It’s triple I, not chorio!
The obstetric perspective

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Overview

- No conflicts to disclose
- Chorioamnionitis
  - Definition
  - Pathophysiology
- Triple I
  - What is it?
  - Why the change?
- Maternal management
- Neonatal management
- Questions
Definition - Chorioamnionitis

- Infection of the chorion, amnion, or both
- A histologic diagnosis?
  - Microscopic findings without clinical findings can be seen
- Chorio typically involves
  - Membranes
  - Amniotic fluid
  - Placenta
  - Umbilical cord
  - Fetus
  - Mother
Intraamniotic infection pathways

- Ascending - common
- Hematogenous - rare
- Retrograde - rarer
- Procedures

- Host factors
  - Cervical mucus plug
  - Fetal membranes
  - Vaginal flora
Incidence

- Term - 1-4%
  - PROM 7%
  - C/S in labor 12%
  - > 8 exams in labor 20%
- Preterm 40-70%
  - Major risk factor is PPROM
    - No antibiotics 20-25%
Risk factors

- Long labor
- Length of time of ruptured membranes
- Multiple vaginal examinations in labor
- Less important factors
  - Cervical insufficiency
  - Nulliparity
  - Meconium stained fluid
  - Internal monitoring
  - Genital tract pathogens (STD’s, GBS, BV)
  - Alcohol and tobacco use
  - Prior pregnancy with chorio
- Not associated with Foley bulb for cervical ripening
Clinical findings

- Maternal fever (100%)
- Maternal tachycardia (50-80%)
- Fetal tachycardia (40-70%)
- Uterine tenderness (4-25%)
- Maternal leukocytosis (70-90%)
- Purulent or malodorous fluid
- Bacteremia (5-10%)

Differential diagnosis
- Labor
- Epidural fever
- Abruption
- Nonobstetric infection
- Medication effect
Microbiology

- Typically polymicrobial
- Mycoplasma
  - Contamination
  - Colonization
  - Infection
- Anaerobes
- Gram negative bacilli
- Group B Strep
## Microbiology

**Organisms isolated in the amniotic fluid of 404 patients with intraamniotic infection**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ureaplasma urealyticum</td>
<td>190</td>
<td>47.0</td>
</tr>
<tr>
<td>Any gram-negative anaerobe</td>
<td>155</td>
<td>38.4</td>
</tr>
<tr>
<td>Mycoplasma hominis</td>
<td>123</td>
<td>30.4</td>
</tr>
<tr>
<td>Bacteroides bivius</td>
<td>119</td>
<td>29.5</td>
</tr>
<tr>
<td>Gardnerella vaginalis</td>
<td>99</td>
<td>24.5</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>59</td>
<td>14.6</td>
</tr>
<tr>
<td>Peptostreptococcus spp</td>
<td>38</td>
<td>9.4</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>33</td>
<td>8.2</td>
</tr>
<tr>
<td>Enteroccci</td>
<td>22</td>
<td>5.4</td>
</tr>
<tr>
<td>Fusobacterium spp</td>
<td>22</td>
<td>5.4</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>14</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Adverse outcomes

**Maternal**
- Dysfunctional labor
- Uterine atony and hemorrhage
- Endomyometritis
- Wound infection
- Sepsis

**Neonatal**
- Pneumonia
- Meningitis
- Sepsis
- Asphyxia
- PVL/IVH
- Cerebral palsy
- Death
Secondary analysis of the BEAM study
1574 preterm deliveries, with mean GA 29 weeks
12% with chorio

Did find that the presence of sepsis was associated with significantly decreased MDI score
Conclusion: Exposure to chorio was not associated neurocognitive defects measured by Bayley II

Table 3. Adjusted Model of Adverse Bayley II Scores in Neonates by Exposure to Chorioamnionitis

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted RR (95% CI)</th>
<th>Adjusted RR (95% CI)*</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDI less than 70</td>
<td>1.06 (0.79–1.44)</td>
<td>0.90 (0.63–1.27)</td>
<td>.53</td>
</tr>
<tr>
<td>PDI less than 85</td>
<td>1.12 (1.00–1.27)</td>
<td>1.14 (0.94–1.38)</td>
<td>.18</td>
</tr>
<tr>
<td>MDI less than 70</td>
<td>1.16 (0.91–1.48)</td>
<td>0.96 (0.70–1.31)</td>
<td>.81</td>
</tr>
<tr>
<td>MDI less than 85</td>
<td>1.04 (0.91–1.20)</td>
<td>0.98 (0.84–1.14)</td>
<td>.79</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval; PDI, Psychomotor Developmental Index; MDI, Mental Developmental Index.
* Adjusted for age, race, body mass index, estimated gestational age, days membranes ruptured, magnesium exposure, delivery route, 5-minute Apgar score less than 7, culture-proven sepsis, and maternal antibiotic exposure.
Treatment in L&D

