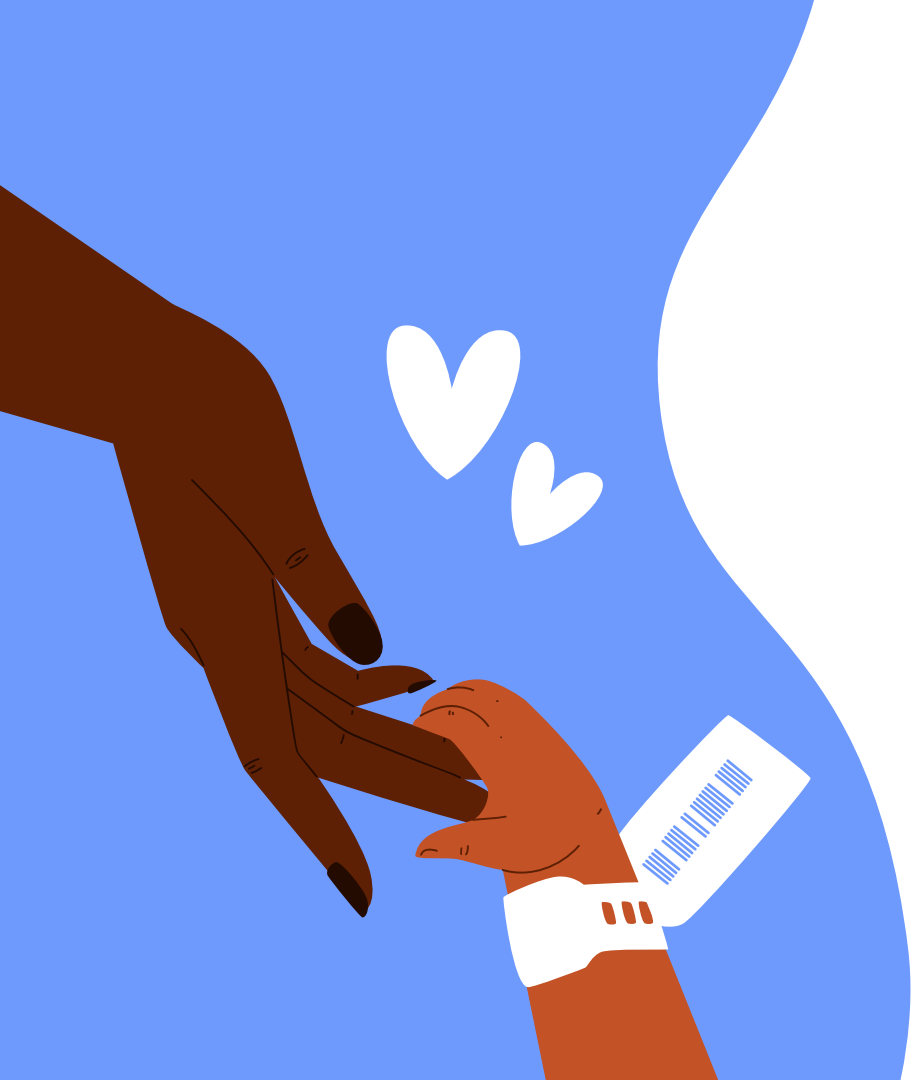


# Management of Clinical Chorioamnionitis: An Evidence-Based Approach

American Journal of Obstetrics and Gynecology
Expert Review

# Introduction

Clinical chorioamnionitis is **the most common infection-related complication** in labor and delivery units worldwide, affecting 1–6% of pregnancies in the United States.

# Maternal & Fetal adverse Outcome

## Maternal

postpartum hemorrhage
secondary to uterine atony.
uterine rupture
unplanned hysterectomy
blood transfusion
postoperative wound infection.
Endometritis.
pelvic abscess.
septic pelvic thrombophlebitis.
Sepsis.
and intensive care unit
admission, among others.

