Intrapartum Management of Intraamniotic Infection

ABSTRACT: Intraamniotic infection, also known as chorioamnionitis, is an infection with resultant inflammation of any combination of the amniotic fluid, placenta, fetus, fetal membranes, or decidua. Intraamniotic infection is a common condition noted among preterm and term parturients. However, most cases of intraamniotic infection detected and managed by obstetrician–gynecologists or other obstetric care providers will be noted among term patients in labor. Intraamniotic infection can be associated with acute neonatal morbidity, including neonatal pneumonia, meningitis, sepsis, and death. Maternal morbidity from intraamniotic infection also can be significant, and may include dysfunctional labor requiring increased intervention, postpartum uterine atony with hemorrhage, endometritis, peritonitis, sepsis, adult respiratory distress syndrome and, rarely, death. Recognition of intrapartum intraamniotic infection and implementation of treatment recommendations are essential steps that effectively can minimize morbidity and mortality for women and newborns. Timely maternal management together with notification of the neonatal health care providers will facilitate appropriate evaluation and empiric antibiotic treatment when indicated. Intraamniotic infection alone is rarely, if ever, an indication for cesarean delivery.

Recommendations
The American College of Obstetricians and Gynecologists (ACOG) makes the following recommendations:

- 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 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.
- For the purposes of this Committee Opinion, the diagnosis of suspected intraamniotic infection is made when the maternal temperature is greater than or equal to 39.0°C or when the maternal temperature is 38.0–38.9°C and one additional clinical risk factor is present.
- For the purposes of this Committee Opinion, isolated maternal fever is defined as any maternal temperature between 38.0°C and 38.9°C with no additional risk factors present, and with or without persistent temperature elevation.
- 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.
- Intraamniotic infection alone is rarely, if ever, an indication for cesarean delivery.
- Regardless of institutional protocol, when obstetrician–gynecologists or other 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.
Background

Intraamniotic infection, also known as chorioamnionitis, is an infection with resultant inflammation of any combination of the amniotic fluid, placenta, fetus, fetal membranes, or decidua. Recently, some authors have suggested changing the name of this condition to “intraamniotic infection and inflammation” to more accurately reflect the full spectrum of the disease process (1). This remains an evolving area, and for the purposes of this document, which focuses on the management of suspected or confirmed infection, the use of the term intraamniotic infection is retained to identify this condition.

Intraamniotic infection often is polymicrobial in origin, commonly involves aerobic and anaerobic bacteria, and frequently originates from the vaginal flora (2). 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). However, most cases of intraamniotic infection detected and managed by obstetrician–gynecologists or other obstetric care providers will be noted among term patients in labor. Estimates suggest that approximately 2–5% of term deliveries are complicated by a clinically apparent intraamniotic infection (3, 4). More recent data suggest that the relative risk for intraamniotic infection and neonatal infection may increase after 40 completed weeks of gestation (3–5).

Intraamniotic infection can be associated with acute neonatal morbidity, including neonatal pneumonia, meningitis, sepsis, and death (3). The use of intrapartum antibiotic treatment given either in response to maternal group B streptococcal colonization or in response to evolving signs of intraamniotic infection during labor has been associated with a nearly 10-fold decrease in group B streptococcal–specific neonatal sepsis (6–8). Decreases in non–group B streptococcal neonatal infections also have been noted (9–11). The protective effect of maternal intrapartum antibiotic administration has been demonstrated in recent multivariate risk models of individual infant risk of neonatal sepsis (5, 12).

Intraamniotic infection can be associated with long-term complications for the infant, such as bronchopulmonary dysplasia and cerebral palsy (13, 14), potentially due to the effect of inflammation alone. A recent meta-analysis of 15 studies found a significantly higher relative risk of cerebral palsy among primarily premature infants exposed to either histologic chorioamnionitis (odds ratio [OR], 1.8; 95% CI, 1.17–2.89) or clinical chorioamnionitis (OR, 2.4; 95% CI, 1.52–3.84) (13). It is nonetheless important to acknowledge that the overall absolute risk of cerebral palsy remains quite low (approximately 2 per 1,000 live births) (15).

Maternal morbidity from intraamniotic infection also can be significant, and may include dysfunctional labor requiring increased intervention, postpartum uterine atony with hemorrhage, endometritis, peritonitis, sepsis, adult respiratory distress syndrome and, rarely, death (16, 17).

