Peripartum Uterine Infection

Background
Intraamniotic infection, also referred to as chorioamnionitis, is an infection with resultant inflammation of any combination of the amniotic fluid, placenta, fetus, fetal membranes, or decidua.

Intraamniotic infection often is polymicrobial in origin, commonly involves aerobic and anaerobic bacteria, and frequently originates from the vaginal flora. It predominantly occurs by ascending bacterial invasion from the lower genital tract to the typically sterile amniotic cavity. Intraamniotic infection also can occur, although rarely, after invasive procedures (eg, amniocentesis or chorionic villus sampling) or by a hematogenous route secondary to maternal systemic infection (eg, Listeria monocytogenes).

Intraamniotic infection can be associated with acute neonatal morbidity, including neonatal pneumonia, meningitis, sepsis, and death, as well as long-term infant complications such as bronchopulmonary dysplasia and cerebral palsy.

Administration of intrapartum antibiotics is recommended whenever an intraamniotic infection is suspected or confirmed. Antibiotics should be considered in the setting of isolated maternal fever unless a source other than intraamniotic infection is identified and documented.

Obstetric care providers diagnose an intraamniotic infection, or when other risk factors for early-onset neonatal sepsis are present in labor (eg, maternal fever, prolonged rupture of the membranes, or preterm birth), communication with the neonatal care team is essential to optimize neonatal evaluation and management.

A. Intrapartum definitions
The diagnosis of intraamniotic infection can be established objectively by amniotic fluid culture, or gram stain, or both and biochemical analysis, but for most women at term who are in labor the diagnosis is primarily made using clinical criteria.

In clinical practice, confirmed intraamniotic infection among women in labor at term will most commonly be made after delivery, based on histopathologic study of the placenta. Therefore, until better and less invasive intrapartum diagnostic tools become available, any practical distinction between suspected and confirmed intraamniotic infection will remain meaningful only in research settings and not for the obstetrician–gynecologist or other obstetric care provider managing a patient in labor. Diagnosis of confirmed histologic intraamniotic infection in the postpartum period does not alter postdelivery maternal treatment.

Suspected intraamniotic infection:
- maternal temperature is greater than or equal to 39.0°C (102.2 F)
  or
- maternal temperature is 38.0–38.9°C (100.4 – 102.1 F) and one additional clinical risk factor is present. (maternal leukocytosis, purulent cervical drainage, or fetal tachycardia)

Isolated maternal fever:
- maternal temperature between 38.0°C and 38.9°C (100.4 – 102.1 F) with no additional risk factors present, and with or without persistent temperature elevation.
**Intrapartum Management**

Multivariate models of neonatal sepsis risk demonstrate the positive effect of intrapartum antibiotics on the risk of culture-confirmed neonatal infection. Intrapartum antibiotics also have been shown to decrease maternal febrile morbidity and length of hospital stay. Therefore, in the absence of any clearly documented overriding risks, administration of intrapartum antibiotics is recommended whenever intraamniotic infection is suspected or confirmed. (See Table 1)

Antipyretics can be considered in addition to antibiotics. Proper labor progression should be ensured, given the association between intraamniotic infection and dysfunctional labor progression.

In the absence of contraindications, augmentation of protracted labor in women with intraamniotic infection appears prudent. However, intraamniotic infection alone is not an indication for immediate delivery, and the route of delivery in most situations should be based on standard obstetric indications. Intraamniotic infection alone is rarely, if ever, an indication for cesarean delivery.

In addition, given the potential benefits for the woman and newborn, antibiotics should be considered in the setting of isolated maternal fever unless a source other than intraamniotic infection is identified and documented. (See Table 1)

**If planning a cesarean delivery...**

**Prevention**

**Single dose**

A meta-analysis of 51 antibiotic trials demonstrated no differences in efficacy when first-generation cephalosporins were compared with broader-spectrum second-generation cephalosporins or third-generation cephalosporins for the purpose of surgical prophylaxis in general. After a single 1-g intravenous dose of cefazolin, a therapeutic level is maintained for approximately 3–4 hours.

Regimen:

- **Cefazolin**
  - < 80 kg: one gram IV 15 to 60 minutes before skin incision
  - > 80 kg: two grams IV 15 to 60 minutes before skin incision
  - > 40 BMI: three grams IV 15 to 60 minutes before skin incision

If anaphylaxis to penicillin or cephalosporin

Gentamicin 5 mg / kg IV and

Clindamycin 900 mg IV

Give a second dose of any antibiotic if > 1500 cc EBL

- Cefazolin if > 4 hr procedure
- Clindamycin if > 6 hr procedure

**Extended coverage**

Due to the rate of post op wound complications and endometritis, we suggest extended coverage against ureaplasma for patients with Cesarean delivery performed:

- during labor
- greater than or equal to 4 hrs of ruptured membranes

Treat with:
Vancomycin 500 mg IV 15 to 60 minutes before skin incision

**Local antibiotic resistance**
Due to local bacterial resistance patterns, in consultation with the ANMC Antimicrobial Stewardship Program, we suggest adding metronidazole 500 mg IV q 8 hrs in addition to surgical prophylaxis. (Table 1)

**Table 1 Treatment of Intraamniotic infection**

<table>
<thead>
<tr>
<th>Primary Regimen</th>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>2 mg IV q 6</td>
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<tr>
<td>and</td>
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<tr>
<td>Gentamicin</td>
<td>5 mg/ kg IV per pharmacy</td>
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<td></td>
<td></td>
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<tr>
<td><strong>PCN allergy, no anaphylaxis</strong></td>
<td></td>
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<tr>
<td>Ceftriaxone</td>
<td>2 gm IV q 24 hrs</td>
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<tr>
<td>and</td>
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<tr>
<td><strong>PCN allergy - anaphylaxis</strong></td>
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<tr>
<td>Vancomycin</td>
<td>1 gm IV q 12 hrs &lt; 80 kg*</td>
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<td>5 mg/ kg IV per pharmacy</td>
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<td></td>
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<tr>
<td>* Consult pharmacy 1.5-2.0 g</td>
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</tbody>
</table>

**Planning a cesarean** | **Add to surgical prophylaxis** |
| Metronidazole | 500 mg IV q 8 hr |

**Post vaginal delivery** | No additional doses |

**Post cesarean delivery** | One additional dose of antimicrobial agents |

**Post-delivery with Intraamniotic infection**
Data suggest that women who have vaginal deliveries are less likely to have endometritis and may not require postpartum antibiotics.