- Delivery
  - Duration of labor does NOT correlate with adverse outcomes
- Antibiotics
  - Broad spectrum
  - Early treatment- to reduce frequency and severity of neonatal infection
- Cover beta-lactamase producing aerobes and anaerobes
- Antipyretics- acetaminophen
- Continuous fetal monitoring
- Ampicillin and Gentamicin
- Gent- daily or TID
- Alternatives
  - Ampicillin sulbactam (Unasyn)
  - Ticarcillin clavulanate (Timentin)
  - Cefoxitin
- With Cesarean delivery add better anaerobic coverage
  - Clindamycin
  - Metronidazole (Flagyl)
- Penicillin allergic- Vancomycin
Executive Summary

Evaluation and Management of Women and Newborns With a Maternal Diagnosis of Chorioamnionitis

Summary of a Workshop

Rosemary D. Higgins, MD, George Saade, MD, Richard A. Polin, MD, William A. Grobman, MD, MBA, Irina A. Buhimschi, MD, Kristi Watterberg, MD, Robert M. Silver, MD, and Tonse N.K. Raju, MD, for the Chorioamnionitis Workshop Participants*

Convened in January 2015
Purpose of workshop

• Address knowledge gaps
• Provide evidence-based guidelines
  • Pregnant women
  • Neonates
• Proposed replacing the term chorio with triple I
  • Intrauterine Inflammation or Infection or both
• Triple I classification system
• Evaluation and management based on triple I classification
• Research agenda
Why triple I?

- The term chorioamnionitis:
  - Has been around for many years
  - Is a misnomer
  - May imply inflammation, a suspicion for infection, or actual infection
  - Has a certain connotation that triggers many things, especially in the neonate
  - Does not convey degree or severity of infection
  - Is there lots of unnecessary treatment?
    - Anaphylaxis
    - Additional lab evaluations, unnecessary treatment, prolonged hospitalization, NICU stays in neonates

- Maternal fever
  - Many etiologies: epidural, dehydration, medications
Dagnosis of triple I

• Requires maternal fever plus one of the following:
  • Fetal tachycardia
  • Maternal WBC count > 15,000 in absence of corticosteroid therapy
  • Purulent fluid from cervix
  • Biochemical or microbiologic amniotic fluid results consistent with microbial invasion

• What is a fever?
  • Temp ≥ 39.0° C (102.2° F) on one occasion
  • Repeat temps ≥ 38.0° C (100.4° F) at least 30 minutes apart
Categorization of triple I

- **Isolated maternal fever - not triple I**
- **Suspected triple I**
- **Confirmed triple I**
  - Objective findings in amniotic fluid
    - Positive gram stain or culture
    - Low AF glucose
    - High WBC count (absence of bloody tap)
  - Histopathologic findings - retrospective
    - Placenta
    - Membranes
    - Umbilical cord (funisitis)

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**Table 1. Features of Isolated Maternal Fever and Triple I with Classification**

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Features and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isolated maternal fever</strong> (<em>documented</em> fever)</td>
<td>Maternal oral temperature 39.0°C or greater (102.2°F) on any one occasion is documented fever. If the oral temperature is between 38.0°C (100.4°F) and 39.0°C (102.2°F), repeat the measurement in 30 minutes; if the repeat value remains at least 38.0°C (100.4°F), it is documented fever</td>
</tr>
<tr>
<td><strong>Suspected Triple I</strong></td>
<td>Fever without a clear source plus any of the following: 1) baseline fetal tachycardia (greater than 160 beats per min for 10 min or longer, excluding accelerations, decelerations, and periods of marked variability) 2) maternal white blood cell count greater than 15,000 per mm³ in the absence of corticosteroids 3) definite purulent fluid from the cervical os</td>
</tr>
<tr>
<td><strong>Confirmed Triple I</strong></td>
<td>All of the above plus: 1) amniocentesis-proven infection through a positive Gram stain 2) low glucose or positive amniotic fluid culture 3) placental pathology revealing diagnostic features of infection</td>
</tr>
</tbody>
</table>

* Discontinue the use of the term “Chorioamnionitis.” See the text for discussion.
Management - Mother

- Infection is not an indication for Cesarean delivery
- Isolated fever- observation is acceptable
- Treatment- based on prevalent microorganisms
  - Ampicillin and Gentamicin
  - Add anaerobic coverage (Clindamycin or Metronidazole) if C/S needed
- After delivery
  - Vaginal- can be stopped
  - C/S- at least one more dose, unclear if more doses are needed
Management - Neonate

- Guided by:
  - Maternal category - fever, suspected triple I, confirmed triple I
  - Gestational age - preterm, late preterm, term
  - Neonatal clinical evaluation

- Preterm < 34 weeks
  - Higher risk of early onset sepsis
  - Suspected or confirmed triple I - treat
  - Isolated fever - “might be observed”, no evidence-based guidelines
Fig. 1. Proposed algorithm for neonatal management.

