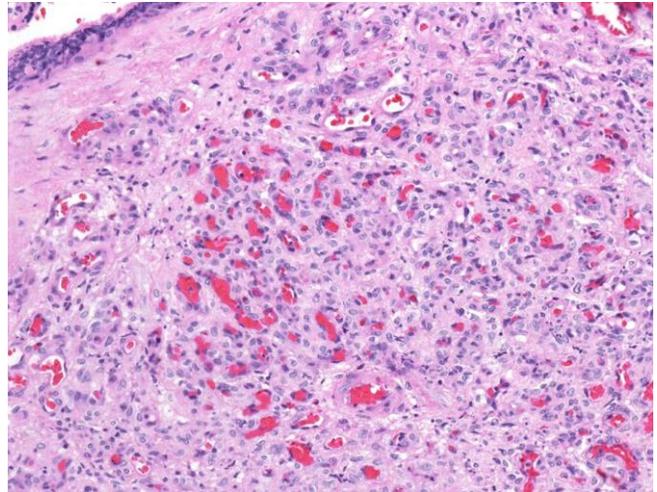
Often associated with **reactive and/or necrotic amnion** and/or bluish myxoid amniotic-chorionic cleft (helpful hints to look for meconium!)

Often best to correlate with clinical findings and gross findings as other pigments (e.g., hemosiderin) can be present.



Chorangioma

Relatively common. Benign placental "tumors."
Well-circumscribed expansile nodule of capillary proliferation with a continuous layer of pericytes within a stem villus.
Can be grossly visible.
Display similar profiles as infantile hemangiomas with staining for GLUT-1.
Large lesions >4 cm can cause fetal morbidity such as thrombocytopenia and shunting.
Associated with fetal hemangiomas and twins.



Placenta Creta

Decidua is deficient or absent, at least focally.
Villi come into direct contact with myometrium.

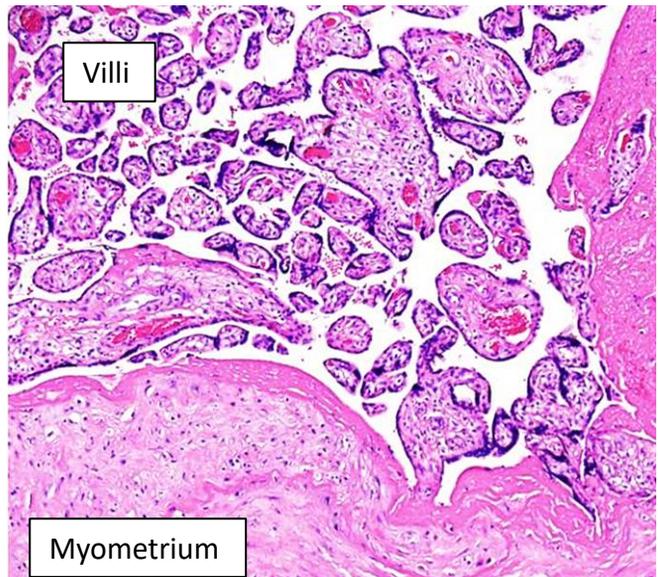
Placenta accreta → villi touch myometrial surface directly

Placenta increta → villi invade into myometrium

Placenta percreta → villi invade completely through uterine wall to peritoneum or other structures.

Increta and percreta may in part be due uterine anomalies like scarring or thin myometrium

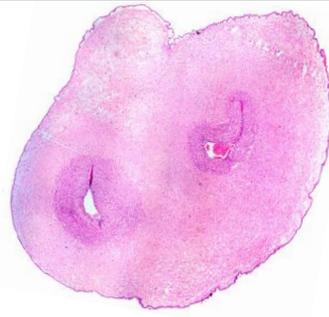
Trophoblasts stain with CK IHC, so if you're unclear if villi are really touching the muscle (vs decidualized stromal cells), IHC can help!



Single Umbilical Artery

Frequently seen in the context of ***other anomalies***, often urinary tract/kidney and heart anomalies.

