Disclosures / Conflict of Interest

- No FDA “off label” pharmaceutical or medical devices will be discussed in today’s presentation.
- No commercial support was received for this presentation.
- No conflict of interest

Objectives

1. Define intraamniotic infection (chorioamnionitis) and potential risk factors for development of perinatal sepsis.
2. Identify key nursing assessments and protocols for early recognition and management of perinatal sepsis
3. Identify critical elements for patient education including warning signs
Maternal sepsis Morbidity

- Maternal sepsis is the leading cause of maternal death, accounting for 15% of maternal deaths worldwide
- Sepsis kills and disables millions, more than breast cancer, lung cancer, and stroke combined.
- In the United States and the United Kingdom, maternal sepsis is considered to be the leading cause of death in the Peripartum period

Padilla & Pankajwar, 2017
**Maternal Sepsis**

**Definition of Terms**

- **Chorioamnionitis**: Infection of the chorion, amnion, or both. Historical term.
- **Intraamniotic Infection (IAI)**: Infection involving the amniotic fluid, fetus, umbilical cord, or placenta and fetal membranes.
- **Triple I (suspected)**: Fever without a clear source plus any of the following: 1) Baseline fetal tachycardia; 2) Maternal WBC >15,000 per mm$^3$ in the absence of corticosteroids; 3) Purulent fluid from the cervical os.
- **Triple I (confirmed)**: All of the above plus laboratory findings of infection e.g.: Positive amniotic fluid Gram stain for bacteria, low amniotic fluid glucose (≤14 mg/dL), amniotic fluid white cell count (>30 cells/mm$^3$), or positive amniotic fluid culture results, or histopathologic evidence of infection or inflammation or both in the placenta, fetal membranes, or the umbilical cord vessels (funisitis).

**Sepsis definitions**

- **Sepsis**: Life threatening organ dysfunction caused by a dysregulated host response to infection.
  - SBP <100mmHg
  - Significantly decreased urine output
  - Abnormal change in mental status
  - Decrease in platelet count
  - Difficulty breathing (RR>22)
  - Abnormal heart pumping function
  - Abdominal pain

- **Septic Shock**: Circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality.
  - Hypotension that does not respond to fluid boluses,
  - Requirement for vasopressors to sustain a MAP of at least 65mmHg, and
  - Serum lactate >2mmol/L.
Maternal sepsis

Is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion or postpartum period

WHO consensus definition, 2018

Immune Response in Pregnancy

- Pregnancy modulates the immunologic response
- Immunologic alterations with advancing pregnancy may impair pathogen clearance resulting in increased severity of disease
- Infants and pregnant women may be at a higher risk and more susceptible to or more severely affected by infectious diseases.

Organisms/ Invasion

- Group B streptococcus (GBS)
- Group A streptococcus
- Escherichia coli
- Coagulase-negative staphylococcus
- Any gram-negative anaerobe
- Mycoplasma hominis
- Ureaplasma urealyticum

Polymicrobial infection is common with 2 or more organisms present

- Gardnerella vaginalis
- Haemophilus influenzae
- Listeria monocytogenes
- Parovirus
- Toxoplasmosis
- Coxsackie
- Zika?
4 pathways of invasion

Maternal colonization can be:
• Intermittent
• Transient
• Persistent

Maternal infection
• Preterm labor
• Preterm Premature Rupture Of Membranes
• Preterm Birth

Case study
• 33y/o G1P0 39/2 weeks
• GBS negative
• Labs negative
• Normal pregnancy, 41 lb. wt, gain BMI 26
• Thinks she may be leaking fluid
• Balloon ripening, induction of labor for “intermittent gestational hypertension”
Risk factors of chorioamnionitis / IAI...

