New Triple I Classification Scheme: Updates in Diagnosis and Management

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Project ECHO
Pathogenesis of Intraamniotic Infection
Incidence and Risk Factors

• 1-4% of TERM pregnancies
• 40-70% of PRETERM pregnancies

• Risk Factors:
  • Prolonged labor
  • Prolonged membrane rupture
  • Meconium staining
  • Genital tract pathogens (STIs, GBS)
  • Alcohol or tobacco use
  • History of intraamniotic infection
  • 🤔 Internal monitoring
Microbiology

Streptococcus sp.
- Fusobacterium;
- Ureaplasma;
- Lactobacillus;
- Bacteroides;
- Streptosporangium;
- Roseovarius;
- Rhodococcus;
- Pseudobacteriaceae and Klebsiella sp.
- Pantoa and Eubacterium sp.

Adenovirus

Candida sp.
- Ureaplasma; Gardnerella;
- Peptostreptococcus;
- Enterococcus;
- Streptococcus;
- Fusobacterium; Leptotrichia;
- Sneathia; Haemophilus and Escherichia sp.
- Mycoplasma sp.

Bacteria

Viruses

Yeast

Dark shading = PTB
Medium shading = PTB/Term
Light shading = Term
### 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><em>Ureaplasma urealyticum</em></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><em>Mycoplasma hominis</em></td>
<td>123</td>
<td>30.4</td>
</tr>
<tr>
<td><em>Bacteroides bivius</em></td>
<td>119</td>
<td>29.5</td>
</tr>
<tr>
<td><em>Gardnerella vaginalis</em></td>
<td>99</td>
<td>24.5</td>
</tr>
<tr>
<td>Group B <em>Streptococcus</em></td>
<td>59</td>
<td>14.6</td>
</tr>
<tr>
<td>Peptostreptococcus spp</td>
<td>38</td>
<td>9.4</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>33</td>
<td>8.2</td>
</tr>
<tr>
<td><em>Enterococci</em></td>
<td>22</td>
<td>5.4</td>
</tr>
<tr>
<td><em>Fusobacterium</em> spp</td>
<td>22</td>
<td>5.4</td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
<td>14</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Adverse Maternal Outcomes

- Abnormal labor
- Uterine atony and postpartum hemorrhage
- Endometritis
- Wound infection
- Sepsis
Adverse Neonatal Outcomes

- Pneumonia
- Meningitis
- Early-onset sepsis
- Asphyxia
- Periventricular leukomalacia
- Intraventricular hemorrhage
- Cerebral palsy
- Death
How do we diagnose it?

- Fever?
- Uterine tenderness?
- Maternal or fetal tachycardia?
- Foul-smelling fluid?
- Leukocytosis?
- Hypotension?
- Amniocentesis?
## Amniocentesis

<table>
<thead>
<tr>
<th>Gram stain</th>
<th>Any bacteria and leukocytes (6/hpf)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>&lt; 15</td>
</tr>
<tr>
<td>WBC</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>Leukocyte esterase</td>
<td>Trace or more</td>
</tr>
<tr>
<td>Culture</td>
<td>Positive</td>
</tr>
<tr>
<td>Maternal immune response</td>
<td>Neutrophilic inflammation of the chorioamnion</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Fetal immune response</td>
<td>Neutrophilic inflammation of the:</td>
</tr>
<tr>
<td></td>
<td>Umbilical cord (funisitis)</td>
</tr>
<tr>
<td></td>
<td>Fetal vessels (chorionic plate vasculitis)</td>
</tr>
</tbody>
</table>
What the heck is Triple I?

- **Intrauterine inflammation, infection, or both**

  - Why the change?
    - Chorioamnionitis is ambiguous
    - Heterogeneous array of conditions
    - Implies potentially serious consequences for mothers and fetuses
    - Management tends to be irrespective of probable cause or clinical findings

  - Isolated maternal fever is NOT synonymous with chorioamnionitis
"Chorioamnionitis"

• Prior to Triple I classification, chorio diagnosed by fever PLUS 1 or 2 of the following:
  • Maternal leukocytosis (>15,000)
  • Maternal tachycardia
  • Fetal tachycardia
  • Uterine tenderness
  • Foul smelling amniotic fluid

• However, this evolved into fever +/- clinical suspicion → lots of moms and babies getting treated
Classification

Temperature greater than 39 on one occasion or greater than 38 on two occasions 30 minutes apart

Fever PLUS any of:
1. Fetal tachycardia
2. Maternal WBC > 15,000
3. Purulent fluid

Suspected Triple I PLUS any of:
1. Amnio + gram stain
2. Amnio + Cx or low glucose
3. Placental path