Increased risk of stillbirth and death.

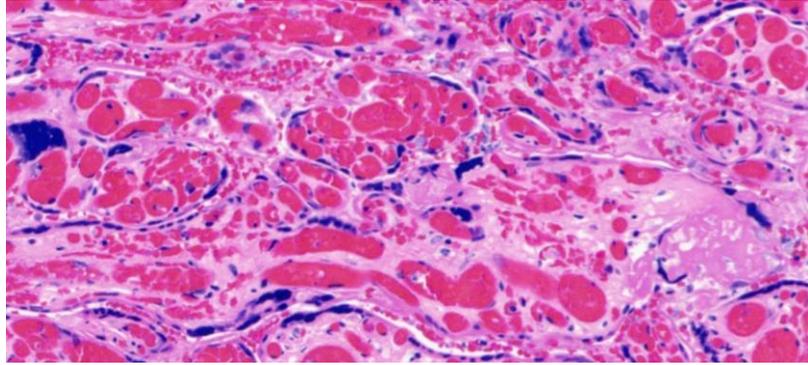


Fetal Capillary Rupture

AKA "***Intravillous hemorrhage***"

Hemorrhage into interstitium of villi.
(look like "bags of blood")

Results from **placental trauma** (e.g., manual extraction, cesarean section, acute abruption, etc...)

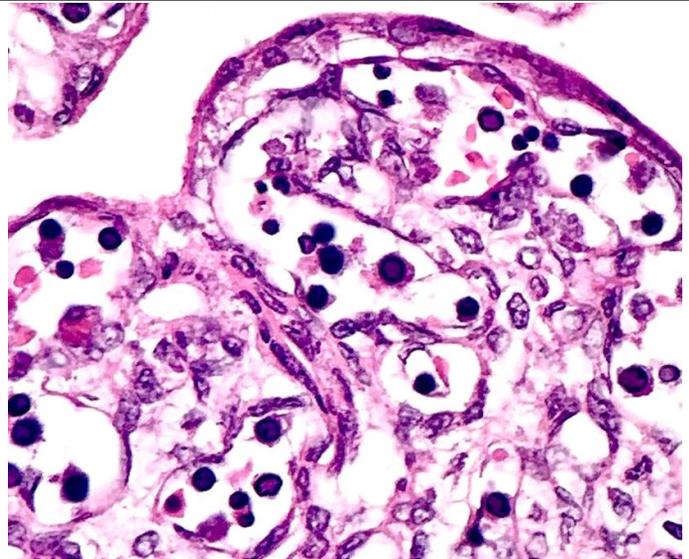
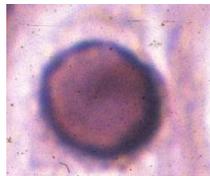


Parvovirus Infection

Characteristic violet, glassy intranuclear inclusions in erythroblasts.

Infects nucleated RBCs → causes hemolysis and transient erythroid aplasia → fetus often die from **anemia or hydrops**

Often placental hydrops. No inflammatory response.



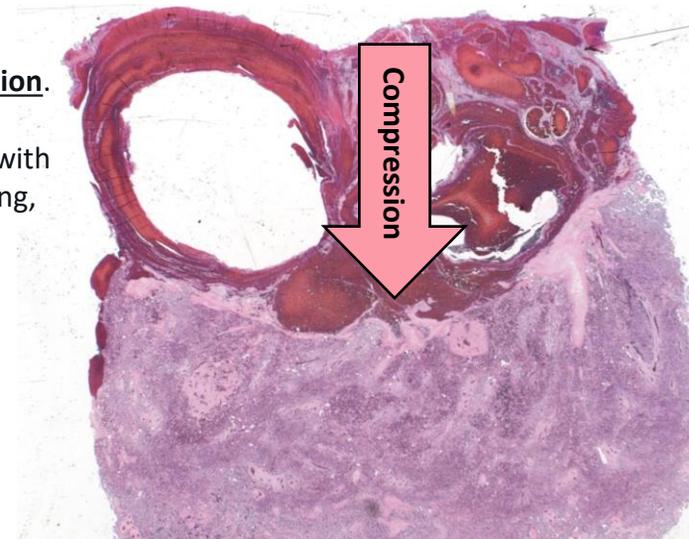
Retroplacental Hemorrhage

Pathologic term for clinical entity of **placental abruption**.