- Low parity
- Spontaneous labor
- Longer length of labor
- Membrane rupture
- Multiple digital vaginal exams especially with ROM
- Internal fetal or uterine monitoring
- Presence of genital tract microorganisms


Diagnosis of chorioamnionitis / IAI

Fever of ≥100.4°F (38°C) present on 2 occasions 30 minutes apart or any temp ≥102.2°F (39°C) and 1 or more of the following:

- Maternal tachycardia (greater than 100 bpm)
- Fetal tachycardia (baseline greater than 160 bpm)
- Maternal leukocytosis (>15,000/mm³)
- Uterine tenderness and irritability
- Purulent or foul odor of the amniotic fluid

- Clinical suspicion to warrant antibiotic administration to the mother
- Diagnosed antepartum, during labor or within 24 hours after birth.

Clinical Characteristics

- Maternal Tachycardia
- Fetal Tachycardia
- Malodorous amniotic fluid
- Maternal fever
- Uterine tenderness
- Leukocytosis

TEMP+
**Presumptive Diagnosis of Intraamniotic Infection**

ACOG Committee Opinion 712, August 2017

- **Isolated maternal fever**
  - Suspected intraamniotic infection
  - Fever + 1:
    - WBC,
    - Purulent cervical drainage, fetal tachycardia

- **Confirmed intraamniotic infection**
  - Amniotic fluid culture or gram stain or both

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**Maternal Fever**

- Maternal fever of 100.4°F (38°C) or greater persisting more than 1 hour or any temperature of 102.2°F (39°C) or greater
- Difficult to differentiate infectious from non-infectious fever during labor
- Accurate indicator of culture proven infection is about 30%
  - Epidural anesthesia
  - Inflammation
  - Other infections
  - Dehydration
- Associated with serious adverse neonatal morbidity (hypotonia, seizures, low APGAR, assisted ventilation)

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**Epidural?**

- 6-30% of laboring women with epidural develop a fever compared with 6% of women with no epidural analgesia
- Cause of maternal hyperthermia with epidural is debated in the literature
  - Possible alteration in thermoregulatory physiology leading to an imbalance between heat-producing and heat-dissipating mechanisms
  - Longer labor (11 hours vs. 6.7 hours without epidural)
  - Infectious cause cannot be discounted therefore more maternal antibiotic treatment
  - Results in increase in neonatal sepsis evaluations
Inflammation?

- Natural body response to an injury (physical, chemical or infectious) and a necessary prelude to healing
- Placental inflammatory process are part of labor
- Protective nature but effect on tissue and organs may be excessive and cause damage.
- Fever induces an inflammatory response leading to increased interleukin (IL-6) levels
- Effects of intrauterine infection on the fetus and newborn depend on the duration and timing of the inflammatory process. Inflammation that involves the fetus is Fetal Inflammatory Response Syndrome (FIRS)

Inflammatory Process During Labor

- Dysfunctional labor
  - Second stage > 2 hours
  - Active labor > 12 hours
- Internal uterine or fetal monitoring
- Multiple cervical exams (> 3)
- Meconium stained amniotic fluid

Other infections associated with fever

- Pyelonephritis
- Influenza
- Appendicitis
- Pneumonia

Can cause maternal tachycardia, leukocytosis and fetal tachycardia
Conditions present with different symptoms
• Maternal heart rate > 100 bpm at any time during labor

• **Alternate causes:**
  - Normal hemodynamic demand of labor
  - Medication
  - Somatic and psychological responses with sympathetic nervous system activation (e.g.: pain, fear, anxiety, loss of control)

Present in 91% with chorio Diagnostic accuracy 56.1%

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• Baseline FHR > 160 BPM

• Other causes:
  - Maternal fever leading to increase in fetal metabolic rate
  - Evolving fetal hypoxemia, hypercarbia and/or respiratory acidosis
  - Elevated maternal catecholamine level
  - Maternal medications

• FHR was normal in 46% of confirmed cases
• One of the indicators with Triple I.

