The Placenta as a Fetal Organ

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How do you …

• Accession Placentas?
• Identify the Baby’s Physician?
• Route Routine Reports?
• Define and Communicate “Critical” Values?
Practice Guideline for Examination of the Placenta

Developed by the Placental Pathology Practice Guideline Development Task Force of the College of American Pathologists

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The Placental Pathology Practice Guideline Development Task Force, a multidisciplinary group, has prepared this guideline to assist those involved with placental examination. It provides recommendations related to indications and methods for placental examination as well as sample worksheets. An algorithm for the handling of placentas summarizes the recommendations of the guideline. A summary of specific findings of placental examination together with their pathogenesis and clinical associations is also provided. Recommendations related to reporting with sample reporting formats are included. The guideline is intended as an educational tool, and its use should be guided by the individual circumstances and care setting of specific cases.

(Arch Pathol Lab Med. 1997;121:449-476)

3. Practice guidelines should be as comprehensive and specific as possible.
4. Practice guidelines should be based on current information.
5. Practice guidelines should be widely disseminated.

Several definitions are important to the development, understanding, and use of practice guidelines.

Parameters.—Practice parameters are strategies for patient management developed to assist physicians in clinical decision making. Practice parameters include standards, guidelines, and other patient management strategies.

Standards.—Standards are accepted principles for patient management. Practice variation owing to patient- or physician-specific factors is not expected.
## Indications for Placental Examination

<table>
<thead>
<tr>
<th>Maternal</th>
<th>Fetal/neonatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery at &lt;37 wks or more than 42 wks <em>(alternative: &lt;34 wks only)</em></td>
<td>Stillbirth or neonatal death</td>
</tr>
<tr>
<td>Unexplained or recurrent pregnancy complications</td>
<td>NICU admission</td>
</tr>
<tr>
<td>Systemic disorders, gestational or underlying, including malignancy with concern for mother or infant</td>
<td>SGA/LGA <em>(birthweight &lt;10th or &gt;90th percentile for gestational age)</em></td>
</tr>
<tr>
<td>Peripartum fever or infection</td>
<td>Birth depression/pH &lt;7.0 / 5-minute Apgar &lt;7/assisted ventilation &gt;10 min</td>
</tr>
<tr>
<td>Excessive third-trimester bleeding</td>
<td>Neonatal hematocrit &lt;35</td>
</tr>
<tr>
<td>Thick or prolonged meconium</td>
<td>Neonatal seizures</td>
</tr>
<tr>
<td>Severe oligohydramnios/polyhydramnios</td>
<td>Suspected infection or sepsis</td>
</tr>
<tr>
<td></td>
<td>Hydrops fetalis of unknown etiology</td>
</tr>
<tr>
<td></td>
<td>Multiple pregnancy <em>(alternative: fused placentas, same-sex twins, and/or twins with discordant fetal growth)</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Placental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural abnormalities or masses involving the placental disc, umbilical cord, or membranes</td>
</tr>
<tr>
<td>Abnormal size for gestational age</td>
</tr>
<tr>
<td>Fragmented, possibly incomplete placenta</td>
</tr>
</tbody>
</table>

Source: College of American Pathologists Practice Guideline, 1997
Society for Pediatric Pathology, Perinatal Section
Nosology Committees


Sampling and definitions of placental lesions: Amsterdam Placental Workshop Group Consensus Statement.


Archives of Pathology and Laboratory Medicine; in Press
Amsterdam 2014 Placental Consensus

• To establish an agreed protocol for sampling the placenta, and for diagnostic criteria for placental lesions

• Assist international comparability of clinico-pathologic and scientific studies and assist in refining the significance of lesions associated with adverse pregnancy and later health outcomes.
Amsterdam 2014 Consensus
Gross Examination Recommendations

- Trimmed Weight
- Fixation (May add 3-6%)
- Prior histologic sampling
- Disruption of the basal plate
- Reference to contemporary weight standards
Weight References

• Pinar et al: Pediatric Pathology and Laboratory Medicine 16:901-907, 1996. (Singleton & Twins)

• Pinar et al: Pediatric and Developmental Pathology 5:495, 2002 (Triplets)