## Fetal

low Apgar scores at 5 minutes.
neonatal seizures.
neonatal sepsis.
bronchopulmonary dysplasia.
intraventricular hemorrhage
(IVH).
periventricular leukomalacia.
use of mechanical ventilation.
admission to the neonatal
intensive care unit (NICU).
neonatal death,
and long-term infectious
morbidity.

# Clinical chorioamnionitis has been traditionally diagnosed by:

the presence of maternal fever (temperature ≥37.8ºC or ≥38.0ºC) plus two or more of the five following clinical signs:

- maternal tachycardia (heart rate >100 beats/min)
- fetal tachycardia (heart rate >160 beats/min)
- uterine tenderness
- purulent or foul-smelling amniotic fluid or vaginal discharge
- maternal leukocytosis (white blood cell count >15,000/mm3)

The diagnostic accuracy of these criteria to identify patients with proven intra-amniotic infection is about 50%.

## Clinical chorioamnionitis as a syndrome:

Patients diagnosed with clinical chorioamnionitis at term can be classified into 3 groups according to the results of amniotic fluid analysis of bacteria and inflammation:

01

**intraamniotic infection 65%**

ie, the presence of microorganisms and intraamniotic inflammation detected by culture and PCR

02

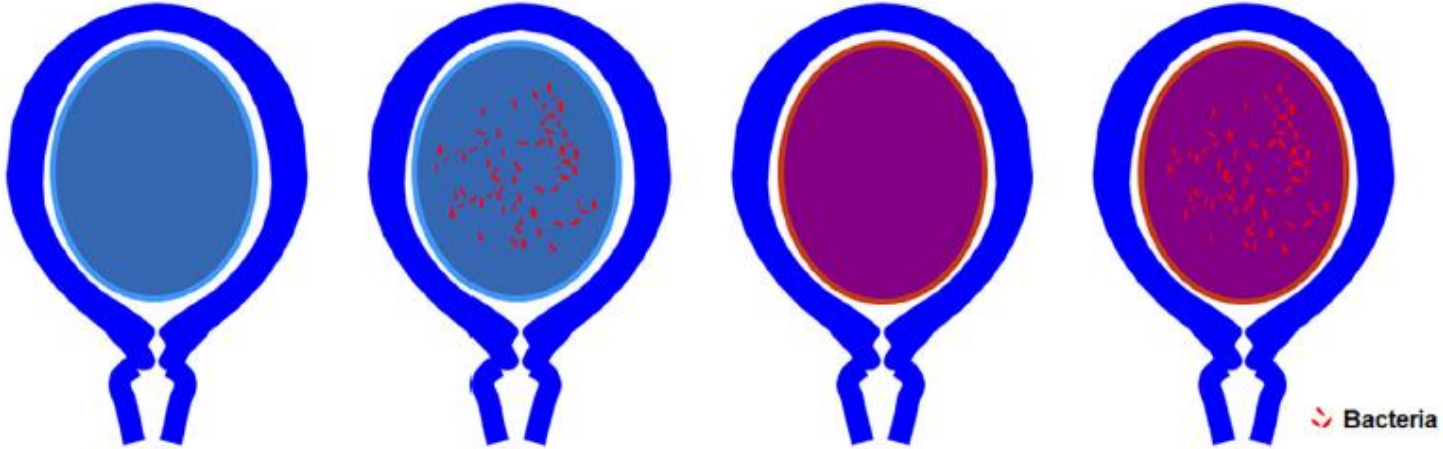
**sterile intraamniotic inflammation 15%**

the presence of inflammatory cells (white blood cell count more than 50 cells/mm3) or by an elevated concentration of a biomarker of inflammation (eg, an interleukin-6 concentration more than 2.6 ng/mL).