Present in 36% with chorio Diagnostic accuracy of 53.8%

---

• Maternal serum WBC count of > 15,000 cells/mm³ in the absence of corticosteroids

• May be elevated in labor and increase linearly with labor duration without evidence of infection

• Corticosteroid therapy

• Measurements of acute phase reactants such as C-reactive protein (CRP) have not been helpful in establishing diagnosis

• One of the markers with Triple I

Present in 33% of cases of chorio Diagnostic accuracy of 55.6%
Subjective finding

Pain continued beyond the effects of contractions alone

Possible causes

- Triggered by inflammatory mediators and prostaglandins which will increase uterine contractility and tenderness
- Decreased uterine perfusion leading to uterine muscle hypoxia
- Abruptio or uterine rupture

Malodorous / purulent amniotic fluid

- Least accurate and least common finding with poor sensitivity
- More likely to be present with preterm infection
- One of the markers for Triple I.

Chorio management in labor

- Plans are made for prompt delivery. Vaginal delivery is usually possible.
- Treated very aggressively, with broad-spectrum, intravenous antibiotics:
  - Ampicillin 2gm IV over 60 minutes every 4-6 hours
  - Gentamicin IV over 60 minutes
  - 1.5 mg/kg every 8 hours
  - Alternative: 5mg/kg once daily
  - Routine monitoring of gentamicin levels is unnecessary
  - Women with renal insufficiency gentamicin levels and creatinine clearance are monitored to guide dosing
  - Clindamycin 900mg IV over 30 minutes q8h (if C/S delivery)
- Maternal temperature is treated with oral or rectal acetaminophen, 1gm every 4 hours.
Maternal sepsis

“Pregnancies complicated by severe sepsis and septic shock are associated with increased rates of preterm labor, fetal infection and preterm delivery. Sepsis onset in pregnancy can be insidious, and patients may appear deceptively well before rapidly deteriorating along with the development of severe shock, multiple organ dysfunction syndrome or death. The outcome and survivability in severe sepsis and septic shock in pregnancy are improved with early detection, prompt recognition of the source of infection, and targeted therapy.”

Barton & Sibai, 2012

Sepsis Screening systems

Consider the physiologic changes of pregnancy

Sepsis pathophysiology

Source of infection

C/S, prolonged labor, PROM, chorio, multiple vag. exams, retained products, anemia, UTI, pyelo-pneumonia, endometritis

Bacteria in the blood

Releases cytokines, histamines, serotonin

Capillary permeability

Leaking blood vessels, Plasma extravascular

Reduced circulating volume

Platelet consumption leads to coagulopathy

Organ dysfunction

Kidneys, liver, lungs, uterus

Vasodilation, hypotension, poor perfusion

Decreased oxygen to tissues leads to Tachycardia

Lactic acid (serum lactate)

Metabolic acidosis
### Signs of septic shock in mother

- Fever (100.4) or abnormally low temp (96.8)
- Tachycardia > 110 bpm
- Hypotension
- Difficulty breathing, tachypnea > 24 bpm
- Significantly decreased urine output
- Areas of mottled skin / jaundice
- Abrupt change in mental status
- Decrease in platelet count
- Lactate > 2mmol/L

2 or more of these symptoms

### Symptoms of sepsis

#### Hypotension

<table>
<thead>
<tr>
<th>A systolic blood pressure of</th>
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</thead>
<tbody>
<tr>
<td>• &lt;90 mm Hg,</td>
</tr>
<tr>
<td>• mean arterial pressure &lt;70 mm Hg, or</td>
</tr>
<tr>
<td>• reduction of &gt;40 mm Hg from baseline.</td>
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BP may decrease due to:

- Vasodilation induced by pregnancy
- Epidural anesthesia
- Blood loss

Normal physiological changes during pregnancy can cause abnormal readings when compared with the non-pregnant population, potentially leading to a missed diagnosis of sepsis.

#### Decreased urinary output

- Trauma
- Retention due to loss of tone
- Cesarean birth
- Dehydration with prolonged labor
- Antidiuretic effect of oxytocin
Symptoms of sepsis

Changed mental state

• Exhaustion following labor
• Effect of narcotic administration

Elevated Serum Lactate

• Lactic acid is a by-product of anaerobic metabolism (serum lactate)
• Poorly perfused tissue beds result in global tissue hypoxia which result in increased serum lactate
• A serum lactate is correlated with increased severity of illness and poorer outcomes even if hypotension is not present
• May be elevated in labor...