• Kalousek et al: Pathology of the human embryo and previable fetus. Springer-Verlag 1990. (Developmental ages 8-18 weeks)

(Tables reprinted in AFIP/ARP Placenta Non-Tumor Fascicle)
Amsterdam 2014 Consensus
Gross Examination Recommendations

• Chorionic Disk Dimensions x 3
  (maximum and minimum thickness)

• Membranes – color-opacity, completeness
  Percentage involved by circumvallation or circummargination

Distance from rupture site to disk edge –
No consensus    (Previa if at edge)
Amsterdam 2014 Consensus
Gross Examination Recommendations

• Umbilical Cord
  – Average diameter
  – Length
  – Insertion site – distance to nearest edge if < 3 cm
  – Strictures and knots
  – Coiling (<1 or >3 / 10 cm)
    • Segmental hypercoiling
    • Deep grooves
  – Coil direction (‘handedness’)

Gross Examination Recommendations

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Coil direction (‘handedness’)

Left Hand - Counterclockwise
<table>
<thead>
<tr>
<th>Coiling Pattern</th>
<th>Frequency</th>
<th>Abnormal cord insertion</th>
<th>Fetal thrombi</th>
<th>Avascular villi</th>
<th>Fetal thrombotic vasculopathy</th>
<th>Stillbirth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Left twist</td>
<td>261 (81)</td>
<td>45 (17)</td>
<td>51 (20)</td>
<td>45 (17)</td>
<td>16 (6)</td>
<td>12 (5)</td>
</tr>
<tr>
<td>Right twist</td>
<td>61 (19)</td>
<td>9 (15)</td>
<td>22 (36)</td>
<td>18 (30)</td>
<td>9 (15)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>P-value</td>
<td>NS</td>
<td>0.006</td>
<td>0.030</td>
<td>0.023</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>
Amsterdam 2014 Consensus
Gross Examination Recommendations

• Routine Histologic Sampling
  1. Membrane roll + umbilical cord: fetal end & 5 cm from insertion
  2. Full thickness close to umbilical cord insertion site
  3 and 4. Full thickness from central 2/3 of Disc
Amsterdam 2014 Consensus 
Gross Examination Recommendations

• Lesions
  – Number and Location
  – Size (Dimensions and Estimate of Placental Volume
  – Sample each type of lesion with adjacent normal parenchyma (up to 3 additional blocks)

Microscopically different lesions may appear similar grossly.
Amsterdam 2014 Consensus Terminology

• Maternal Vascular Malperfusion
  Preferred over “Underperfusion”

Gross Features

  Hypoplasia (< 10th Percentile)
  Thin umbilical cord (<8 mm at term or 10th Percentile)
  Infarcts (Any preterm; >5% non-peripheral at term)
  Retroplacental hemorrhage
Multiple Infarcts, Different Ages
Maternal Vascular Malperfusion
Microscopic Features

Distal villous hypoplasia
Accelerated villous maturation
Decidual arteriopathy
   Acute atherosis
   Fibrinoid necrosis or thrombosis
Absence of remodeling & mural hypertrophy
3rd trimester persistence of intramural trophoblast
Normal Endometrial Spiral Arteries

Before Remodeling

After Remodeling
Failure of Remodeling of Spiral Arteries
Decidual arteriopathy with narrowing classic for but not limited to preeclampsia.

Atheroîs, fibrinoid necrosis, and thrombosis.
Distal Villous Hypoplasia

Usually <32 Weeks Gestation
Widened Intervillous Space with Paucity of Terminal Villi Relative to Stem Villi
Thin Elongated Terminal Villi

Lower 2/3 Chorionic Plate
30% full thickness slide

Focal = 1 slide
Diffuse ≥ 2 slides
Accelerated Villous Maturation (NB 28 Wk GA IUGR)

28 Week IUGR

29 Week Normal
Maternal Vascular Malperfusion

Insufficient Evidence / Inconclusive

Chorionic pseudocysts
≥ 3 microscopic chorionic lakes per section of a membrane roll or grossly unremarkable placental parenchyma

Membranous (Laminar) Decidual Necrosis
A band of coagulative necrosis of choriodecidual interface of placental membranes (at least 10% of membrane roll)