Systems issues

- Communication of critical importance
- Including postpartum course
- Checklist?
- Info flow goes both ways
  - Placental pathology
  - Neonatal cultures
- Education, program development, audit and feedback mechanisms

Box 1. Checklist of Items to Include in Communication Between the Obstetric and Neonatal Teams

- Gestational age
- Maternal tachycardia
- Fetal tachycardia
- Maternal white blood cell count greater than 15,000
- Maternal group B streptococci status
- Duration of rupture of membranes
- Duration of labor
- Purulent fluid
- Amniotic fluid evaluation
- Highest maternal temperature
- Epidural anesthesia use
- Prostaglandin use
- Antimicrobial agent(s) used
- Antipyretic used
- Spontaneous preterm birth
- Prior spontaneous preterm birth
### Table 2. Research Gaps and Opportunities

<table>
<thead>
<tr>
<th>Area</th>
<th>Maternal Topics</th>
<th>Neonatal Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of infection</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prediction of infection</td>
<td>Yes, colonization vs infection</td>
<td>Yes</td>
</tr>
<tr>
<td>Scoring system for probability of</td>
<td>Yes, placental histology, microbiome</td>
<td>Yes, need to define by gestational age, microbiome</td>
</tr>
<tr>
<td>sepsis; infection prediction</td>
<td></td>
<td></td>
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<tr>
<td>models to guide clinical</td>
<td></td>
<td></td>
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<tr>
<td>management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated fever in labor</td>
<td>Management—antipyretics, nonsteroidal anti-inflammatory drugs, antimicrobial</td>
<td>Management evaluation and antimicrobial agents</td>
</tr>
<tr>
<td>agents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biomarkers</td>
<td>Prediction, consensus for design of biomarker validation studies,</td>
<td>Prediction, guidance for management, consensus for design of biomarker</td>
</tr>
<tr>
<td>Outcomes</td>
<td>reporting of accuracy, or all of these</td>
<td>validation studies or reporting of accuracy</td>
</tr>
<tr>
<td>Antimicrobial agents</td>
<td>In hospital subsequent reproductive outcomes</td>
<td>In hospital, morbidities; longer term outcomes including neurodevelopment</td>
</tr>
<tr>
<td>Postpartum events</td>
<td>Timing, duration, selection of antimicrobial agents used</td>
<td>Timing, duration, selection of antimicrobial agents used</td>
</tr>
<tr>
<td>“Epidural fever” investigation</td>
<td>Fever, clinical course, and its relationship to newborn’s care and management</td>
<td></td>
</tr>
<tr>
<td>Maternal fever</td>
<td>Management and treatment</td>
<td>Management and treatment</td>
</tr>
<tr>
<td>Duration of antimicrobial therapy</td>
<td>Timing, duration, height, and effect on clinical care and course</td>
<td>Timing, duration, height, and effect on clinical care and course</td>
</tr>
<tr>
<td>Link studies—mother and neonate</td>
<td>Timing and selection of antimicrobial agents</td>
<td>Term neonate—well-appearing</td>
</tr>
<tr>
<td>cohorts</td>
<td></td>
<td>Term neonate—symptomatic</td>
</tr>
<tr>
<td>Observation vs treatment</td>
<td></td>
<td>Term neonate—resolved minor symptoms</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td>Preterm neonate</td>
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<tr>
<td>Microbiome—maternal-fetal</td>
<td>Effects—short and long term</td>
<td>Effect of infection on neurodevelopment</td>
</tr>
<tr>
<td>microbiome ecosystem</td>
<td>Perturbations, influence of gastrointestinal flora on genitourinary flora</td>
<td>Impairment or cerebral palsy</td>
</tr>
<tr>
<td>Low-risk cohorts</td>
<td></td>
<td>Low-risk cohorts</td>
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<td></td>
<td></td>
<td>Effects prenatal and postnatal</td>
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<td></td>
<td>Symbiosis vs pathology</td>
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</tbody>
</table>
Editorial

Lost in Translation
The Changing Language of Our Specialty

- I know we overdiagnose chorio- is that bad?
- Commonly seen in Path reports when there are no/minimal clinical findings- what does this mean?
- Triple I reduces the role of clinical findings- is that good?
- A new classification system should:
  - Bring clarity to areas of confusion and discord
  - Foster development of more robust quality efforts by improving precision of data
- Is triple I really an improvement?
  - Nonspecific
  - De-emphasis of physical exam