Infections of the Newborn: Evaluation & Management

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Today's Menu

- Background statistics
- Why babies are more vulnerable
- Risk factors
- Clinical signs
- Screening
- Workups
- Treatment
- Aftermath
- Future Trends
Background Statistics

- Neonatal literature says:
  - Actual infection rate 1-8/1000 newborns
  - LBW infection rate 1-2/100 newborns
Historical Changes in Predominant Infectious Agent

- 1930’s: Group A Strep
- 1940’s: E.coli
- 1950’s: Staph aureus
- 1970’s: Group B Strep
Setting Priorities

- Newborn are not small children
- Remember that 10 babies are worked up for each proven case
Neonatal Vulnerability

- Immature immune system (slow to react, decreased IgG and complement production, poor phagocytosis, poor migration)
- Unavoidable exposure to pathogenic organisms in birth canal
- Peripartum stress
- Invasive procedures
- Exposure to highly resistant nosocomial organisms in NICU
# CHARACTERISTICS OF NEONATAL SEPSIS

<table>
<thead>
<tr>
<th></th>
<th>EARLY ONSET</th>
<th>LATE ONSET</th>
<th>LATE, LATE ONSET</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing</strong></td>
<td>Less than 4-7 days of life</td>
<td>7 days to 3 months</td>
<td>More than 3 months</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Vertical; organism often acquired from mother’s genital tract</td>
<td>Vertical or via postnatal environment</td>
<td>Usually postnatal environment</td>
</tr>
<tr>
<td><strong>organisms</strong></td>
<td>GBS, E.coli, listeria, non-typeable haemophilus influenza and enterococcus</td>
<td>Staph coag-negative, staph.aureus, pseudomonas, GBS, E.coli and listeria</td>
<td>Candida, staph coag-negative,</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td>Fulminant course, multisystem involvement, pneumonia common</td>
<td>Insidious, focal infection, meningitis common</td>
<td>Insidious</td>
</tr>
<tr>
<td><strong>manifestation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>mortality</strong></td>
<td>5%-20%</td>
<td>5%</td>
<td>Low</td>
</tr>
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Risk Factors

- Maternal risk factors for early onset sepsis (EOS)
- Neonatal risk factors for infection
Maternal risk factors for early onset sepsis (EOS)

- chorioamnionitis
- PPROM
- GBS colonization of current pregnancy. The infant of a colonized mother is at 25 times the risk for EOS
- A previous affected infant with GBS
- GBS bacteriuria and untreated maternal urinary tract infection
- Prolonged ROM is taken as 18 hours
- Intrapartum or immediate postpartum maternal fever > 38°C
- Malnutrition
- Sexually transmitted disease
- Lower socioeconomic status
- Maternal substance abuse
Mother to Infant Transmission

GBS colonized mother

50% Non-colonized newborn

50% Colonized newborn

98% Asymptomatic

2% Early-onset sepsis, pneumonia, meningitis
Neonatal risk factors for infection

- Prematurity
- Low birth weight
- Indwelling catheter
- Endotracheal tube
- Low Apgar score (<6 at 1 or 5 min); birth asphyxia
- Meconium staining
- Congenital anomalies
- Multiple gestation
Prevention strategy for early-onset (GBS) disease

Vaginal/Rectal cultures at 35 to 37 weeks in ALL pregnant women

- Intrapartum prophylaxis indicated
- Previous infant with invasive GBS OR
- GBS bacteriuria in current pregnancy OR
- Positive GBS screening culture OR
- Unknown GBS status AND
  - Delivery at < 37 OR
  - ROM ≥ 18 hours OR
  - Intrapartum Tem ≥ 38 C

- Intrapartum prophylaxis not indicated
- Previous pregnancy with positive culture
- Planned section with intact Membranes (regardless of maternal GBS culture status)
- Negative GBS screening culture (regardless of intrapartum risk factor)

ACOG Committee Opinion #279, Dec 2002
**BOX 2. Recommended regimens for intrapartum antimicrobial prophylaxis for perinatal GBS disease prevention**

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Penicillin G, 5 million units IV initial dose, then 2.5 million units IV every 4 hours until delivery</th>
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</thead>
<tbody>
<tr>
<td>Alternative</td>
<td>Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hours until delivery</td>
</tr>
<tr>
<td><strong>If penicillin allergic†</strong></td>
<td></td>
</tr>
<tr>
<td>Patients not at high risk for anaphylaxis</td>
<td>Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hours until delivery</td>
</tr>
<tr>
<td>Patients at high risk for anaphylaxis$§</td>
<td></td>
</tr>
<tr>
<td>GBS susceptible to clindamycin and erythromycin$</td>
<td>Clindamycin, 900 mg IV every 8 hours until delivery</td>
</tr>
<tr>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Erythromycin, 500 mg IV every 6 hours until delivery</td>
<td></td>
</tr>
<tr>
<td>Clindamycin resistant to erythromycin or GBS susceptibility unknown</td>
<td>Vancomycin, **1 g IV every 12 hours until delivery</td>
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</table>
Updated algorithm for women with threatened preterm delivery

Onset of labor OR ROM at < 37 wk, with significant risk for imminent preterm delivery

- No GBS culture
  - Obtain vaginal & rectal GBS culture and initiate penicillin
    - No growth At 48 hr
      - Stop penicillin
    - Penicillin (IV) ≥ 48 hr (during tocolysis)
      - IAP at delivery

- GBS positive
  - No GBS prophylaxis

- GBS negative
Management of Patients with PPROM

Clinical history of PPROM

Confirm diagnosis (pooling, nitrazine and fern tests, ultrasound)