For women undergoing cesarean deliveries, at least one additional dose of antimicrobial agents after delivery is recommended.

However, the presence of other maternal risk factors such as bacteremia or persistent fever in the postpartum period may be used to guide continuation of antimicrobial therapy, duration of antimicrobial therapy, or both in vaginal and cesarean deliveries.

Isolated maternal fever and suspected or confirmed intraamniotic infection should be communicated to neonatal caregivers at birth. Regardless of evolving national recommendations and local variations in approach, such infants will require enhanced clinical surveillance for signs of developing infection.
**B. Endomyometritis**

A patient may also develop a fever after delivery. In terms of infectious morbidity, the first 24 hours are often excluded because isolated low grade fever during this period is common and often resolves spontaneously, especially after vaginal birth.

The infection begins in the decidua, and then may extend into the myometrial and parametrial tissues. As above the infection is polymicrobial, usually involving a mixture of two to three aerobes and anaerobes from the lower genital tract.

There are no characteristic sonographic findings associated with postpartum endometritis.

The time of onset of signs and symptoms depends upon several factors, including whether intrauterine infection developed antepartum, intrapartum, or postpartum and the bacterium or bacteria causing the infection. For example, group A streptococcus (GAS) infection should be suspected in patients with early onset, high fever.

An elevated lactic acid concentration is a marker for serious infection.

**Definition**

Postpartum endomyometritis is defined as a persistent oral temperature of ≥38.0 degrees Celsius (≥100.4 degrees Fahrenheit) with one of the following:

- tachycardia
- midline lower abdominal pain
- uterine tenderness

Other non-specific supporting factors may be:

- Foul lochia, chills, and lower abdominal pain.
- Uterus may be soft and subinvovled, which can lead to excessive uterine bleeding.
- Initial sepsis is an unusual presentation

**Laboratory**

- Leukocytosis is present, but this can be a normal finding in postpartum women secondary to the physiologic leukocytosis of pregnancy and the effects of labor
- Vaginal, cervical, endometrial or uterine cultures are not helpful.
- Blood cultures can be useful in guiding the choice of antimicrobial treatment if the patient fails to respond to empiric therapy, if the patient is immunocompromised, or if the patient is septic

**Differential diagnoses include:**

- Surgical site infection (cesarean delivery incision, episiotomy incision, perineal lacerations)
- Mastitis or breast abscess
- Pyelonephritis
- Aspiration pneumonia
- Unexplained fever with significant back pain after a neuraxial anesthetic, especially when accompanied by neurologic symptoms, may be due to infection or inflammation of the spinal cord.
- Pseudomembranous colitis due to Clostridium difficile is a rare, but potentially serious, cause of postpartum fever. It should be considered in postpartum women who have low-grade fever, abdominal and gastrointestinal symptoms, and recent antibiotic exposure
- Any disorder associated with fever, such as appendicitis or viral syndrome

**Management**
Treatment is indicated for relief of symptoms and to prevent sequelae, such as peritonitis, salpingitis, oophoritis, phlegmon or abscess, and septic pelvic thrombophlebitis. Prompt administration of appropriate antibiotics is critical in septic patients. Treatment is the same, regardless of mode of delivery. (See Table 2)

### Table 2: Treatment of Endomyometritis

<table>
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<tr>
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<tr>
<td>Ceftriaxone</td>
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**Duration**
Continue intravenous treatment until the patient is clinically improved (no fundal tenderness) and afebrile for at least 24 to 48 hours. Oral antibiotic therapy after successful parenteral treatment is not required, as randomized trials have shown that it does not improve outcome.

If bacteremia was present with a positive blood culture, oral antibiotic therapy is indicated after parenteral antibiotics to complete a seven-day total course of antibiotic therapy. If the bacteremia is related to group A streptococcal or staphylococcal infection, then consultation with an infectious disease specialist is advised as a longer course of therapy may be indicated.

**Intravenous access not available**
If intravenous access is not available:
- Amoxicillin-clavulanic acid 875 mg orally every 12 hours OR
- Cefotetan 2 g intramuscularly every 8 hours OR
- Meropenem or imipenem-cilastatin 500 mg intramuscularly every 8 hours OR
- Amoxicillin 500 mg plus metronidazole 500 mg orally every 8 hours

If a prolonged oral antibiotic regimen must be administered for logistics, then use a 14 day course. If an intramuscular antibiotic regimen is used, use 48 to 72 hours of intramuscular therapy and then switch to an oral antibiotic to complete a seven day course.

**Sepsis**
Endomyometritis can progress rapidly to sepsis. Please consult the ANMC Adult Sepsis / Systemic Inflammatory Response (SIRS) guideline.

**References**

Royal College of Obstetricians and Gynaecologists. Sepsis in Pregnancy, Bacterial (Green-top Guideline No. 64a) https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg64a/ (Accessed 8/20/17)