Blood accumulation beneath/dissecting the decidua with **compression of the overlying villi**, with villous crowding, congestion, and/or intravillous hemorrhage.

→ Can see associated infarction.

→ After a few days see hemosiderin deposition



A Quick Microscopic Approach

Adapted from: *Diagnostic Gynecologic and Obstetric Pathology*.
Crum, Nucci, and Lee. 2nd Edition 2011.

In each compartment, look for the common pathologic changes:

1. Evaluate Membrane Roll:

- **Inflammation** → Look for neutrophils in chorioamnion → Chorioamnionitis
- **Vascular changes** → Spiral arteries should have NO muscle and thin walls. If retained muscle layer → mild decidual arteriopathy. If fibrinoid necrosis → severe decidual arteriopathy.
- **Abruption** → Retromembranous hemorrhage in varying states of organization depending on age
- **Pigment** → Look for meconium (faint yellowish-orange-brown) in macrophages. A good clue to look for this is reactive-appearing amniotic cells.

2. Evaluate Cord:

- **Count number of vessels** → Should be 2 arteries and 1 vein.
- **Inflammation** → look for neutrophils in/around vessels → funisitis;
- **Thrombosis** → Look for vascular thrombosis (rare)

3. Evaluate Disk Surface:

- Look for the same surface **inflammation** and **pigments** you looked for in the membrane rolls
- **Vascular changes** → look at large surface fetal vessels for thrombosis. Myocyte necrosis can be seen with meconium.

4. Evaluate Stem Villi:

- **Thrombosis** → Look for vascular changes like thrombi or loss of vascularization
- **Microorganisms** → look for viral inclusions
- **Fetal blood** → increased neutrophils or nucleated RBCs could indicate fetal infection/stress

5. Evaluate Terminal Villi:

- **Look at maturity** → After 37 wks, almost all villi should be mature terminal villi (small, peripheral capillaries, prominent syncytial knots). If mature but preterm, could be “hypermaturation” as is seen with placental ischemia.
- **Chorangiosis** → >10 capillaries in >10 contiguous villi → due to hypoxia
- **Infarcts** → Coagulative necrosis with loss of basophilia
- **Acute villitis** → Neutrophils in villi and intervillous space → suggests maternal bacteremia → bug stains
- **Chronic villitis** → Histiocytes with some lymphocytes and plasma cells → associated with either TORCH infections (so get CMV and Syphilis stains) or immune-mediated Villitis of Unknown Etiology
- **Diffuse Stromal Edema** → look for clear, watery, hypocellular stroma → often caused by fetal hydrops
- **Avascular villi** → loss of capillary vessels with collagenization → due to interruption of fetal blood flow upstream. If multifocal → multifocal upstream thrombi → indicative of fetal thrombotic vasculopathy.
- **Fetal Capillary rupture** → *intravillous* hemorrhage → see with trauma (e.g., manual extraction)

6. Evaluate between Villi:

- **Collapse of intervillous space** → See with infarction of stem villi
- **Perivillous Fibrin** → normal as long as <25% intervillous space. Otherwise, “massive” perivillous fibrin → can compromise perfusion
- **Chronic histiocytic intervillitis** → large numbers of mononuclear cells within the maternal intervillous space → associated with miscarriage, IUGR, fetal death

7. Evaluate Maternal Surface:

- **Maternal floor infarct** → Grossly looks like a white rind → extensive fibrin in decidua
- **Decidual arteriopathy** (look for fibrinoid necrosis, same as in step 1)
- **Hemorrhage** → Large adherent clots with associated placental depression and ischemia suggest abruption
- **Villi on myometrium** → decidual deficiency like placenta creta