Infant of Mother/Fetus with Chorioamnionitis

Review and Proposed Evaluation
And Management at LLUMC
T. Allen Merritt, M.D., MHA
Chorioamnionitis

The term chorioamnionitis is used to describe an intrauterine status of inflammation in tissues of either mixed fetal-maternal (choriodecidual space) or fetal origin (chorioamnioniotic membranes, amniotic fluid, and umbilical cord)

Acute chorioamnionitis (ACA) is a very common histopathologic finding of a neutrophilic infiltrate in the placental membranes. It is considered to be nearly always due to a microbial infection of the amionic fluid. There are some specific single-organism organism infectious etiologies of ACA that are diagnosable from placental histopathology…….
A Pathologists Perspective

• The sequellae of ACA includes preterm rupture of membranes, preterm delivery, and thus all the sequellae of prematurity. The less commonly associated fetal sepsis, is difficult to predict; the only histopathologic finding associated with fetal sepsis is the presence of umbilical cord “arteritis” (fetal exudae through the umbilical arteries into Wharton jelly)”

Roberts, D. MGH 2008
Placental Findings and Their Timing Relative to Delivery

• Chronic in utero compromise >48 hr
• Necrotizing funisitis, villitis

• Findings associated with subacute in utero compromise (18-48 hr)
• Necrotizing acute chorioamnionitis
• Roberts, D. Arch Path Lab Med 2008
Maternal & Fetal Factors and Chorioamnionitis - Thomas and Speer 2011

- Elevated cytokines in amniotic fluid
- Maternal fever, tachycardia, leukocytosis, CRP, vaginal discharge, uterine tenderness. Fetal tachycardia.

Histological: Polymorphonuclear infiltration of placenta, membranes and umbilical cord

Biochemical: Elevated proinflammatory cytokines in umbilical cord blood

Microbiological

Clinical: Vasculitis in umbilical cord or chorionic plate

Fetal inflammatory response syndrome
Chorioamnionitis and Cerebral Palsy: OR 4.8 for Term 10.0 for Preterm-Thomas/Speer 2011 and confirmed in recent Canadian Study 2012.
Concerns of Neonatologists

• Existing data support a role of chorioamnionitis for cystic PVL, CP, and IVH in preterm infants, but its association with noncystic white matter necrosis is not yet as clear.

• Prenatal inflammation/infection is a significant risk factor for neonatal sepsis (term or preterm)   Thomas and Speer 2011
The diagnosis of choriamnionitis must be considered even when maternal fever is the sole abnormal finding. Although fever is common in women who received epidural anesthesia (15-20%), histologic evidence of acute chorioamnionitis is very common in women who become febrile after an epidural (70.6%). Furthermore, most of these women with histologic chorioamnionitis do not have a positive placental culture.
The incidence of clinical chorioamnionitis varies inversely with gestational age. In the NICHD (14%-28%) of women delivering preterm infants at 22 through 28 wk gestation exhibited signs compatible with chorioamnionitis. The major risk factors for chorioamnionitis include:
Major Risk Factors for chorioamnionitis:

- Low Parity, spontaneous labor, longer length of labor and membrane rupture, multiple digital vaginal examinations (with or without ROM), meconium-stained amniotic fluid, internal fetal or uterine monitoring, and the presence of genital tract mycoplasma hominis.” Committee of Fetus and Newborn
Mother to Infant Transmission of GBS

GBS colonized mother

- 50% Non-colonized newborn
- 50% Colonized newborn

- 98% Asymptomatic
- 2% Early-onset sepsis, pneumonia, meningitis
Rate of Early-onset GBS Disease in the 1990s, United States

Group B Strep Association formed
1st ACOG & AAP statements
CDC draft guidelines published
Consensus guidelines

Year

Cases per 1,000 live births
0 0.5 1 1.5 2 2.5

Prepartum Maternal Risk factors → Neonatal Early Onset Sepsis

- In the 70’s the main organism GBS
- 1996 CDC guidelines: Consensus for: appropriate intra-partum abx if + for GBS plus for neonatal workup / start of abx:
  - Prolonged ROM (>18h)
  - Maternal fever
  - Maternal UTI
  - Prior infant with GBS infection
  - Prematurity (<37 weeks)
Rate of Early- and Late-Onset GBS, 1990-2008