03

**maternal signs or symptoms of systemic inflammation without evidence of intraamniotic inflammation or intraamniotic Infection 20%**

The etiology is unclear and has been attributed to a neuroinflammatory process after the administration of epidural analgesia.




| | No intraamniotic infection | Microorganisms in amniotic fluid without intraamniotic inflammation | Sterile intraamniotic inflammation | Intraamniotic infection |
|---|---|---|---|---|
| Microorganisms in amniotic fluid | No | Yes | No | Yes |
| Intraamniotic inflammation | No | No | Yes | Yes |

# Whoa!

In 2015, an expert panel proposed to replace the term clinical chorioamnionitis with the term “**intrauterine inflammation or infection or both**”, abbreviated as “**Triple I**”. However, this proposal has not gained popularity because it implies that the inflammatory status of the amniotic cavity and the presence of microorganisms have been established, and this is rarely the case. Therefore, we continue to use the term “**clinical chorioamnionitis**” to refer to this syndrome.

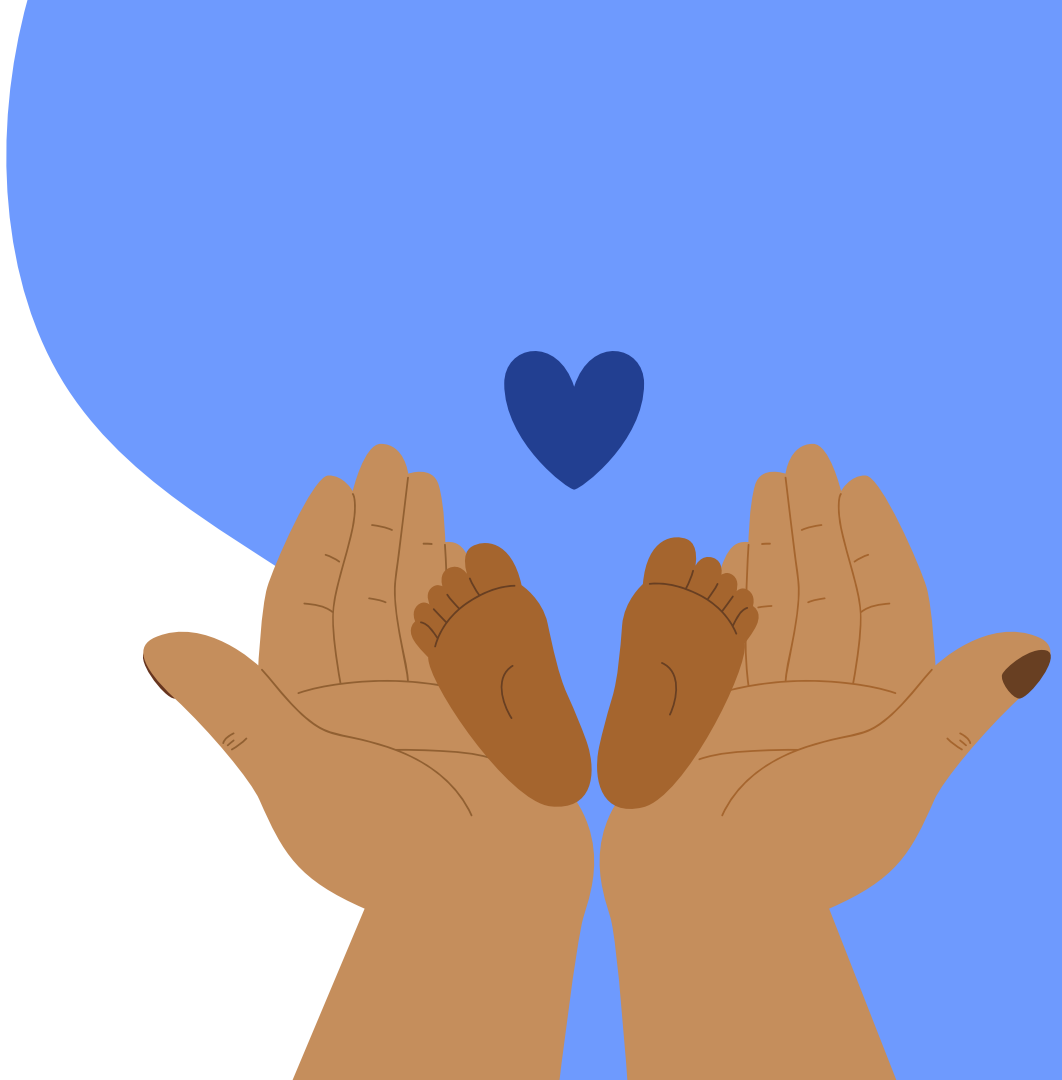
# The standard treatment for clinical chorioamnionitis has been:

- Antibiotics.
- Antipyretics.
- expedited delivery.

01

# Antibiotics

Timing of antibiotic therapy initiation

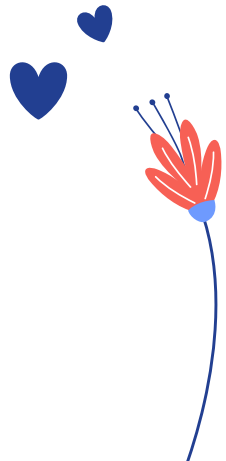


# Timing of antibiotic therapy initiation

Evidence suggests that antibiotic administration should be initiated in the intrapartum period when the diagnosis of clinical chorioamnionitis is made.

The antimicrobial agents used are ampicillin and gentamicin.
Patients who undergo cesarean delivery also receive clindamycin after cord clamping to extend coverage for anaerobic organisms.

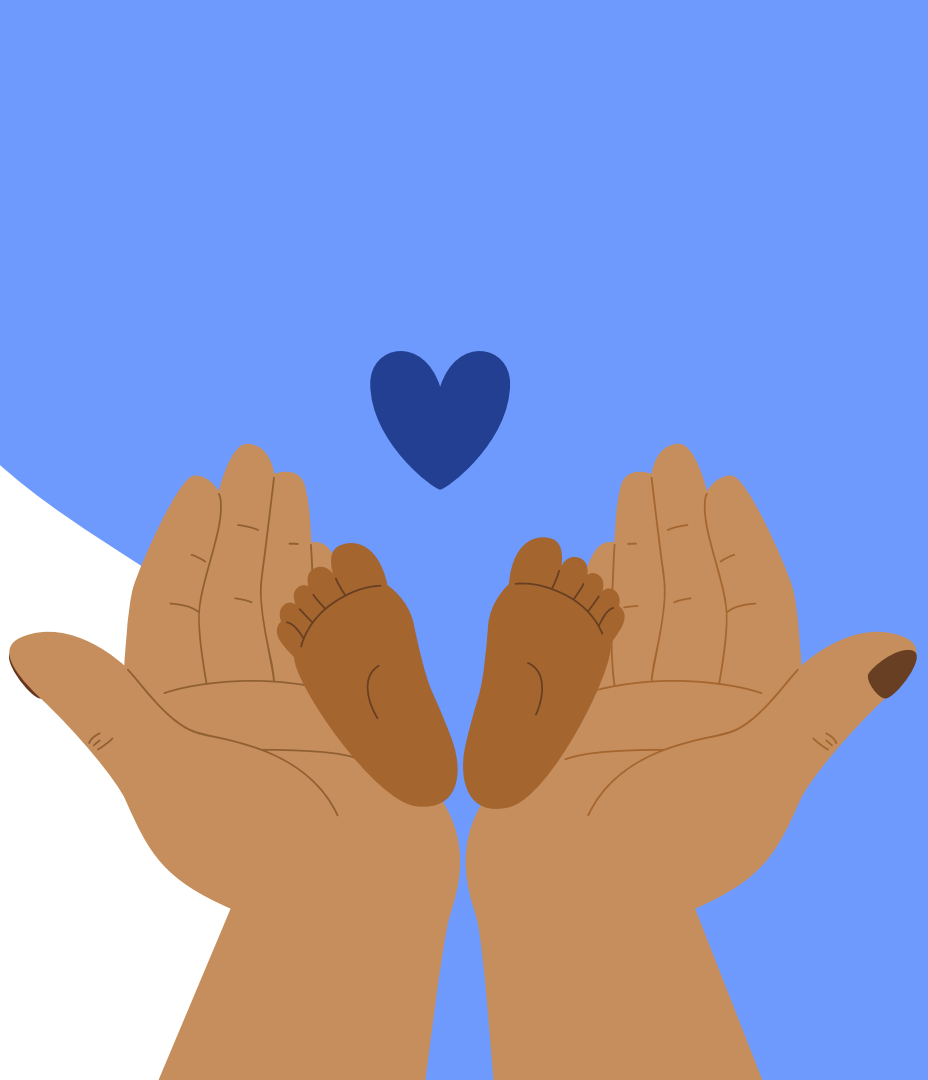
Intrapartum antibiotic treatment was associated with a significant reduction in the frequency of neonatal pneumonia or sepsis, and a decrease in neonatal hospital stay, maternal postpartum hospital stay, and maternal febrile days.