Maternal Treatment Regimens and Practice Implications

- Antepartum management
- Labor management
- Antibiotic therapy
- Lab assessment
**Antepartum**

- **PPROM - Preterm Premature Rupture of Membranes**
  - Expectant management until 34 weeks, signs of labor or suspected infection. May continue up to 37 weeks.
  - Infection may be subclinical and the clinical findings are not yet present
  - < 34 weeks antenatal corticosteroids

- **Preterm Labor – Labor between 20 - 37 weeks gestation**
  - MgSO4 for neuroprotection up to 32 weeks
  - Antibiotics
  - Glucocorticoids
  - If chorio is suspected, no attempt to stop labor

ACOG: Prelabor Rupture of Membranes, 2018
ACOG: Management of Preterm Labor, 2016

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**Corticosteroids for expectantly managed 34-37 weeks**

- Betamethasone may be considered in a woman with a singleton pregnancy between 34 0/7 and 36/6/7 weeks gestation if at risk for imminent risk of preterm birth within 7 days
- Should not be used if antenatal corticosteroids already administered during pregnancy
- Specifically mentioned, an indicated delivery, such as with development of severe features in preeclampsia, should not be delayed in this time frame for administration of corticosteroids
- Use of corticosteroids during this time frame for patients with pregestational diabetes, is still being evaluated

ACOG: 2017 Antenatal Corticosteroid Therapy for Fetal Maturation

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**Intrapartum Antimicrobial Prophylaxis (IAP) for GBS**

- **PCN Allergy?**
  - YES: Antenatal GBS testing?
    - Low
      - Yes: Cefazolin 2Gm, 1Gm q8h
    - No: Penicillin 5Mu, 2.5 Mu q4h
  - NO
    - Anaphylaxis Risk?
      - High
        - Vancomycin 1Gm q12h
      - Low
        - GBS susceptibility
          - 99%
            - Clindamycin 900mg q8h
          - 1%
            - Erythromycin 500mg q6h
          - Vancomycin 1Gm q12h

Treatment for GBS is prophylactic. If the woman has IAP, follow guidelines for broader antibiotic coverage
New or suspected infection

Evaluate for 2 or more sepsis criteria
- T. 100.4
- HR > 110
- RR > 24
- WBC > 15,000
- Altered mental state
- Urine output < 30ml/hr for 2 hours
- Blood glucose > 140

Interventions for sepsis
- Draw lactate
- CBC, CMP, PT, PTT, INR, serum creatinine
- UA
- Blood cultures
- IV access
- Give antibiotics
- Chest x-ray
- Rapid response team
- Consider source of infection

The most important change in the revision of the Surviving Sepsis Campaign bundles is that the 3-hour and 6-hour bundles have been combined into a single “Hour-1 Bundle” with the explicit intention of beginning resuscitation and management immediately.

1 hour bundle

The most important change in the revision of the Surviving Sepsis Campaign bundles is that the 3-hour and 6-hour bundles have been combined into a single “Hour-1 Bundle” with the explicit intention of beginning resuscitation and management immediately.

1 hour bundle
- Measure Blood Lactate
  - Remeasure if initial lactate is >2 mmol/L.
  - A high lactate level indicates that the tissues are not getting enough oxygen

- Perform Blood Culture
  - Blood cultures identify the cause of the infection.
  - Should be taken before antibiotics are administered, if possible.

- Antibiotics
  - Broad-spectrum antibiotics that are active against the causative organism

- IV Fluids
  - Rapid administration of 30ml/kg crystalloid for hypotension or lactate > 4mmol/L

- Vaspressors
  - Raise blood pressure
  - This is a critical resuscitation step in patients with septic shock

Effective 5/11/18
Maternal Morbidity: Effects on Labor and Delivery

- Increased risk for dysfunctional labor
- Approximately 75% require oxytocin for augmentation of labor
- 30 to 40% deliver by cesarean, usually for failure to progress

Postpartum complications

- Endomyometritis
- Wound infection
- Pelvic abscess
- Venous thrombosis
- Bacteremia, septic shock
- Postpartum hemorrhage
  - Uterine atony (Hemabate may not work)
  - Inflammation leads to dysfunctional uterine tone
- DIC
- ARDS
- Maternal death