Early-onset GBS

Late-onset GBS

Before national prevention policy  Transition  Universal screening

Source: Active Bacterial Core surveillance / Emerging Infections Program
CDC GBS Guidelines

CDC GBS 2002 Guidelines:

• Screening of all pregnancies at 35-37 weeks with Cultures or Intrapartum NAAT for GBS
• IPA: All + or unknown /Fever, PROM, hX GBS
  – IPA: Pen/Amp > 2 doses 4 hours before delivery
  – IPA ↓ neonatal sepsis by 80%
• Algorithm for all newborns
CDC GBS 2010 Guidelines:

• Chorioamnionitis can be present even if GBS culture is negative
• Chorioamnionitis frequently leads to fetal infection and may also lead to neonatal infection
<table>
<thead>
<tr>
<th>Clinical scenario</th>
<th>2002</th>
<th>2010</th>
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<tbody>
<tr>
<td>Newborn with signs of sepsis, no IAP</td>
<td>No guidance</td>
<td>Full evaluation +antibiotics</td>
</tr>
<tr>
<td>Well appearing newborn, maternal chorioamnionitis</td>
<td>No guidance</td>
<td>Limited evaluation +antibiotics</td>
</tr>
<tr>
<td>Well appearing newborn, GBS+ mother, no IAP</td>
<td>No guidance</td>
<td>Depends on GA and ROM</td>
</tr>
<tr>
<td>Well appearing newborn, mother w/ indication for IAP, received clindamycin or</td>
<td>No guidance</td>
<td>Depends on GA and ROM</td>
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<tr>
<td>vancomycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well appearing newborn, mother w/ indication for IAP, received ampicillin,</td>
<td>Limited evaluation</td>
<td>Depends on GA and ROM</td>
</tr>
<tr>
<td>penicillin or cefazolin &lt;4 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well appearing newborn, mother w/ indication for IAP, received ampicillin,</td>
<td>Limited evaluation</td>
<td>Observation for ≥48 hours</td>
</tr>
<tr>
<td>penicillin or cefazolin ≥4 hours, GA 35-36 weeks</td>
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FIGURE 9. Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns

- Signs of neonatal sepsis?
  - Yes → Full diagnostic evaluation
  - Antibiotic therapy
  - No → Maternal chorioamnionitis?
    - Yes → Limited evaluation
    - Antibiotic therapy
    - No → GBS prophylaxis indicated for mother?
      - Yes → Mother received intravenous penicillin, ampicillin, or cefazolin for ≥4 hours before delivery?
        - Yes → Observation for ≥48 hours
        - No → Observation for ≥48 hours
      - No → Routine clinical care

- ≥37 weeks and duration of membrane rupture <18 hours?
  - No → Either <37 weeks or duration of membrane rupture ≥18 hours?
    - Yes → Limited evaluation
    - Observation for ≥48 hours
  - Yes → Observation for ≥48 hours
CDC GBS 2010 Guidelines Q&A:

• All well appearing infants of mothers suspected of chorioamnionitis should:
  – Undergo limited diagnostic evaluation (CBC/Culture [frequently only aerobic culture])
  – Receive antibiotics pending culture result
  – Neither choice of antibiotic treatment or durations is recommended by CDC
Maternal risk factors for neonatal infection are expanded beyond what seems to be associated with GBS, focuses on mother symptoms but also at fetal surroundings and are better defined and identified as CHORIOAMNIONITIS.
Prevalence: Several studies

- 21-24 we $\rightarrow$ 40-70%
- 33-36 we $\rightarrow$ 15-22%
- Term $\rightarrow$ 1-5%
CHORIOAMNIONITIS

Definition of clinical acute chorioamnionitis

- Maternal fever: 100.4 for >1 hour/ plus 2 other factors maternal temp of 101 plus 1 other factor

- Other factors:
  - Maternal tachycardia (>100)
  - Fetal tachycardia (>160)
  - Maternal leukocytosis (12000-15000), B >9%
  - Abnormal amniotic fluid (foul smelling, purulent)
  - Uterine tenderness
CHORIOAMNIONITIS