01

# Antibiotics

Selection of antibiotics and regimens

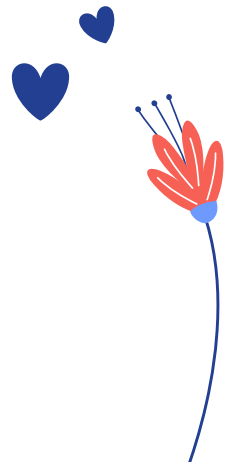


# Selection of antibiotics and regimens

There were no significant differences in maternal and neonatal infectious morbidity between the antibiotic regimens assessed in deferent trials.

Ampicillin 2 g intravenously (IV) every 6 hours combined with Gentamicin 1.5–2.0 mg/kg IV every 8 hours or 4.0–5.0 mg/kg IV every 24 hours. Patients who undergo cesarean delivery also receive clindamycin at the time of umbilical cord clamping (usually 900 mg IV single dose)

The second most frequently used antibiotic regimen during the intrapartum period was ampicillin/sulbactam 3 g IV every 6 hours.

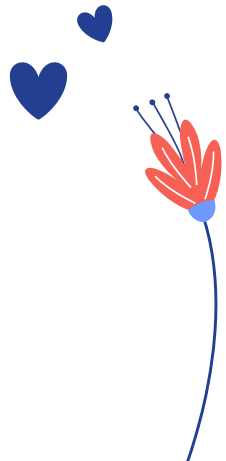


# Selection of antibiotics and regimens

Based on expert opinion, metronidazole 500 mg IV has been proposed as an alternative to clindamycin in the event of cesarean delivery.

Ureaplasma species are the most common microorganisms isolated from the amniotic fluid of patients with clinical chorioamnionitis. The antibiotics that were used in the randomized controlled trials  do not provide coverage against Ureaplasma species and mycoplasma species.

Recently, the successful use of an antibiotic regimen, i.e., ceftriaxone 1 g IV every 24 hours, clarithromycin 500 mg orally every 12 hours, and metronidazole 500 mg IV every 8 hours, has been reported among women with (PROM), and a subset of patients with confirmed intra-amniotic infection/inflammation and preterm labor with intact membranes or cervical insufficiency



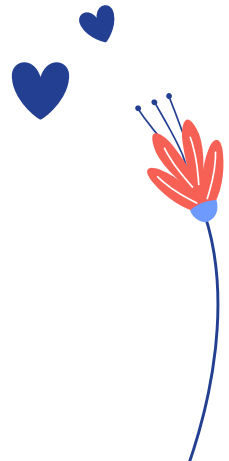
# Selection of antibiotics and regimens

The rationale for using this antibiotic regimen was as follows: clarithromycin for its much higher rate of transplacental passage than erythromycin or azithromycin and its effectiveness against Ureaplasma species and mycoplasma species;

ceftriaxone for its enhanced coverage of aerobic bacteria and high rate of transplacental passage;

and metronidazole for its optimal coverage of anaerobic microorganisms.

