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Janice M. Lage, MD, FASCP
**Fetoplacental circulation**

- Two circulatory systems
  - Maternal: from spiral arteries in decidua, around villi, intervillous space, back via sinuses
  - Fetal: through umbilical cord, chorionic plate vessels on surface of placenta, down stem villi to secondary and tertiary villi, reverse to cord

**Mature Placenta-- Gross Anatomy**

- Placental disc (villi)
  - Fetal surface, chorionic plate, umbilical cord
  - Maternal surface, decidua
- Umbilical cord (2 arteries and 1 vein)
- Placental membranes: amnion, chorion, and decidua
Mature Placenta: Maternal and Fetal Surfaces

- Succenturiate lobe

Normal Umbilical Cord

- 45-55 cm normal
- 32/35-70 cm, range
- left:right spiral twist 4-7:1, 0.21 coils/cm
- Short, <30 cm, decr fetal motion, IUGR, incr perinatal mortality, neurologic abn, decr IQ, seizures
- Long cord, >70 cm, thrombosis and congestion, associated with hyperactivity syndromes
Umbilical Cord Insertion

- Normal, eccentric
- Marginal, battledore
- Membranous, velamentous-compression injury
  - Associated with multiple gestations, congenital syndromes (4x), diabetes mellitus (4x), adv maternal age (2x), smoking
  - Neurologic abnormalities (2x), hyperactive syndromes (2-3 x)
  - Catastrophic fetal blood loss with rupture, most frequent in ruptured vasa previa:
    - velamentous cord vessels overlying cervical os, trauma causes exanguination
Abnormalities of Umbilical Cord

- **False knot**
- **True knot**—1% of all deliveries, inconsequential
- **Occlusive true knot**
  - Cause of fetal death in utero due to thrombosis or hemorrhage
  - Indentation when untied
  - Edematous cord on placental side due to umbilical vein obstruction

True and False Cord Knots
Single umbilical artery

- Single umbilical artery—1% of deliveries
- Associated with renal anomalies and major congenital anomalies (2x)
- Stillbirth (4x)
- Intrauterine growth retardation, preterm delivery (2x)
Histopathologic Lesions of the Placenta

- Infections: maternal/fetal/both
- Structural lesions:
  - Hemorrhages/thrombi/abruptions
  - Infarcts
- Reactive changes:
  - Pigment: meconium, hemosiderin
  - Upstream occlusions/downstream effects (dam on a river)
- Chronic inflammatory lesions
- Chronic fibrinoid depositions
- Failure of the placenta to deliver

Cerebral Palsy in Term Infants: 159 medicolegal case reviews

- Clinical/sentinel events (20%)
- Severe, large fetoplacental vascular lesions (34%)
- Chronic placental dysfunction (22%)
- Subacute/chronic hypoxia (15%)
- Idiopathic (8%)


Placental lesions associated with neurologic impairment in >37 wks

- Severe fetal chorioamnionitis
  - Severe fetal chorionic vasculitis with:
    - Subintimal expansion
    - Dissolution of individual smooth muscle cells
- Extensive avascular villi
- Diffuse chorioamnionic hemosiderosis
  - Chronic peripheral separation
  - Macrophages with hemosiderin, 1-3 days (3-8 days in other tissues, Redline)

Redline, O’Riordan, Arch Path Lab Med 2000, 124:1785-1791

Severe fetal placental vascular lesions in term infants with neurologic impairment:

- Fetal thrombotic vasculopathy (avascular villi)
- Chronic obliterator villitis
- Severe fetal vasculitis
- Meconium-associated fetal vascular necrosis
- 51% of cases/10% controls
- 52% of cases had one/more lesion(s)

Infections of umbilical cord

- Acute funisitis, various vessels, associated with chorioamnionitis
- Long-standing acute funisitis calcifies and becomes necrotic
- Lymphoplasmacytic funisitis is associated with syphilis or herpes simplex infections
- Candidal funisitis
Circummarginate membrane insertion (extrachorial)

