PLACENTA – Part 1 – BIG 4
ASPEN 2014
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Maternal-Fetal-Placental Unit
Extra powerpoint posted covering Gross Placental Pathology

Acknowledge: Dr. Linda Ernst (Head of NMH Perinatal Pathology).

EXTENSIVE USE OF TEMPLATES.

General References:
GOALS

Review placental development.

Review pathologic criteria and clinical implications of amnionic infection syndrome.

Review pathologic criteria and clinical implications of maternal vascular underperfusion.

Review pathologic criteria and clinical implications of fetal vascular obstruction (fetal thrombotic vasculopathy).

Review pathologic criteria and clinical implications of chronic villitis.
PLACENTAL DEVELOPMENT
First differentiation event: morula to inner cell mass and outer trophectoderm.

From: Langman’s Medical Embryolgy 11th ed. TW Sadler
Early Placental Development – Day 7.5

**Figure 4.1** A 7.5-day human blastocyst, partially embedded in the endometrial stroma. The trophoblast consists of an inner layer with mononuclear cells, the cytotrophoblast, and an outer layer without distinct cell boundaries, the syncytiotrophoblast. The embryoblast is formed by the epiblast and hypoblast layers. The amniotic cavity appears as a small cleft.

From: Langman’s Medical Embryology 11th ed. TW Sadler
Early Placental Development – Day 9

**Figure 4.3** A 9-day human blastocyst. The syncytiotrophoblast shows a large number of lacunae. Flat cells form the exocoelomic membrane. The bilaminar disc consists of a layer of columnar epiblast cells and a layer of cuboidal hypoblast cells. The original surface defect is closed by a fibrin coagulum.

From: Langman’s Medical Embryology 11th ed. TW Sadler
Early Placental Development – Day 13

1 – Completely embedded in endometrial stroma.

2 - Lacunae open into maternal spiral arteries – sinusoids. Utero-placental circulation established.

3 – Extraembryonic mesoderm layer forms and lines the cytotrophoblast layer (to become chorion).

4 – Amnionblast (derived from epiblast) will form separate layer amnion later.

5 – Connecting stalk will become UC.

6 – Primary villi form.

7 – chorionic cavity forms.

Figure 4.6 A 13-day human blastocyst. Trophoblastic lacunae are present at the embryonic as well as the abembryonic pole, and the uteroplacental circulation has begun. Note the primary villi and the extraembryonic coelom or chorionic cavity. The secondary yolk sac is entirely lined with endoderm.

From: Langman’s Medical Embryolgy 11th ed. TW Sadler
VASCULOGENESIS OF THE PLACENTA (Beginning day 14)

New vessels formed from mesodermic mesenchyme.

Cytotrophoblast cells invade through syncytiotrophoblast and results in altered differentiation of extravillous trophoblast (EVT).

From: Langman’s Medical Embryolgy 11th ed. TW Sadler
Early Placental Development – Day 21

Figure 5.13 Presomite embryo and the trophoblast at the end of the third week. Tertiary and secondary stem villi give the trophoblast a characteristic radial appearance. Intervillus spaces, which are found throughout the trophoblast, are lined with syncytiun. Cytotrophoblastic cells surround the trophoblast entirely and are in direct contact with the endometrium. The embryo is suspended in the chorionic cavity by means of the connecting stalk.

From: Langman’s Medical Embryolgy 11th ed. TW Sadler
Archoring (primary) villi.

Branching to secondary and tertiary villi.

**Figure 7.8** Structure of villi at various stages of development. A. During the fourth week. The syncytiotrophoblast penetrates the stem villi in the direction of the decidua. B. During the fourth month. In many villi, the capillaries are in direct contact with the syncytiotrophoblast. C, D. Enlargement of the villus as shown in [image].

From: Langman’s Medical Embryology 11th ed. TW Sadler
Overview of Placenta

Figure 7.10 Relation of fetal membranes to wall of the uterus. A. End of the second month. Note the yolk sac in the chorionic cavity between the amnion and chorion. At the abembryonic pole, villi have disappeared (chorion laeve). B. End of the third month. The amnion and chorion have fused, and the uterine cavity is obliterated by fusion of the chorion laeve and the decidua parietalis.