Increased Extravillous trophoblast (“X-cell”) Islands
≥ 5 cell islands and/or placental septa with ≥ 50 extravillous trophoblastic cells per placental section or membrane migratory trophoblastic layer > 7 cells thick
Acute Retroplacental Hematoma

Loosely adherent clot (a)

Early organizing, adherent clot (b) with compression of maternal surface (c)
Retroplacental Hemorrhage
Microscopic Features

Blood beneath or within decidua
Villous compression with crowding and congestion
Intravillous hemorrhage
Coagulative necrosis of syncytiotrophoblast
Infarction Above Retroplacental Hemorrhage
Amsterdam 2014 Consensus Terminology

• Fetal Vascular Malperfusion
  Preferred over “Thrombotic Vasculopathy”
  Umbilical cord lesions
  Thrombophilia
  Cardiac dysfunction

Chronic thrombo-occlusive lesions in fetal circulation of the placenta due to chronic or sudden cessation of blood flow to distal chorionic villi.
Obstruction to *venous* drainage due to intermittent or chronic mechanical cord obstruction *much more common*

- Overlong and often hypercoiled cords
- Nuchal or complex cord loops
- Tight Cord knots
- Velamentous cords

Obstruction to *anterograde* arterial blood flow associated with:

- 2º fetal hypercoaguable state (hypovolemia, erythrocythemia)
- Fetal cardiac dysfunction (decreased perfusion pressure)
- 1º fetal thrombophilia
Fetal Vascular Malperfusion

*Chorionic Surface (Large) Vessel*
- Thrombosis (arterial or venous)
- Vascular intramural fibrin deposition
  (preferred over “intimal fibrin cushion”)
- Vascular (venous) ectasia (fourfold vs. artery)

*Distal (Small) Vessel*
- Stem vessel fibromuscular sclerosis/obliteration
  (preferred over “endovasculopathy”)
- Segmental avascular villi
- Villous stromal-vascular karyorrhexis
  (preferred over “hemorrhagic endovasculitis”)
Fetal Vascular Malperfusion

Segmental/Global Patterns

*Segmental* – complete occlusion with downstream obstruction to umbilical blood flow

*Global* – partial/intermittent obstruction, but widespread

- Numerous small (< 5 villi/focus) of avascular or karyorrhectic villi
- Intramural fibrin deposition
- Venous ectasia
Umbilical Cord Thrombosis
Chorionic and Stem Villous Venous Ectasia
Chorionic Vascular Intramural Fibrin Deposition
Chorionic and stem villous thrombi
Thrombosis in chorionic villous tree → involutional changes in dependent villi
Spectrum of Villous Changes with Fetal Vascular Malperfusion: Karyorrhexis to Diffuse Stromal Sclerosis
Fetal Vascular Malperfusion

Avascular/Karyorrhectic Villi Quantitation

Required for diagnosis: $\geq 3$ foci of 2-4 affected villi

Intermediate foci: 5 -10 affected villi/focus

Large foci: $> 10$ affected villi/focus
Fetal Vascular Malperfusion

High Grade

> 1 focus of avascular villi with ≥45 cumulative affected villi over 3 sections or averaging >15 affected villi; with or without thrombus

≥ 2 occlusive or non-occlusive thrombi in chorionic plate or major stem villi

Umbilical cord thrombus
High Grade Fetal Vascular Malperfusion

Chorionic Plate Thrombus

Chronic propagating venous thrombi
High Grade Fetal Vascular Malperfusion
> 15 Contiguous Avascular Fibrotic Villi
Fetal Vascular Malperfusion

Associations:

• Impedance to blood flow in placenta (AEDBF)

• Fetal growth restriction (IUGR) related to loss of functional placental parenchyma

• Fetal demise, especially if extensive (30-50% of placental parenchyma)

• Thromboembolic phenomena in fetus

• Neurologic sequelae in liveborn infants
Postmortem placental involutional changes of intrauterine retention can resemble *antemortem* pathology of Fetal Vascular Malperfusion

Multifocal stem villous vascular luminal abnormalities due to ingrowth of fibroblasts, resulting in “septation” and obliteration

Progressive terminal villous endothelial and stromal karyorrhexis, loss of capillaries, and sclerosis leading to a hyalinized appearance