- 4% (3-25%) of placentas to some degree
- Major fetal malformations
- Decidual necrosis

Circumvallate membrane insertion (extrachorial)

- 6% (2-18%) of placentas to some degree
- Multiparity
- Early fluid loss
- Intrauterine growth retardation (IUGR)
- Pre-eclampsia
- Bleeding disorders during pregnancy – chorionic hemosiderosis
- Decidual necrosis

Amniotic band

- Slight fluid loss-- no sequelae
- Ongoing loss of much fluid-- amniotic bands form, webs of amniochorion entrap fetal parts ...amputation, malformation, deformations

Abnormalities of membranes

- Amnion nodosum
  - Severe oligohydramnios
    - Due to prolonged, premature rupture of membranes
    - Due to marked decreased urine production
  - Poor fetal lung development
  - Congenital absence of kidneys, ureters, urethra, obstruction, such as a posterior urethral valve
  - Ulceration of amnion, deposits of squames and vernix on denuded amnion
Amnion nodosum: severe oligohydramnios

Meconium
- Meconium release, acute, turns fetal membranes green initially, then cord:
  - Amnion, 1-3 hours
  - Chorion, 3-6 hours
  - Decidua, 3-6 hours
  - Cord and chorionic plate, > 6 hours
Abnormalities of membranes and chorionic plate

- Chronic meconium exposure
  - After 16 hours gets apoptosis of smooth muscle cells of cord—meconium associated vasonecrosis (really apoptosis)
  - Longer, membranes turn yellow
  - Eventually meconium disappears

Meconium-associated vascular necrosis

- Altshuler, 1989, necrosis of smooth muscle, vasoconstriction of cord vein
- Myocytes of chorionic blood vessels exposed to meconium exhibit apoptotic changes, like pyknotic nuclei in heart

Need picture of apoptotic smooth muscle chorionic plate
Placental Inflammations and Infections

- Two types of placental infections:
  - Ascending infection, most common type, bacterial, associated with or causes PROM
    - acute chorioamnionitis
    - maternal neutrophils in membranes
  - Hematogenous infection, bacterial or viral, including syphilis, listeriosis, toxoplasmosis, candida, rubella, CMV, HSV, parvovirus, mycoplasma,
    - villitis, acute or chronic

Chorioamnionitis

Chronic vasculitis: Fetal neutrophils and eosinophils headed for amnionic sac
<table>
<thead>
<tr>
<th>T-cell and eosinophilic chorionic vasculitis, Jacques et al. Ped Dev Pathol 2011;14:198-205</th>
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</thead>
<tbody>
<tr>
<td>CD3 + T cells and eosinophils</td>
</tr>
<tr>
<td>To intervillous space in 23.5%</td>
</tr>
<tr>
<td>To amniotic cavity in 15.7%</td>
</tr>
<tr>
<td>No specific direction in 60.8%</td>
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<td>Asso with villitis of unknown origin and avascular villi</td>
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**Chronic villitis**
- Lymphocytes, plasma cells and histiocytes in villi
- Maternal in origin
- May result in villous sclerosis or massive intervillositis

**Granulomatous villitis**
Parvovirus
Placental Parenchymal Lesions

- Infarcts
  - 5-15%, esp if central, associated with pre-eclampsia, diabetes, lupus erythematosis, uteroplacental insufficiency
  - Fetal complications: intrauterine growth retardation (IUGR), fetal distress, intrauterine fetal demise (IUFD)
Infarct and surrounding accelerated maturation

Placental Parenchymal Lesions

- Thrombi
  - Intervillous
    - Fetal and maternal blood, 6/1000 births
    - Associated with fetomaternal hemorrhage, isoimmunization, erythroblastosis, SLE, antiphospholipid antibodies, trauma, vigorous fetal movements; check Kleihauer-Betke
  - Retroplacental
  - Retromembranous

