CHORIOAMNIONITIS: WHAT IS THE EVIDENCE FOR CLINICAL MANAGEMENT?

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Disclosures
• No Financial Disclosures

Definition
• Chorioamnionitis
  • Amnionitis
  • Intramamniotic infection

Pathogenesis
• Ascending of cervicovaginal flora
  • Facilitated by ROM
• Tranplacental
  • Listeria moncytogenes
• Iatrogenic
  • Amnio, CVS, fetal surgery
**EPIDEMIOLOGY**

**Preterm**
- Intramamniotic infection with pPROM
  - Less than 27 weeks → 41%
  - 28 to 36 weeks → 15%
- Intraamniotic infection 1/3 of spontaneous preterm labor with intact membranes

**Term**
- 2 to 4% term deliveries
- 12% in labor who undergo a cesarean delivery

Risk Factors

- Low parity
- Prolonged labor
- Prolonged rupture of membranes
- Multiple vaginal examinations in labor (consequence of longer labors)
- Internal fetal monitoring
- Genital tract pathogens (STI, GBS, BV)

Microbiology

- Clinical intraamniotic infection
  - Bacteroides species (25 %)
  - G. vaginalis (24 %)
  - GBS (12 %)
  - Aerobic streptococci (13 %)
  - E. coli (10 %)
  - Aerobic gram-negative rods (10 %)

Microbiology

- 35 % of patients with clinical chorioamnionitis yield Mycoplasma hominis
Clinical Presentation

- Clinical chorioamnionitis
- Subclinical absence of clinical findings:
  - Most commonly presents as spontaneous preterm labor or pPROM

Clinical Chorioamnionitis

- Maternal fever (oral temp ≥ 38.0°C or 100.4°F)
  (all cases)
- At least two of the following:
  - wbc > 15k (70-90% of cases)
  - maternal tachycardia (> 100 bpm) (50-80% of cases)
  - fetal tachycardia (> 160 bpm) (50-80% of cases)
  - uterine tenderness or foul odor of the amniotic fluid (4-25% of cases)

Amniocentesis

- Refractory to tocolytics
- pPROM to determine whether induction is indicated
- Discriminate between chorioamnionitis and other causes of fever and abdominal pain

<table>
<thead>
<tr>
<th>Test</th>
<th>Clinical parameters</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Temperature &gt;100.4 F</td>
<td>95 – 100 sensitive</td>
</tr>
<tr>
<td>Maternal tachycardia</td>
<td>&gt; 100/min</td>
<td>50 – 80% sensitive</td>
</tr>
<tr>
<td>Fetal tachycardia</td>
<td>&gt;160/min</td>
<td>40 – 70% sensitive</td>
</tr>
<tr>
<td>Fundal tenderness</td>
<td>Tenderness on palpation</td>
<td>4 – 25% sensitive</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>Foul-smelling discharge</td>
<td>5 – 22% sensitive</td>
</tr>
</tbody>
</table>
### Amniocentesis

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal Finding</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal white blood cell count (WBC)</td>
<td>≥15,000 cells/mm³ with preponderance of leukocytes</td>
<td>Labor and/or corticosteroids also may result in elevation of WBC</td>
</tr>
<tr>
<td>Amniotic fluid glucose</td>
<td>≤10 to 15 mg%</td>
<td>Excellent correlation with positive amniotic fluid culture and clinical infection</td>
</tr>
<tr>
<td>Amniotic fluid interleukin-6</td>
<td>≥7.9 ng/mL</td>
<td>Excellent correlation with positive amniotic fluid culture and clinical infection</td>
</tr>
<tr>
<td>Amniotic fluid leukocyte esterase</td>
<td>≥1+ reaction</td>
<td>Good correlation with positive amniotic fluid culture and clinical infection</td>
</tr>
</tbody>
</table>

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### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal Finding</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amniotic fluid gram stain</td>
<td>Any organism in an oil immersion field</td>
<td>Allows id of particularly virulent organism: GBS. However, very sensitive to inoculum effect. Cannot id pathogens such as mycoplasmas.</td>
</tr>
<tr>
<td>Amniotic fluid culture</td>
<td>Growth of aerobic or anaerobic microorganism</td>
<td>Results are not immediately available</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>Growth of aerobic or anaerobic microorganism</td>
<td>+ in 5% to 10% of patients; done in seriously ill pts or at risk for bacterial endocarditis, immunocompromised, or has a poor response to initial tx</td>
</tr>
</tbody>
</table>