From: Langman’s Medical Embryology 11th ed. TW Sadler
AMNIONIC FLUID INFECTION
Acute Amniotic Fluid Infection

Ascending maternal bacterial infection.

5.31. Routes of fetal infection.
Histologic Staging of Amnionic Fluid Infection

<table>
<thead>
<tr>
<th>Maternal inflammatory response</th>
<th>Stage</th>
<th>Suggested diagnostic terminology</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute marginating choriodeciduitis</td>
<td>1—Early</td>
<td>Acute subchoriitis or choriitis</td>
<td>PMN in subchorionic fibrin and/or membrane trophoblast (Fig. 1a,b)</td>
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<tr>
<td></td>
<td>2—Intermediate</td>
<td>Acute chorioamnionitis</td>
<td>Diffuse-patchy PMN in fibrous chorion and/or amnion (Fig. 1c)</td>
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<td></td>
<td>3—Advanced</td>
<td>Necrotizing chorioamnionitis</td>
<td>PMN karyorrhexis, amnioncye necrosis, and/or amnion basement membrane thickening/hyperesinophilia (Fig. 1d)</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Grade</th>
<th>1—Mild-moderate</th>
<th>No special terminology required</th>
<th>Not severe as defined below</th>
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<tbody>
<tr>
<td></td>
<td>2—Severe</td>
<td>Severe acute chorioamnionitis or with subchorionic microabcesses</td>
<td>Confluent PMN (≥ 10 × 20 cells in extent) between chorion and decidua, ≥ 3 isolated foci or continuous band (Fig. 1e)</td>
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<td></td>
<td>Other</td>
<td>Chronic (or subacute) chorioamnionitis</td>
<td>Subamnionc mononuclear cell infiltrate with occasional PMN (meconium and hemosiderin-laden macrophages excluded) (Fig. 1f)</td>
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<tr>
<th>Fetal inflammatory response</th>
<th>Stage</th>
<th>With chorionic vasculitis or umbilical phlebitis</th>
<th>Intramural PMN-chorionic vessels and/or umbilical vein (Fig. 2a,b)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1—Early</td>
<td>With umbilical vasculitis (one or two arteries ≤ vein) or umbilical panvasculitis (all vessels)</td>
<td>Intramural PMN-umbilical artery or arteries (≥ umbilical vein) (Fig. 2c)</td>
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<td></td>
<td>2—Intermediate</td>
<td>With (subacute) necrotizing funisitis or with concentric umbilical perivasculitis</td>
<td>PMN ± associated debris in concentric bands-rings-halos around one or more umbilical vessels (Fig. 2d)</td>
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<tr>
<td></td>
<td>3—Advanced</td>
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<td>2—Severe</td>
<td>With a severe fetal inflammatory response or with intense chorionic (umbilical) vasculitis</td>
<td>Near confluent intramural PMN-chorionic and/or umbilical vessels with attenuation/degeneration of VSMC (Fig. 2e,f)</td>
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<td></td>
<td>Other</td>
<td>With associated fetal vessel thrombi</td>
<td>Recent thrombosis associated with intramural PMN (Fig. 2f)</td>
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<tr>
<th>Other specific features</th>
<th>Peripheral funisitis</th>
<th>Focal aggregates of PMN at the umbilical cord surface (Fig. 3a)</th>
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<tbody>
<tr>
<td></td>
<td>Acute villitis</td>
<td>PMN in villous stroma (or between trophoblast and stroma) (Fig. 3b)</td>
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<td></td>
<td>Acute intervillitis with intervillous abscesses</td>
<td>Patchy-diffuse PMN in intervillous space (Fig. 3c)</td>
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<td>Decidual plasma cells</td>
<td>Unequivocal plasma cells in decidua basalis or capsularis (Fig. 3d)</td>
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PMN, polymorphonuclear leukocyte; VSMC, vascular smooth muscle cell.
HISTOLOGIC STAGING OF ACUTE AMNIOTIC FLUID INFECTION

MATERNAL INFLAMMATORY RESPONSE
(look at membranes and at the chorionic plate)
Stage 1  Subchorionitis (acute marginating choriodeciduitis)
Stage 2  Acute chorioamnionitis
Stage 3  Acute necrotizing chorioamnionitis

FETAL INFLAMMATORY RESPONSE
(look at umbilical cord & vessels and chorionic plate vessels)
Stage 1  Acute umbilical phlebitis and/or chorionic plate vasculitis
Stage 2  One or more umbilical arteries involved +/- vein & CP vessels
Stage 3  Necrotizing funisitis or concentric perivasculitis

Terms:  FUNISITIS reserved for inflammation in Wharton’s jelly
        VASCULITIS reserved for inflammation in wall of fetal vessel

Stage thought related to duration of infection and therefore likelihood of fetal infection!