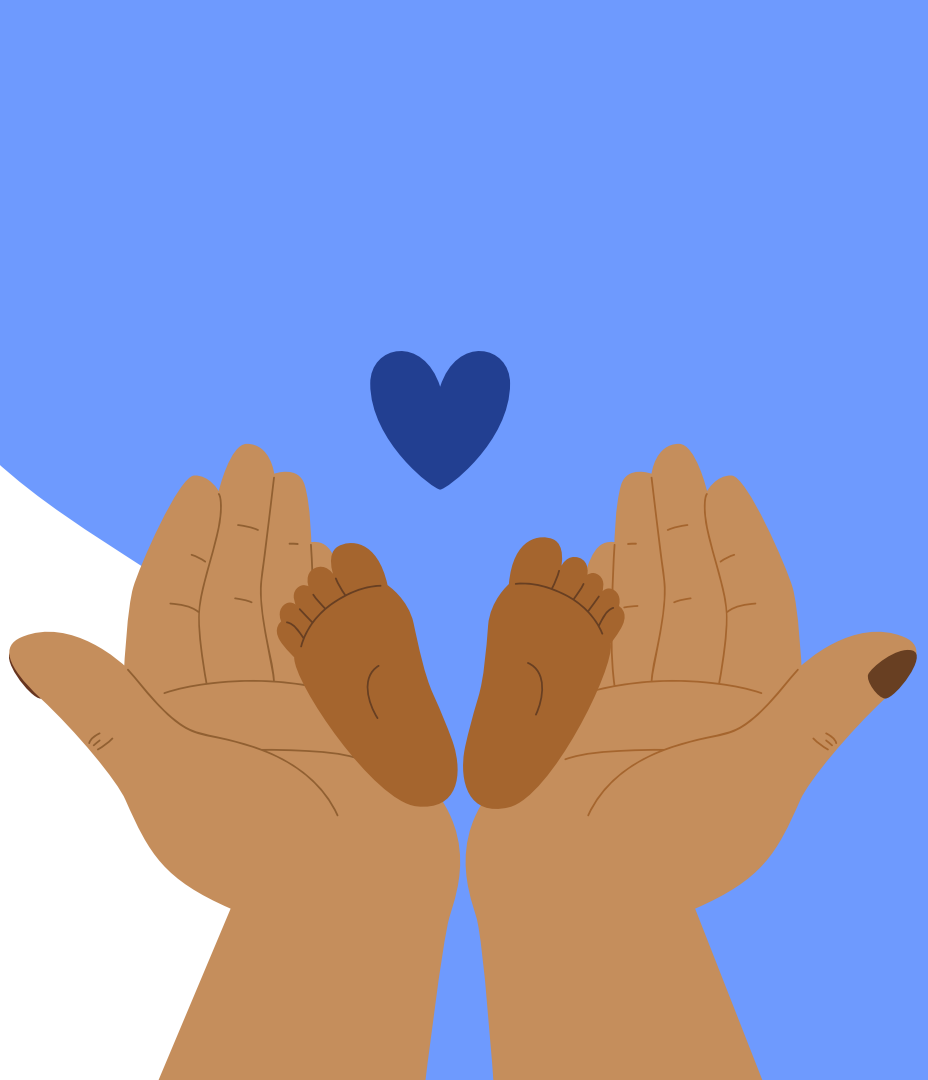
We believe that this new antibiotic regimen, using clarithromycin 500 mg IV (instead of orally) every 12 hours, should be the subject of study in patients with clinical chorioamnionitis given the high concordance between microorganisms associated with clinical chorioamnionitis and those associated with confirmed infection/inflammation and preterm PROM.