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### Clinical Management

- **Maternal bacteremia:**
  - 3 – 12 % of infected patients

- **Cesarean delivery is required:**
  - 8 % develop a wound infection
  - 1 % develop a pelvic abscess
  - Increase risk of endomyometritis and venous thrombosis

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**Clinical Management**

- Three separate investigations show intrapartum treatment is superior to treatment after delivery.
  - Decrease in bacteremia
  - Decrease pneumonia
  - Decrease in maternal fever and hospitalization


**Regimen**

- Antibiotic should be initiated as soon as Dx is made
- Administer broad spectrum antibiotics to cover:
  - Beta-lactamase producing aerobes
  - Anaerobes
- Main goal is to target GBS and *E.coli*

**Clinical Management**

- 2002 meta-analysis (N = 181) compared intrapartum versus postpartum antibiotic therapy
  - Intrapartum:
    - Reduction in neonatal sepsis (RR 0.08; CI 0.00 - 1.44)
    - Pneumonia (RR 0.15; CI 0.01 – 2.92)

Hopkins L, *Cochrane Database Syst Rev* 2002

**Regimen**

- Ampicillin (2 g every 6 hours) or penicillin (5 million units every 6 hours) plus
- Gentamicin (1.5 mg/kg every 8 hours or 7 mg/kg/ideal body weight every 24 hours)
Other Regimens

- Ampicillin-sulbactam
  - 3 grams intravenously every six hours
- Ticarcillin-clavulanate
  - 3.1 grams intravenously every four hours
- Cefoxitin
  - 2 grams intravenously every six hours

Regimen

- Penicillin-allergic patients
  - Substitute ampicillin for:
    - Vancomycin 1 gram every 12 hours
      - If GBS+ and Clinda resistant/resistance unknown: Vancomycin /Gentamicin
      OR
    - Clindamycin 900 mg every 8 hours
      - If GBS-negative or Clinda-sensitive GBS: Clindamycin /Gentamicin

Chorioamnionitis and Cesarean delivery:

- If Amp/Gent or Vanco/Gent used
  - add Clindamycin
    or
  - Metronidazole

(ideally prior to skin incision) for anaerobic coverage

Duration Postpartum

- Post-partum management if vaginal delivery:
  - antibiotics are continued for one dose after delivery unless the woman is diagnosed with endometritis

No difference in treatment failure or infection-related complications in RCT evaluating:

- single postpartum dose of antibiotics (Amp/Gent in study) versus
- continuing until 24 hours afebrile postpartum

## Duration Postpartum

- **Post-partum management of chorioamnionitis if Cesarean delivery:**
  - If Amp/Gent or Vanco/Gent used
    - add Clindamycin
    - or Metronidazole

Edwards' study included vaginal delivery and cesarean.

Underpowered to compare single-dose vs. continued dose just including Cesarean.

Given the high risk of endometritis in the setting of chorioamnionitis and Cesarean, continue antibiotics until 24 hours afebrile postpartum


## Antipyretics

- Maternal fever + fetal acidosis confers a **12.5%** risk of neonatal encephalopathy (OR 94, 95 % CI 29 - 307)

- Independent effect:
  - Fever OR 8.1, 95 % CI 3.5 - 18.6
  - Neonatal acidosis OR 11.5, 95 % CI 5.0 – 26.5


## Regimen

- There is **NO evidence for oral antibiotics after discontinuation of parental therapy.**


## Route of Delivery

- Bactericidal concentrations in fetus one-half to one hour after infusion

- Average time between diagnosis and delivery is 3 to 5 hours

- No evidence that duration of infection correlates with outcomes

Prolonged first or second stage of labor has been associated with an increased risk of chorioamnionitis. Whether this relationship is causal is unclear → evolving chorioamnionitis may predispose to longer labor.