Histologic Staging of Amnionic Fluid Infection in the Placenta
Opaque Chorionic Plate (Chorioamnionitis)

Normal Chorionic Plate
Normal Placental Membranes

Maternal Inflammatory Response - Membranes

Acute Necrotizing Chorioamnionitis (stage 3)
Acute Chorioamnionitis, Stage 2
Acute Marginating Choriodeciduitis or Subchorionitis (Stage 1)
Maternal Inflammatory Response at the Chorionic Plate
(Acute subchorionitis, chorionitis, and amnionitis.)
Approximation of timing of the infection based on maternal response:

Stage 1 – acute subchorionitis          6-12h
Stage 2 – acute chorioamnionitis       12-36h
Stage 3 – necrotizing chorioamnionitis >36h

Multiple factors can affect the actual timing. We do not put this in our reports.
Fetal Inflammatory Response

Phlebitis (stage 1), arteritis or panvasculitis (stage 2), concentric panvasculitis or necrotizing vasculitis/funisitis (stage 3).
Chorionic plate vasculitis (stage 1).

Acute umbilical phlebitis – stage 1

Acute umbilical arteritis – stage 2

Acute necrotizing vasculitis – stage 3
AFI can increase the risk of marginal, subchorionic and retroplacental hemorrhages.
FINDINGS CONSISTENT WITH AMNIONIC INFECTION SYNDROME:

MATERNAL INFLAMMATORY RESPONSE, STAGE ____.
MEMBRANES WITH
Pick one:
- ACUTE MARGINATING CHORIODECIDUITIS.
- ACUTE CHORIOAMNIONITIS.
- ACUTE NECROTIZING CHORIOAMNIONITIS.

CHORIONIC PLATE WITH
Pick one:
- ACUTE SUBCHORIONITIS.
- ACUTE SUBCHORIONITIS AND CHORIONITIS.
- ACUTE SUBCHORIONITIS, CHORIONITIS, AND AMNIONITIS

FETAL INFLAMMATORY RESPONSE, STAGE ____.
Pick which apply:
- ACUTE CHORIONIC VASCULITIS.
- ACUTE UMBILICAL PHLEBITIS.
- ACUTE UMBILICAL ARTERITIS.
- ACUTE UMBILICAL PANVASCULITIS WITH FUNISITIS.
Candida Funisitis

Peripheral umbilical microabscesses

Can present as early neonatal sepsis.
Most cases neonate does fine.
We still consider this a critical value.
Clinical implications of amnionic fluid infection.

**Before 32 weeks:**
PPROM with preterm delivery and immature organ systems (intracranial hemorrhages, hyaline membrane disease, necrotizing enterocolitis, infection, etc., death (fetal pneumonia/sepsis)).
Preivable fetus less than 23 weeks.

**Term fetus:**
Amnionic fluid infection common (between 5-25%) with no major sequelae in most cases. [2-3 fold increased risk of intubation, low APGAR, pneumonia, sepsis, seizures, respiratory distress, cerebral palsy].

Fetal inflammatory response (stage 2 or 3) is associated with CP and poor neurologic outcomes.

Increased risk related to fetal infection, thrombi, hemorrhage (abruption), hypoxic-ischemic injury.

Common organisms: GBS, other Strep, Staph, gram negatives (fusobacterium, H. flu, E. coli, others), Listeria, mixed flora, Candida.
An example of an identifiable organism from placental pathology

32 year old G5P1031 at 25w3d by LMP delivered by crash C-section after presenting in preterm labor with advanced cervical dilation and secondary non-reassuring fetal heart tones. Fetal position was footling breech. Stable in NICU. Placenta received for pathologic assessment.