Definition of clinical acute chorio

Presence of diagnostic factors:

• Fever 95-100%
• Maternal tachycardia 50-80%
• Fetal tachycardia 40-70%
• Uterine tenderness/foul odor 4-25%

Subacute chorio:

• Preterm labor/ PROM
• no signs
Differential Diagnosis:

- Plain labor, maternal exhaustion
- Maternal infection in other location
- Fever due to epidural anesthesia (blockade of sympathetic temp control responses)
- Drug induced tachycardia (adrenergic, $\beta$-mimetics, etc)
- Abruptio placenta
CHORIOAMNIONITIS

Hystopathological/bacteriological definition:

• Inflammatory changes, neutrophil infiltrates and or necrosis with or without the presence of bacteria in:
  – Amniotic membranes
  – Amniotic fluid
  – Umbilical cord (funisitis).
CHORIOAMNIONITIS

Specific pathology:
Peripheral funisitis: Candida
Acute intervillous abscesses: Listeria
Acute fetal capillaritis: Gram negative sepsis
Term placentas with chorioamnionitis on left and normal right.
<table>
<thead>
<tr>
<th>Group B streptococcus</th>
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<tbody>
<tr>
<td>Can present without rupture of membranes or chorioamnionitis</td>
</tr>
<tr>
<td>Rarely associated with acute villitis</td>
</tr>
<tr>
<td>Organisms can be present in villous vessels or on amnion, easily identified on hematoxylin-eosin</td>
</tr>
<tr>
<td>Often presents with necrotizing acute chorioamnionitis with intact amnion</td>
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<table>
<thead>
<tr>
<th>Fusobacteria</th>
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<tr>
<td>Necrotizing acute chorioamnionitis with a blurring necrosis of amnion</td>
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<tr>
<td>Filamentous organisms can be seen on hematoxylin-eosin on amniotic surface</td>
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<table>
<thead>
<tr>
<th>Listeria monocytogenes</th>
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<td>Micro and macro placental abcesses</td>
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<tr>
<td>Acute villitis with acute chorioamnionitis</td>
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<tr>
<td>Forms present on silver stain</td>
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<tr>
<th>Candida albicans</th>
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<td>Peripheral abcesses (surface) on the umbilical cord (can be seen grossly)</td>
</tr>
<tr>
<td>Hyphae and cyst forms identifiable in abcesses</td>
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</table>
CHORIOAMNIONITIS

Amnionitc Fluid Diagnostic Analysis:

- Gold standard: positive culture (delayed results /false neg)
- GS >6 bacteria/field  24%  but 99% specif
- Glucose <15mg/dL  57%  74% specif
- IL-6 ≥8 ng/mL  81%  75% specif
- Matrix metallproteinase  90%  80% specif
- Leukocyte esterase (dipstick)  85%  95-100% sp
Diagnostic Dilema

• There are 3 fold histological chorio cases compared with 1 clinical chorioamnionitis
  – Other reasons for inflammation (antigenic conceptus)
• 1/3 of clinical chorioamnionitis do not have pathology correlation
  – Difficulty culturing
  – Infection at different site
• Funisitis present: always chorio
• Funisitis absent in 1/3 of chorios
CHORIOAMNIONITIS

Maternal Outcome:
- Bacteriemia in 10%

Neonatal Outcome:
- Perinatal death in infants born to mothers with chorio:
  - (term 6%, preterm 25%)
  - 10% vs. 6%

Sherman and Rosenkrantz, Medscape Ref, Drugs, Diseases and procedures. 97237-
Soraishan Am J Obstet Gynecol 2009
CHORIOAMNIONITIS

Neonatal Outcome:

Infection

– EOS (terms 2-8%, preterms 7-28%) OR 5.5
Chorio is present in 40% of EOS
If chorio is present in symptomatic baby → 13% blood +Cx
If chorio is present in asymptomatic baby → 1.5% blood +Cx
If chorio is not present in term baby → 0.12% blood +Cx

Tita. Clinics of Perinatology 37, 2010

In term/late preterms if there is PROM and Chorio there is 3% blood +Cx vs 0.6% if chorio without ROM.