Postpartum antibiotics

- Optimal duration of antibiotic therapy after delivery has not been determined conclusively.
- Reasonable to continue antibiotics for one additional postpartum dose or until the woman is afebrile and asymptomatic for 24 hours.
- No evidence that oral antibiotics are beneficial after discontinuing IV therapy.
- Extension based on risk factors for postpartum endometritis. For women undergoing C/S at least one additional dose of antimicrobial agents is recommended

This is for chorioamnionitis not for GBS
Fetal / Neonatal morbidity

- The fetus may suffer from infection AND the maternal temperature elevation.
- Increased core temperatures lead to an increased metabolic rate of the fetal enzyme systems, which in turn need more oxygen than normal.
- Combination of maternal fever and fetal acidosis conferred a 12.5% increased risk of neonatal encephalopathy.

Fetal infection

1. With an ascending infection, bacteria from lower genital tract ascend into the chorionic villus space.
2. Inflammatory mediators (IL-6,8) produced by decidua and/or membranes diffuse into amniotic fluid and the fetal lung.
3. Fetal lung injury is induced by inflammatory mediators (cytokines).

Fetal Inflammatory Response Syndrome (FIRS)

A multiorgan disease

- Necrotizing enterocolitis
- White matter disease / cerebral palsy
- RDS / BPD
- Thymic involution

Adverse Neonatal Outcomes

- Perinatal death
- Asphyxia
- Early onset sepsis
- Septic shock
- Pneumonia
- Meningitis
- Intraventricular hemorrhage
- Cerebral white matter damage (PVL)
- Long term neurodevelopmental disability (cerebral palsy)
- Bronchopulmonary dysplasia (BPD)

Proactive, Cautious Management Approach

- MB separation
- Risk/benefit of antibiotic exposure
- Microbiome
- Lab tests, sepsis evaluation
- Resource utilization

Incidence of neonatal early-onset sepsis has declined but the approach to sepsis risk assessment practices remains controversial, especially among initially well-appearing term.
Early Onset Sepsis Risk Calculator (Kaiser)

https://neonatalsepsiscalculator.kaiserpermanente.org/infectionProbabilityCalculator.aspx

- >34 weeks
- Maternal temp
- Duration of ROM
- GBS status
- Intrapartum antibiotics

Nursing implications

- Review prenatal and intrapartum history
- Aware of potential maternal and/or neonatal deterioration
  - Vigilance with vital sign and symptom assessment
  - Prompt administration of antibiotics
  - Delivery is not always the ‘cure’ for the mother
- Invasive procedures: artificial rupture of membranes, digital cervical exams, and internal monitoring devices need to be avoided without clear indication
- Promotion of breastfeeding / breastmilk/colostrum
- Minimize separation with neonatal antibiotic administration
- Patient education for signs of maternal infection and neonatal infection
- Attend / participate in severe maternal morbidity review sessions

Maternal Education

- Incision that is not healing
- Red or swollen leg, that is painful or warm to touch
- Temperature of 100.4°F or higher
Advise parents to seek urgent medical help if concerned

- Abnormal behavior
- Feeding difficulty
- Signs / symptoms of early onset sepsis
- Temp below 36C or above 38C
- Jaundice
- Lethargy
- Tachypnea

**Participate in Severe Maternal Morbidity Reviews**

1. Was the diagnosis of sepsis or infectious disease made in a timely fashion? Did the Early Warning System alert the team?
2. Were appropriate antibiotics used after diagnosis? How long to treatment?
3. Did the woman receive appropriate volume of IV fluids?
4. Were significant modifiable risk factors for infectious complications identified?

**Summary**

- Chorioamnionitis (IAI, Triple I) is associated with significant maternal, fetal and neonatal adverse outcomes.
- Clinical signs are nonspecific
- Early recognition and prompt treatment is crucial.
- Early warning scoring systems are not consistent
- A neonatal emergency that may lead to pneumonia, meningitis or sepsis