01

# Antibiotics

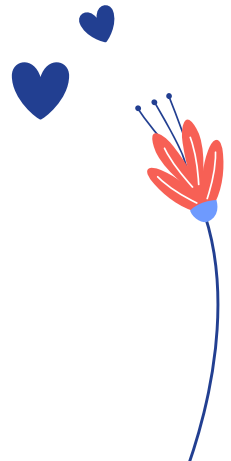
Use of antibiotics after delivery



# Use of antibiotics after delivery

Even though there is limited information to guide the appropriate use of antibiotics after delivery in patients with clinical chorioamnionitis, current evidence suggests that antibiotic administration **may not be necessary after vaginal or cesarean delivery**. However, if post-delivery antibiotics are prescribed**, one additional dose of the antibiotic regimen appears to be as effective as continued use of antibiotics** to reduce the risk of maternal infection.

A longer duration of antibiotic therapy may be required in patients with persistent fever, bacteremia, or sepsis in the postpartum period.



# 02

# Antipyretics

## Maternal intrapartum fever has been associated with a higher frequency of:

01

**Fetal tachycardia**

02

**intervention for non-reassuring electronic fetal monitoring**

03

**operative vaginal delivery**

04

**Cesarean delivery**

05

**Neonatal,**

Depression
Seizures
Encephaopathy

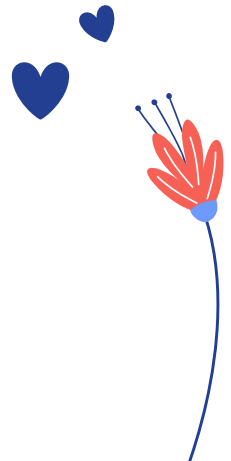
06

**NICU admission**

# Antipyretics

Acetaminophen has been the most recommended antipyretic in patients with clinical chorioamnionitis.
It can be administered orally, rectally, or IV.
Serum peak levels (~12 µg/ml) and half-life (~1.5 hours) of acetaminophen in pregnant women are similar to those in non-pregnant adults.
The conventional oral dose of acetaminophen is 325–650 mg every 4–6 hours; total daily doses should not exceed 4 g.

There is no clear evidence that the treatment of intrapartum fever reduces the risk of adverse obstetric and neonatal outcomes. Nevertheless, antipyretics, mainly acetaminophen, have been used to treat hyperthermia in patients with clinical chorioamnionitis.



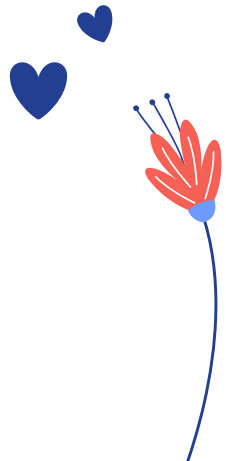
# 03

# Antenatal corticosteroids

# Antenatal corticosteroids

Current available evidence suggests that the administration **of at least one single dose of ACS** to patients with clinical chorioamnionitis has an overall **beneficial effect** on the neonate without increasing the risk of sepsis or other adverse neonatal outcomes.
Thus, it appears reasonable to administer ACS to women with clinical chorioamnionitis between 24 0/7 and 33 6/7 weeks of gestation and to consider its administration to those with a gestational age between 23 0/7 and 23 6/7 weeks.

**Delivery should not be delayed in order to complete the full course of ACS**.



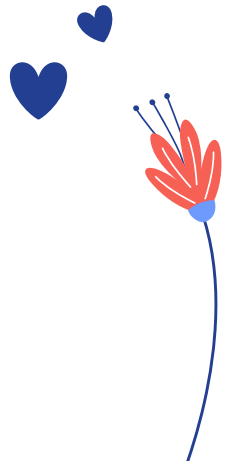
# 04

# Magnesium sulfate for fetal neuroprotection

# Magnesium sulfate for fetal neuroprotection

The current evidence supports the administration of antenatal magnesium sulfate to women with clinical chorioamnionitis between 24 0/7 and 33 6/7 weeks of gestation for preventing cerebral palsy in their offspring. It also may be considered for women with a gestational age between 23 0/7 and 23 6/7 weeks.