Jackson, Peds IDJ 31: 2012
CHORIOAMNIONITIS

Neonatal Outcome:
Infection cont

- Pneumonia  (terms 2%, preterms 10-20%)
- Meningitis  3%  Up to 15% of –blood Cx could have +CSF Cx
- Ratio of treated to infected infants  (+ blood Cx) is 10-20:1
CHORIOAMNIONITIS

Neonatal Outcome:

Fetal Inflammatory Response in preterms:

- Leukomalacia OR 3
- CP OR 4.8-10 (Wu JAMA Nov 26 2003;290:2677 Neufeld J Perinatol)
  (Versland Acta Paediatr 2-2006;95 (2):231)
- IVH 23%
- NEC/intestinal perf 4-5% (Adams Curr Opin Infect Dis Jun 2006;19(3):270)
  (Ragoliaux Pediatrics. 12-2007;120(6):e1458)
- RDS 63%
- BPD ~40% in preterm infants
CHORIOAMNIONITIS

Etiology  Usually polymicrobial

- Ureaplasma/Mycoplasma  *(in lower genital tract of 70% of women)* responsible for  47-30%
- Anaerobes: Gardnerella/Bacteroids  25-30%
- GBS  15%
- E. Coli  8%
- Enterococci  5%
- Fungus (candida)  2%
- Others
NICU Workup and TX for Term infants

• NICU admission; Rapid placental pathology needs to be available within 24 hours

• If Asymptomatic:
  – CBCs, CRPs, Blood cx, PCR for Ureaplasma
  – Amp/Gent 48 hs

• If Symptomatic
  – CBCs, CRPs, Blood Cx, Ureaplasma PCR, LP
  – Amp/Gent/Clynda/ Azythro? for ≥7 days
NICU Workup and TX for Preterm infants

• NICU Admission and Rapid Placental Histopathology

• Asymptomatic:
  – CBCs, CRPs, Blood cx Ureaplasma PCR, Mycoplasma culture
  – Amp/Gent /Flagyl/Azythro 48 hs

• Symptomatic
  – CBCs, CRPs, Blood Cx, Ureaplasma PCR, Mycoplasma culture and perform LP
  – Amp/Gent/Clinda or Flagyl Azythbro for 7-10 days
Is all this Really Necessary?

• Obstetric diagnosis of chorioamnionitis must be taken seriously by neonatologists and WE DO!

• Placental/Cord histopathology needs to be within 24 hours.

• Aerobic Cultures takes a minimum of 48-72 hr, Ureaplasma, Mycoplasma much longer, Candida takes days

• Duration of treatment is empiric, NICU admission currently is mandatory
FIGURE 2
Evaluation of asymptomatic infants ≥37 weeks’ gestation with risk factors for sepsis. aThe diagnosis of chorioamnionitis is problematic and has important implications for the management of the newborn infant. Therefore, pediatric providers are encouraged to speak with their obstetrical colleagues whenever the diagnosis is made. bLumbar puncture is indicated in any infant with a positive blood culture or in whom sepsis is highly suspected on the basis of clinical signs, response to treatment, and laboratory results. WBC, white blood cell; Diff, differential white blood cell count.
FIGURE 1
Evaluation of asymptomatic infants <37 weeks’ gestation with risk factors for sepsis. aThe diagnosis of chorioamnionitis is problematic and has important implications for the management of the newborn infant. Therefore, pediatric providers are encouraged to speak with their obstetrical colleagues whenever the diagnosis is made. bLumbar puncture is indicated in any infant with a positive blood culture or in whom sepsis is highly suspected on the basis of clinical signs, response to treatment, and laboratory results. IAP, intrapartum antimicrobial prophylaxis; WBC, white blood cell; Diff, differential white blood cell count.
Treatment Recommendations Pediatrics May 2012