Obstetric risk factors for intraamniotic infection at term have been delineated, including low parity, multiple digital examinations, use of internal uterine and fetal monitors, meconium-stained amniotic fluid, and the presence of certain genital tract pathogens (eg, group B streptococcal infection and sexually transmitted infections) (3, 18–20). It should be recognized that many of these proposed risk factors also are associated with longer duration of labor and membrane rupture, and may not be independently associated with intraamniotic infection. For example, a recent retrospective investigation of more than 2,000 parturients specifically analyzed the number of cervical examinations performed during labor and found that women who developed an intrapartum fever had more digital cervical examinations than women who did not (21). However, this relationship was not significant after adjusting for spontaneous labor, the Bishop score, and rupture of membranes on admission.

Maternal intraamniotic infection is reasonably sensitive but lacks specificity with regard to the diagnosis of neonatal sepsis, particularly among preterm infants. Multivariate risk models for predicting neonatal sepsis among term and late-preterm infants have been developed based on objective data, including gestational age, duration of rupture of membranes, highest maternal intrapartum temperature, group B streptococcal colonization, and the type and timing of intrapartum antibiotic administration (5, 12, 22). These neonatal sepsis risk models do not affect maternal intrapartum management, but the use of maternal intrapartum data underscores the importance of communication with pediatric care providers as well as of appropriate maternal medical record documentation.

Presumptive Diagnosis of Intraamniotic Infection

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 a recent executive summary of proceedings from a joint workshop sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the Society for Maternal–Fetal Medicine, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists, a panel of maternal and neonatal experts recommended separating intraamniotic infection into three different categories: 1) isolated maternal fever,
2) suspected intraamniotic infection, and 3) confirmed intraamniotic infection (1). The new definitions distinguish suspected and confirmed intraamniotic infection according to clinical and laboratory/pathologic findings, and provide standardized temperature criteria to diagnose intrapartum fever. According to the expert workshop executive summary, isolated maternal fever is defined as either a single oral temperature of 39°C or greater, or an oral temperature of 38–38.9°C that persists when the temperature is repeated after 30 minutes. Suspected intraamniotic infection is based on clinical criteria, which include maternal intrapartum fever and one or more of the following: maternal leukocytosis, purulent cervical drainage, or fetal tachycardia. Confirmed intraamniotic infection is based on a positive amniotic fluid test result (gram stain, glucose level, or culture results consistent with infection) or placental pathology demonstrating histologic evidence of placental infection or inflammation. 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. Although the expert workshop executive summary included patients with temperature 39°C or greater with no other clinical risk factors present in the isolated maternal fever group, it is the opinion of the Committee on Obstetric Practice that absent an obvious alternative source, these patients be included in the suspected intraamniotic infection group. The American College of Obstetricians and Gynecologists’ recommendation optimizes sensitivity given that markedly elevated maternal temperatures are most likely due to infection, while transient lower temperature elevations may be due to infection or may be spurious, or related to noninfectious factors such as dehydration or epidural analgesia (23–25).

Management of Suspected or Confirmed Intraamniotic Infection

As demonstrated in a randomized clinical trial, intrapartum antibiotic therapy for intraamniotic infection decreases the rate of neonatal bacteremia, pneumonia, and sepsis (26). Multivariate models of neonatal sepsis risk demonstrate the positive effect of intrapartum antibiotics on the risk of culture-confirmed neonatal infection (5, 12). 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 (26). Antipyretics should be administered in addition to antibiotics. Proper labor progression should be ensured, given the association between intraamniotic infection and dysfunctional labor progression (3, 16, 17, 27). 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.

Management of Isolated Maternal Fever

For the purposes of this document, isolated maternal fever is defined as any temperature between 38°C and 38.9°C with no other clinical criteria indicating intraamniotic infection, and with or without persistent temperature elevation. In clinical care, an isolated maternal fever is a common scenario facing obstetrician–gynecologists or other obstetric care providers and, even absent additional criteria or persistent temperature elevation (as defined in the expert workshop executive summary), in practice clinicians often choose to treat for intraamniotic infection. Few data exist to guide appropriate management of women with isolated intrapartum fever in the absence of other clinical signs suggesting intraamniotic infection. Isolated intrapartum fever alone, whether due to infection or not, also has been associated with poor short-term and long-term neonatal outcomes (28–30). The exact mechanism of such an effect remains unclear, although fetal hyperthermia (and associated changes in metabolic rate) is hypothesized to potentiate the negative effects of tissue hypoxia. Prospective, randomized controlled studies are needed to better guide management of isolated intrapartum fever. Currently, 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. In some settings, this approach may result in increased awareness and diagnosis of intraamniotic infection, which will affect subsequent management of newborns. Whether or not a decision is made to initiate intrapartum antimicrobial therapy, the occurrence of maternal intrapartum fever should be communicated to the neonatal care team. Newer pediatric recommendations rely less on the clinical diagnosis of suspected intraamniotic infection, and more on consideration of a variety of risk factors and newborn clinical status to determine neonatal management.