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>Isolated maternal 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>Suspected Triple I</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>Confirmed Triple I</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>
Isolated Maternal Fever

• Variety of causes:
  • Epidural anesthesia
  • Prostaglandin use
  • Dehydration
  • Ambient heat
  • Hyperthyroidism

• Temperature should be taken ORALLY to diagnose fever
Maternal Management

• In cases of isolated fever, it may be appropriate to avoid antimicrobials

• In cases of suspected Triple I, antimicrobials are recommended
  • Ampicillin and Gentamicin for vaginal deliveries
  • Addition of anaerobic coverage for cesarean deliveries
    • Anaerobic coverage: Metronidazole, Clindamycin, Carbapenems, β-lactam/β-lactamase combinations (Piperacillin-tazobactam (Zosyn))
  • Alternatives: Cefoxitin, Ampicillin-sulbactam, Vancomycin (penicillin allergic)
Maternal Management

• Duration of therapy:
  • **Vaginal delivery** → Reasonable to stop antibiotics after delivery vs. one additional dose
  • **Cesarean delivery** → One additional dose after delivery appears as effective as longer course
    • Consider treating until 24-48 hours afebrile in sicker* patients
    • *Sicker= Patients with signs of sepsis, continued fevers, underlying high-risk morbidity (immunosuppression, etc...)*
Neonatal Management - Term Infants

FIGURE 9. Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns

  - GBS prophylaxis indicated for mother? Yes: Mother received intravenous penicillin, ampicillin, or cefazolin for 24 hours before delivery? Yes: Observation for ≥48 hours. No: Observation for ≥48 hours.
    - ≥37 weeks and duration of membrane rupture <18 hours? Yes: Observation for ≥48 hours. No: Observation for ≥48 hours.
      - Either <37 weeks or duration of membrane rupture ≥18 hours? Yes: Limited evaluation. No: Observation for ≥48 hours.
Neonatal Management - Term Infants
Neonatal Management - Preterm Infants

• Isolated fever:
  • Well-appearing infant and no prolonged rupture → screening labs, observe (no blood culture)
  • Not well-appearing or prolonged rupture → screening labs, culture, +/- 48hr antibiotics

• Suspected Triple I:
  • Well-appearing infant: screening labs, culture, 48hrs antibiotics
  • Clinically septic infant: above + lumbar puncture and 5-7 days antibiotics
  • Culture-positive sepsis: above + 7-10 days antibiotics
  • Meningitis: above + 21 days antibiotics

Veroni, CDC, 2010
OB and Neonatology Communication

• Important to note the following at delivery:
  • What was the diagnosis?
  • How sick was mom?
  • Did baby appear sick prior to or at delivery?
  • How was mom treated?
Our Delivery Note (Epic)

<table>
<thead>
<tr>
<th>Complications</th>
<th>Retained Placenta without Hemorrhage</th>
<th>Uterine Rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aesthetic Complications</td>
<td>Abnormal Labor - Prolonged First Stage</td>
<td></td>
</tr>
<tr>
<td>Dysfunctional Labor</td>
<td>Abnormal Labor - Prolonged Second Stage</td>
<td></td>
</tr>
<tr>
<td>Seizures During Labor</td>
<td>Cord Prolapse</td>
<td>Abnormal Labor</td>
</tr>
<tr>
<td>Abruptio Placenta</td>
<td>Malignant</td>
<td>Abnormal Labor</td>
</tr>
<tr>
<td>Shoulder Dystocia</td>
<td>Placenta Accreta Spectrum</td>
<td>Abnormal Labor</td>
</tr>
<tr>
<td>Abnormal Labor - Prolonged Latent Stage</td>
<td>Postpartum Hemorrhage</td>
<td>Abnormal Labor</td>
</tr>
</tbody>
</table>

Intrauterine inflammation or infection (Tripe I, formerly called chorioamnionitis) details:

- Please choose one diagnosis:
  - Isolated maternal fever (38.0 degrees C on any one occasion or two documented temperatures of ≥ = 38.0 at least 30 minutes apart)
  - Suspected Tripe I (maternal fever as defined above AND at least one of the following - fetal tachycardia (> 160 for > 10 minutes), maternal WBC > 15,000, purulent amniotic fluid)
  - Confirmed Tripe I (suspected tripe I as defined above AND at least one of the following - amniocentesis with positive gram stain, amniocentesis with low glucose, amniocentesis with positive

Maternal antibiotic treatment given?  Yes  No

**Please send the placenta to pathology on all suspected Tripe I cases**
Will this lead to better care of mothers and infants?

• May decrease the risk of over-treatment
  • Increase maternal bonding
  • Decrease cost
  • Decrease risk of adverse effects

• May not predict adverse maternal/neonatal outcomes