- Diagnostic tests for EOS other than (Blood with \(\geq 1\text{ml of blood}\)) and/or CSF are useful for identifying infants at LOW RISK
- Superficial cultures, Gastric Aspirate useless
- LPs in those with signs of sepsis and +BC or who do not respond to initial antibiotics
- Optimal Treatment Amp and Gent or based on culture results
- Antibiotics should be DCed by 48hr in low risk situations
Bronx, NY 5045 /29698 infants (17%) were admitted for “evaluation for sepsis”

421/5045 treated with IM antibiotics for 48-72 hrs

14/421 (3.3%) met criteria inadequate treatment using IM antibiotics

7/421 developed symptoms in first 32 hr after birth, and all had positive blood cultures
Lambert et al 2012

• Maternal Chorioamnionitis (intrapartum fever >100.4 or 37.8
• Evaluation for “suspected sepsis” BW>2000 gm, inborn, “well appearing” or asymptomatic
• Evaluation CBC (differential), BC, +/-LP
• Treated in mother’s postpartum room with IM ampicillin/gentamicin and moved to NICU if symptoms developed or + BC
Lambert et al

- Of 421 infants managed with IM antibiotics, 14 developed symptoms and 13 returned to NICU, one was “discharged” but readmitted
- 7/14 had positive BC.
- All but one infant with positive BC had symptoms <24 hr
Lambert et al

• With term or >2000 gm asymptomatic infants receiving IM antibiotics and staying with mother, cost difference was $1735 for LDRP room stay vs $10,850/day for NICU.

• Estimated cost savings of $652,550 at one institution per year. (6.25 reduction in hospital charges). 96.7% of infants could be managed in this way.
Alternative Strategy 2012

- Of 5000 term infants, 13 transferred to NICU for signs of sepsis

- Authors conclude that $600,000 saved per year using this strategy, infants not separated from mother, more consistent breastfeeding

- Pain management for IM injections a success
Legal Consequences of Non-Evaluation or Treatment—Ask Your Patient’s Lawyer!

Bacterial infection: chorioamnionitis, amnionitis, premature birth danger

Chorioamnionitis or amnionitis is an inflammation of the fetal membrane caused by a bacterial infection.

The fetal membrane and amniotic fluid protects the fetus. Chorioamnionitis happens in 1 or 2 percent of all pregnancies but is more common in preterm births. Chorioamnionitis may cause a blood infection for the mother and can lead to preterm birth and serious infection for the newborn.

What causes premature rupture of membranes?

Premature rupture of membrane or PROM happens when a woman’s water breaks before she gets to the hospital. This is a fairly common occurrence happening in one out of 10 pregnancies.

Pelvic examinations during the last three months of pregnancy contribute to premature rupture of membranes. Also previous occurrences with water breaking, chlamydia infections, and past and current smokers put women at risk for premature rupture.

Do You Have A Chorioamnionitis Case? »
Settlement for $5 Million Dollars

When Doctor Negligence Leads to Chorioamnionitis

January 27, 2012
Posted In: Birth Injury


If your child suffered injuries before, during or after labor, and it was caused by doctor negligence, then you could be entitled to receive compensation through an Ohio birth injury claim. You should speak immediately with an Elyria birth injury law firm to discuss your case.

With any labor and delivery, there is the chance that complications will arise. Birth injuries are not uncommon. However, when they are preventable and are caused by some form of negligence, then the doctor may be held liable.

An Overview of Chorioamnionitis

One type of complication that can arise before or during labor is chorioamnionitis. This is a bacterial infection that affects the outer membrane and the amniotic sac. According to Healthline, this condition can strike up to 33% of patients who experience a premature birth and anywhere between 1% to 10% of women who are at full-term.

Not only is the fetus at risk of this infection, but it also can affect the mother. This can lead to serious complications for both the baby and the mother.

Risk Factors for Chorioamnionitis

An awareness of risk factors for chorioamnionitis is important because the more of them that are present, the greater the chances are of developing it. Pregnant mothers should be carefully monitored and doctors need to be able to recognize the risk factors.

Some of the risk factors for chorioamnionitis include:
- early water breakage (premature rupture of the membranes);
- prolonged labor;
- women with ruptured membranes who undergo numerous vaginal examinations;
- internal uterine and fetal monitoring;
- young mother; and
- pre-existing lower genital tract infections.
THANKS!