- Infarcts, aging
Maternal floor infarction

- Misnomer
- Extreme form of perivillous fibrin deposition
- Gross: white, firm, stiff placenta
- Diffuse involvement of maternal surface basal plate extending upward into overlying villi

Maternal floor infarction

- Gitterinfarkt, German literature--gridlike
- Fibrin obliterates normal space between villi (intervillous space) in which maternal blood percolates
- Area of involvement removed from the overall placental function: no exchange of nutrients, oxygen, waste products
Maternal floor infarction

Massive perivillous fibrin deposition

Massive perivillous fibrin
Villous vascular lesions

- Increased vascularity
  - Localized-chorangioma
  - Diffuse-chorangiosis, chorangiomatosis
  - Thrombi, intimal cushions
  - Muscularization of stem veins
  - Acute arteritis
- Obliteration of flow
  - Hemorrhagic endovasculitis
  - Fetal artery thrombosis-downstream
Chorangiosis

- Increased villous blood vessels
- >10 loops/10 villi/medium power field in 3 or more areas
- Often > 20 capillaries
- Large for gestational age, delayed villous maturation, diabetic
Fibrin thrombi and intimal fibrin cushion

Villous stem vessels
- Muscularization of stem vein walls
- Seen in reversed end diastolic blood flow doppler studies

Villous vascular lesions
- Acute arteritis
- Fetal artery thrombosis
- Avascular villi
- Fetal thrombotic vasculopathy

Fetal thrombotic vasculopathy (extensive avascular villi)
- Redline and Pappin, Hum Pathol 1995; 26:80-85
- Greater than 2.5% of total villi
- Foci in multiple sections
- Single lesion greater than 0.25 cm squared
- IUGR, monitoring abnormalities, oligohydramnios, and maternal coagulopathy
Hemorrhagic endovasculitis

- Thrombosis and recanalization of chorionic/villous stem vessels
- Increased perinatal morbidity and mortality
- Abnormalities of neonatal growth and development

Hemorrhagic endovasculitis—Associated clinical conditions in livebirth and stillbirth

- Chronic villitis of unknown etiology
- Chorionic vessel thrombi
- Increased fetal nucleated rbc’s
- Meconium staining
- Maternal hypertension

Villous adrenal cortical nodule
Placental abruption

- **Acute**
  - Due to inflamed decidual vessels, deciduitis and decidual necrosis, or hypertensive rupture
  - Trauma, acute chorioamnionitis, congenital anomalies, pre-eclampsia, smoking
  - Outcome: risk of stillbirth, preterm delivery, neonatal death
  - Life-threatening, generally quick in evolution

Acute placental abruption

- Chronic
  - Retroplacental or marginal sinus bleed
  - May be life-threatening, generally slow in evolution
  - Retroplacental hemorrhage indents placenta, hemosiderin laden macrophages, clot turns brown and stringy
Decidual vasculopathy

- Associated with pre-eclampsia, PIH, chronic hypertension, lupus erythematosus, less commonly, DM
- Acute vascular rejection of transplanted kidney
- Fibrinoid necrosis, foamy macrophages, lymphocytes
- Results in placental infarcts
Changes in maternal blood vessels with hypertensive disorders

- Normal spiral arteries
- Decidual medial hypertrophy

Abnormal placental adherence

- Placenta accreta-abnormal placental adherence, clinical and/or pathologic diagnoses, myometrium attached to maternal surface of placenta
- Placenta increta-often hysterectomy, villi within myometrium
- Placenta percreta-always hysterectomy, villi on uterine serosa

Placenta increta/percreta
Pregnancy and Placenta

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Come on people, one more hill and then we’re finished!
Life-Threatening Placental Lesions

- Abruptio placentae (extensive)
- Placental infarction (extensive)
- Knotted umbilical cord
- Umbilical vascular thrombosis
- Ruptured vasa previa
- Chorionic vascular thrombosis (extensive)
- Giant chorangioma
- Choriocarcinoma