*Suggests premortem*

- Chorionic surface vessel thrombosis
- Discreet population of avascular villi
Amsterdam 2014 Consensus Terminology

• Delayed Villous Maturation
  Preferred over “dysmaturity or maturation defect”
  Rare 34 weeks; usually after 36 weeks
  Monotonous villous population (at least 10)
    Centrally placed capillaries
    Continuous cytotrophoblast layer
    Decreased vasculosyncytial membranes
  Focal: 30% of 1 full thickness section
  Diffuse: Present in more than one slide
Delayed Villous Maturation

Focal Delayed Villous Maturation

Adjacent Normal Villi 36 weeks
Chorioamnionitis/Funisitis

Maternal & Neonatal Sepsis, Morbidity Death

Maternal Inflammation

- Prostaglandin release
- Cervical changes
- Weakened membranes

Preterm Labor

Premature-Prolonged Rupture of Membranes

Preterm Birth

Fetal Inflammation
Fetal Inflammatory Response Syndrome

Cytokines & Chemokines
IL-1, IL-6, IL-8
TNF-α, MMP

Fetal/Neonatal brain and Multi-organ injury

Perinatal death & long-term morbidities including cerebral palsy

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
Maternal response
Stage 2

Maternal response
Stage 3 Grade 2 (severe)

Maternal response
Grade 2 (severe)
Ascending Intrauterine Infection

- 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
Fetal Inflammatory Response

Chorionic vasculitis
Stage 1 = intramural PMNs

Funisitis = PMNs in cord
Stage 1 = phlebitis intramural
Stage 2 = Vein + Art
Stage 3 = Necrotizing funisitis
Severe Fetal Inflammatory Response
Grade 2
Villitis of Unknown Etiology

Subchorial and basal distributions typical

Often has maternal chronic lymphohistiocytic deciduitis

Spares stem villi and mid-parenchymal zone
Villitis of Unknown Etiology

- **Low Grade**
  - At least 2 foci; all with < 10 contiguous affected villi
    - Focal: Confined to one slide
    - Multifocal: More than one slide
  - Ungradable – possible low grade: Solitary focus < 10 contiguous villi

- **High Grade**
  - Multiple foci, >1 sections; at least one with > 10 contiguous affected villi
    - Diffuse: >30% of villi affected
    - Patchy: Not diffuse
  - Ungradable – possible high grade: Solitary focus > 10 contiguous villi
Grading of Villitis of Unknown Etiology

Low grade VUE
≤10 villi/ focus

High grade VUE
> 10 villi/ focus
Chronic Villitis with Stem Vessel Obliteration
Placental “Critical Values”

Gross Diagnoses:
  Candida Funisitis
Candida Funisitis
Candida Funisitis

H/E 20x

H/E 200x

GMS 200x
Placental “Critical Values”

Gross Diagnoses:
- Candida Funisitis
- Listeria Placentitis
Acute necrotizing villitis
Placental “Critical Values”

Gross Diagnoses:
- Candida Funisitis
- Listeria Placentitis

Microscopic Diagnoses:
- Other Specific Infections: Herpes, CMV, Parvovirus, Toxoplasmosis, Syphilis, Malaria, Chagas etc.

- Chorionamnionitis with Grade 2 Fetal Inflammatory Response or Non-occlusive chorionic thrombi
Placental “Critical Values”

Microscopic Diagnoses:

- Diffuse High Grade Chronic Villitis and VUE with Obliterative Vascular Changes
- High Grade Fetal Vascular Malperfusion
- Massive Perivillous Fibrinoid Deposition/Maternal Floor Infarction
- Large Chorangioma
Lotus Delivery Placenta

- Male infant born at home at 38 weeks gestation
- Planned non-severance of the umbilical cord
- Birth weight 2664 grams (7th percentile)
- Presented at two days of age with S. epidermidis sepsis, hypothermia, and hypoglycemic seizures
- 145 gram placenta (< 3rd percentile)
- Fetal:Placental ratio 18.3 (> 97th percentile)
- Hypocoiled, 0.5 cm diameter, peripherally inserted umbilical cord, single umbilical artery
What Happens When a Placenta Works Right?

Thank You