Hospitalize

Overt maternal infection OR unstable fetal presentation OR non-reassuring fetal status

Obtain sample of amniotic fluid for assessment of fetal lung maturity

Deliver

Fetal lung maturity confirmed and gestational age ≥32 weeks

Deliver

Fetal lung maturity confirmed but gestational age <32 weeks

Expectant management* until 32 weeks then deliver

Immature fetal lung profile

Expectant management* until 32 to 34 weeks
Clinical Signs (1)

- Not breathing well
- Not feeding well
- Not looking well
Clinical Signs(2)

- **Respiratory**
  - “dusky spell”
  - *Tachypnea-sensetive but nonspecific-respiratory distress in term newborn is sepsis until proven otherwise*
  - *Apnea in normal newborn-septic W/U and supportive measures*
Clinical Signs(3)

- Feeding
  - “not hungry”
  - Distension
  - Residuals
  - Vomiting
  - Hem-positive stools
  - Watery or mucousy stools
Clinical Signs (4)

- **Appearance**
  - Lethargic
  - Mottled
  - Poor perfusion
  - Temperature instability (not necessarily fever, but fever is more specific)
  - Early-onset jaundice
Clinical Signs(5)

- Ominous Late Signs
  - Apnea
  - Seizures
  - Hypotension/Shock
Sepsis-like Presentations:

- Ductal-dependent congenital heart disease
- CAH
- Inborn errors of metabolism (IEM)
Approach to all neonates born with suspicious EOS

**SIGNS OF INFECTION**
- Suspected Chorioamnionitis or previous EOBGS infants
- **Maternal Risk Factors**
- No or Inadequate Intrapartum Antibiotics
- Adequate Intrapartum Antibiotics

**NO SIGNS OF INFECTION**
- **Maternal Risk Factors**
- NO Risk Factors

- Normal Care

- Gestation <35 wk
  - CBC, IT ratio, CRP
  - Observe for 48 hrs

- Gestation ≥ 35 wk
  - CBC, IT ratio, CRP
  - Observe 24-48 hrs

- Symptomatic infants, or Abnormal CBC, IT ratio, CRP

- **ADMIT TO NEONATAL UNIT**
  - Sepsis workup- CBC, IT ratio, CRP and blood Culture
  - Commence ampicillin and an aminoglycoside IV (include cefotaxime IV for meningitis)
  - Other investigation according to clinical indication (e.g. LP, CXR, gastric aspirate, skin swabs)
Screening

- CBC with manual diff
  - WBC: up, down, or normal
  - ANC, I/C ratio
  - Left shift helpful but may be delayed
  - Unexplained thrombocytopenia

- PT/PTT suddenly abnormal

- Blood sugar may be high or low-change in pattern

- ESR and CRP? Varies from center to center

- CIE or Latex fixation for GBS? Numerous false positives.

- Gastric aspirate or ET aspirate? Not very specific
Workup during early sepsis

- Blood culture
- Amniotic fluid or placenta culture if available
- ET aspirate (if intubated)
- Very low yield for LP or urine cultures in first 24 hours unless specific clinical indication
- LP later if B/C positive or specific symptoms—but note that 10-15% of babies with positive LP’s have negative blood cultures
Classic septic workup (late)

- Blood culture
- LP
- Urine-catherized or suprapubic aspirate
- ET aspirate if intubated
- Surface cultures skin/eye/secretion
- Stool culture if stools abnormal
- CXR
- Abd.X-ray if symptomatic
Goals of workup

- Recover organism
- Determine septic antibiotic
- Determine antibiotic doses
- Determine length of therapy
Treatment(1)

- Antibiotics
- General supportive measures
- IVIG?
- GCSF or GMCSF?
Treatment(2)

- **General supportive measures**
  - Assisted ventilation and/or oxygen as needed
  - IV and possibly arterial access
  - NPO, NG suction if needed
  - Volume support, pressors
  - Transfuse if indicated
  - FFP/cryo if clotting disorders
  - Thermal regulation/support
Selection of antibiotics based on:

- Age of onset
- Location (home vs. hospital)
- Maternal history
- Known colonization
- Epidemic situation
- etc
Treatment(5)

- Antibiotic selection
  - **Early-onset sepsis**: usually Ampicillin & aminoglycoside
  - **Late onset for premie in hospital (nosocomial)**: Vancomycin & Aminoglycoside (or drug specific to known colonization or epidemic situation such as Ceftazidim, Imipenem, cefotaxim, ...)
  - **Abdominal Catastrophes**: Ampicillin & aminoglycoside & metronidazol
  - **Late onset home**: Ampicillin & Cefotaxim
  - **Non-hospitalized meningitis**: ampicillin & aminoglycoside & cefotaxim
  - **Late-onset hospitalized meningitis**: vancomycin & ampicillin & aminoglycoside (or cefotaxim)
  - **Fungus**: Amphotericin B, 5FC, etc.
Aftermath(1)

- How long to treat?
  - Was organism recovered?
  - Where was organism found?
  - Clinical course?
  - Repeat cultures?

- Sequelae?
  - Few in uncomplicated neonatal sepsis
  - Frequent with NEC, gram-ve meningitis
Aftermath (2)

- Negative cultures and course not consistent with infection: 48-72 hours of treatment
- UTI - 7-10 days treatment, screen for renal anomalies
- Sepsis/NEC - 10-14 days of treatment
- Meningitis: 14 days (GBS), 21 days (gram-negative)
- Osteo - prolonged treatment,
Future Trends

- GCSF or GMCSF
- Monoclonal antibodies
- Prophylaxis - various modes