Neither chorioamnionitis nor its duration should be an indication for cesarean delivery.
Short-Term Outcomes
• Case-control study (N = 67) microbiologically confirmed clinical chorioamnionitis at term.
  • Pneumonia 4%
  • Neonatal bacteremia 4%
  • No difference in low Apgar scores


Short-Term Outcomes
• Among preterm neonates those with chorioamnionitis had higher:
  • Perinatal death (13% vs 3%, P < .05)
  • RDS (34% vs 16%, P < .01)
  • Infection (17% vs 7%, P < .05)


Short-Term Outcomes
• More likely to require cesarean
  • Uterine dysfunction
  • Inadequate uterine response to oxytocin
  • Abnormal labor progress

Creasy and Resink 7th Edition 2014

Long-Term Outcomes

PLOS ONE
**Long-Term Outcomes**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRETERM INFANTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral Palsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical chorioamnionitis</td>
<td>11</td>
<td>1.9 (1.4-2.5)</td>
</tr>
<tr>
<td>Histologic chorioamnionitis</td>
<td>5</td>
<td>1.6 (0.9-2.7)</td>
</tr>
<tr>
<td>Cystic Periventricular Leukomalacia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical chorioamnionitis</td>
<td>6</td>
<td>3.0 (2.2-4.8)</td>
</tr>
<tr>
<td>Histologic chorioamnionitis</td>
<td>7</td>
<td>2.1 (1.5-2.9)</td>
</tr>
</tbody>
</table>

CI, confidence interval; RR, relative risk.


**Prevention**

- Ineffective:
  - Chlorhexidine vaginal washes during labor
  - Antepartum treatment of bacterial vaginosis
  - Broad-spectrum antibiotics in patients with preterm labor but intact membranes


**Prevention**

- Intrapartum prophylaxis to prevent neonatal GBS sepsis decrease chorioamnionitis
  - Screening based strategy versus risk-based

**Prevention**

- **Active management of labor**  

- **Induction of labor after PROM at term**  

- **Prophylactic antibiotics in selected patients with pPROM**  

**Prevention**

- Largest randomized study found induction with oxytocin induction in PROM  
  - Reduced:  
    - the time interval between premature rupture of membranes and delivery  
    - chorioamnionitis  
    - postpartum febrile morbidity  
    - neonatal antibiotic treatments  
  - Without increasing cesarean deliveries or neonatal infections  
  ACOG PB Number 107, August 2009.

**Prevention**

- Intravaginal PGE2 for IOL with PROM appears to be safe and effective  
  ACOG PB Number 107, August 2009.

**Prevention**

- Meta-analysis (N = 6,814) PROM at term compared:  
  - IOL with prostaglandins or oxytocin  
  - expectant management  
  - In patients which underwent IOL significant reduction in the risk of:  
    - chorioamnionitis  
    - endometritis  
    - number of neonates requiring admission to NICU  
  Dare MR et al *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD005302.
Summary

- Chorioamnionitis is polymicrobial
  - results from migration of cervicovaginal flora through the cervical canal
  - Other causes include transplacental infection
    - bacteremia
    - invasive procedures
  - Maternal fever ≥100.4 F.
    - Clinical diagnosis is strengthened by risk factors for the disease and excluding sources of fever
    - Nonspecific clinical signs: leukocytosis, maternal and fetal tachycardia, uterine tenderness, malodorous amniotic fluid


Summary

- Amniocentesis may be helpful in cases of diagnostic uncertainty
- Chorioamnionitis may impair myometrial contractility → can result:
  - labor abnormalities
  - need for cesarean delivery (with higher rate of complications)
  - postpartum hemorrhage


Summary

- Broad spectrum antibiotics should be started at diagnosis to minimize maternal and fetal morbidity.
  - Vaginal delivery: a single dose of antibiotics after delivery
  - Cesarean section: afebrile for at least 24 hours


Summary

- In the setting of chorioamnionitis, prompt induction or augmentation of labor
  - cesarean delivery reserved for standard obstetrical indications
  - Immediate cesarean in the setting reassuring intrapartum fetal testing, adequate progress of labor, and administration of antibiotics does not improve neonatal or maternal outcome.
  - Adverse neonatal outcomes associated with chorioamnionitis