Postdelivery Recommendations

Intrapartum antimicrobial agents administered for suspected or confirmed intraamniotic infection should not be continued automatically postpartum; rather, extension of antimicrobial therapy should be based on risk factors
for postpartum endometritis (31–34). Data suggest that women who have vaginal deliveries are less likely to have endometritis and may not require postpartum antibiotics (32). 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.

Common antibiotic choices for treatment of suspected intraamniotic infection are listed in Table 1. Obstetricians–gynecologists and other obstetric care providers also should consider consulting their local microbiology laboratory and infectious disease experts to ascertain whether there are alternative recommended regimens based on local antibiotic resistance patterns.

Table 1. Recommended Antibiotic Regimens for Treatment of Intraamniotic Infection

<table>
<thead>
<tr>
<th>Recommended Antibiotics</th>
<th>Primary Regimen</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Ampicillin and Gentamicin</td>
<td>2 g IV every 6 hours</td>
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</tr>
<tr>
<td>Ampicillin–sulbactam</td>
<td>3 g IV every 6 hrs</td>
<td></td>
</tr>
<tr>
<td>Cefazolin and Gentamicin</td>
<td>2 g IV every 8 hours</td>
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</tr>
<tr>
<td>Cefazolin and Gentamicin</td>
<td>2 mg/kg IV load followed by 1.5 mg/kg every 8 hours or 5 mg/kg IV every 24 hours</td>
<td></td>
</tr>
<tr>
<td>Cefotetan</td>
<td>2 g IV every 12 hrs</td>
<td></td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>2 g IV every 8 hrs</td>
<td></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1 g IV every 24 hrs</td>
<td></td>
</tr>
<tr>
<td>Ampicillin–sulbactam</td>
<td>3 g IV every 6 hrs</td>
<td></td>
</tr>
<tr>
<td>Piperacillin–tazobactam</td>
<td>3.575 g IV every 8 hrs</td>
<td></td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>2 g IV every 8 hrs</td>
<td></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1 g IV every 24 hrs</td>
<td></td>
</tr>
</tbody>
</table>

Postcesarean delivery: One additional dose of the chosen regimen is indicated. Add clindamycin 900 mg IV or metronidazole 500 mg IV for at least one additional dose.

Postvaginal delivery: No additional doses required; but if given, clindamycin is not indicated.

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
</tr>
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<tbody>
<tr>
<td>Clindamycin or Vancomycin* and Gentamicin</td>
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| Postcesarean delivery: One additional dose of the chosen regimen is indicated. Additional clindamycin is not required.
| Postvaginal delivery: No additional doses required, but if given, clindamycin is not indicated. |

Abbreviation: IV, intravenous.

*Vancomycin should be used if the woman is colonized with group B streptococci resistant to either clindamycin or erythromycin (unless clindamycin-inducible resistance testing is available and is negative) or if the woman is colonized with group B streptococci and antibiotic sensitivities are not available.
**Neonatal Implications of an Intraamniotic Infection Diagnosis**

The Centers for Disease Control and Prevention and the American Academy of Pediatrics provide guidelines for assessing risk of neonatal infection (7, 35–37). These guidelines recommend laboratory studies and empiric antibiotic therapy for all newborns delivered from women with a suspected or confirmed intraamniotic infection. Currently such recommendations are being re-evaluated (1, 38). Recent data on the development of the neonatal microbiome and the role of early antibiotic exposures suggest that antibiotic therapy may not be entirely benign (39–46). Multivariate risk assessment and increased reliance on clinical observation may safely decrease the number of well-appearing term newborns treated empirically with antibiotics (5, 12, 22). In all cases, 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 always will require enhanced clinical surveillance for signs of developing infection.

**Conclusion**

Intraamniotic infection is a common condition noted among preterm and term parturients. Recognition of intrapartum intraamniotic infection and implementation of the treatment recommendations are essential steps that can effectively minimize morbidity and mortality for women and newborns. Timely maternal management together with notification of the neonatal health care providers will facilitate appropriate evaluation and empiric antibiotic treatment when indicated. Intraamniotic infection alone is rarely, if ever, an indication for cesarean delivery.

**References**

This information is designed as an educational resource to aid clinicians in providing obstetric and gynecologic care, and use of this information is voluntary. This information should not be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations in practice may be warranted when, in the reasonable judgment of the treating clinician, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology. The American College of Obstetricians and Gynecologists reviews its publications regularly; however, its publications may not reflect the most recent evidence. Any updates to this document can be found on www.acog.org or by calling the ACOG Resource Center.

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