Delivery should not be delayed in order to administer the full course of antenatal magnesium sulfate for fetal neuroprotection.



# 05

# Management of labor

# Mode of Delivery

**Clinical chorioamnionitis, regardless of antibiotic therapy type and duration, was associated with a significantly increased risk of adverse maternal outcomes among women who had a cesarean delivery but not among women who had a vaginal delivery**

Once a diagnosis of clinical chorioamnionitis has been established, delivery should be considered, regardless of the gestational age.

Clinical chorioamnionitis alone is not an indication for cesarean delivery.

Unless contraindicated, induction and trial of labor can be considered.

Vaginal delivery is the safer option and cesarean delivery should be reserved for standard obstetric indications

# Duration of chorioamnionitis and adverse maternal and neonatal outcomes

**The time interval between the diagnosis of clinical chorioamnionitis and delivery is not related to the risk of most adverse maternal and neonatal outcomes**

there is no evidence supporting that immediate delivery after the diagnosis of clinical chorioamnionitis prevents adverse maternal and neonatal outcomes, or long-term neurodevelopmental outcomes.

On the contrary, such an approach would lead to an increase in the frequency of cesarean delivery and, therefore, to an increased risk of adverse maternal outcomes.

# Labor progression

**Women with clinical chorioamnionitis are more likely to have abnormal labor progression or prolonged labor**
**and cesarean delivery for failure to progress or non-reassuring fetal heart rate tracing**

the available evidence supports the hypothesis that clinical chorioamnionitis is associated with reduced uterine contractility.

an in vitro study performed in the early 80s showed that bacteria causing chorioamnionitis, such as anaerobic streptococcus species, Veillonella species, Bacteroides species, and enterococcus faecalis, reduce the contractility of human myometrial tissue and its responsiveness to oxytocin

# Continuous electronic fetal heart rate monitoring

**The most common fetal heart rate (FHR) patterns observed in clinical chorioamnionitis include tachycardia, absence of accelerations, presence of variable and late decelerations, and persistently reduced variability.**

the management of intrapartum fetal heart rate tracings in patients with clinical chorioamnionitis does not differ from that in patients without clinical chorioamnionitis

It is worth noting that isolated fetal tachycardia is a poor predictor of fetal hypoxemia or acidemia, unless accompanied by minimal or absent FHR variability or recurrent decelerations or both, and is not an indication for immediate operative delivery.

# 05

# Promising Interventions

# Vaginal cleansing with antiseptic solutions before cesarean delivery

**Evidence from three recent meta-analyses supports that vaginal cleansing with antiseptic solutions before cesarean delivery reduces postoperative infectious morbidity.**

A network meta-analysis showed that **povidone-iodine 1%** had the highest probability of being the most effective treatment for the prevention of **endometritis** and chlorhexidine had the highest probability for the best agent for the prevention of wound infection.

# Summary

# Here are three important ideas

The first-line antimicrobial regimen for the treatment of clinical chorioamnionitis is **ampicillin combined with gentamicin**, which should be initiated during the **intrapartum period**. In the event of a cesarean delivery, patients should receive **clindamycin** at the time of umbilical cord clamping.

delivery should not be delayed in order to complete the full course of corticosteroids and magnesium sulfate.

Once the diagnosis of clinical chorioamnionitis has been established, delivery should be considered, regardless of the gestational age. Vaginal delivery is the safer option

# Thanks!

## Resources

Am J Obstet Gynecol. 2020 December ; 223(6): 848–869. doi:10.1016/j.ajog.2020.09.044
Clinical chorioamnionitis at term: definition, pathogenesis, microbiology, diagnosis, and treatment. https://doi.org/10.1016/j.ajog.2023.02.002

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