LISTERIA AND PREGNANCY

Dr Laura Guirado, Dr Montse Palacio

1. DESCRIPTION OF PATHOGEN, MATERNAL SYMPTOMS, EPIDEMIOLOGY

Listeria monocytogenes is a facultative, intracellular, anaerobic Gram-positive rod. It is an intracellular microorganism, which is why, in cases of cell-mediated immune deficiency, such as during gestation, there is a higher susceptibility for the infection, especially in the third trimester.

The infection is generally transmitted through the consumption of contaminated food (the rod presents resistance to low temperatures) – phagocytosis by gastrointestinal cells – intracellular proliferation, transplacental intracellular transmission. *Listeria monocytogenes* has **a strong tropism for the placenta**. The most frequently contaminated foods are pre-cooked meat products, non-pasteurised milk and other milk products, and shellfish (***Annex 2***).

The incidence of the infection has increased significantly in recent years, rising from 0.2 to 0.8 per 1000 births since 2002. The incubation period is variable, ranging from 1 to 90 days.

The infection is seasonal, having a higher incidence during summer. The infection can appear as an isolated case or as a small epidemic outbreak.

In pregnant women, the infection causes **fever and flu-like illness**. 20% of cases may present with digestive symptoms and abdominal pain before the fever. 29% of cases are asymptomatic. Most of the infections in immunocompetent pregnant women are mild and self-limiting but can cause **severe fetal effects**. The infection by listeria is an underdiagnosed infection.

2. CONGENITAL INFECTION FOR LISTERIA

Globally, the infection by listeria accounts for **30% of fetal or neonatal deaths.**

When the infection occurs in the **first or second trimester** (20% of cases) it causes **septic abortions and intrauterine fetal demise**. If the infection occurs in the third trimester (80% of cases) it causes **chorioamnionitis**

and preterm delivery in 2/3 of cases, with a 20% perinatal mortality rate. In 1/3 of cases it might be asymptomatic for the fetus/neonate

Neonatal sepsis by listeria:

- **Early** (intrauterine acquisition by hematogenous spread or by infected amniotic fluid deglutition): this is the most common. Symptoms appear during the first and second day of life (<7 days). In general, neonates are born premature from mothers with fever and meconium-stained amniotic fluid. The most frequent neonatal symptoms are: respiratory distress and pneumonia. Up to 20-30% of cases have a fatal outcome.

- **Late** (acquisition through delivery or postnatal acquisition): symptoms appear from 7 days of life. In general, newborns are born at term from asymptomatic carrier mothers. Most frequent symptom: meningitis

There is no relation between infection by listeria and recurrent miscarriages.

3. DIAGNOSIS

Maternal infection can be difficult to diagnose due to unspecific systemic manifestations.

- In the **first and second trimester** the main symptom is **fever ≥ 38ºC** with no other focus. Gastrointestinal symptoms are uncommon (20%) and usually precede the fever.

- During the **third trimester** the infection appears as a **clinical chorioamnionitis** (maternal fever >37.8º, maternal tachycardia (>100 beats/minute), fetal tachycardia (>160 beats/minute), uterine irritability (pain and/or uterine contractions)

Diagnostic confirmation is only possible with fluids or sterile tissue **cultures** (blood, neonatal cerebrospinal fluid, amniotic fluid or placenta).

Symptomatic maternal infection presents analytic parameters that point to bacterial aetiology: leukocytosis with neutrophilia (81%), leukocyte formula deviation with presence of young form** cells (50%). **C-reactive protein** (CRP) is the most sensitive parameter and is high in almost all cases.

The study of a pregnant woman with fever **≥ 38ºC (ruling out other possible causes or focus of infection)** must include a blood test including blood count and CRP. An increase of CRP with leukocytosis without other focus should be approached as listeria infection and a blood culture must be performed at fever spike. When chorioamnionitis is suspected, an **amniocentesis** is indicated if it is feasible for microbiological (Gram and

culture) and biochemical study. It is important to remark that the detection rate of the germ with Gram stain is only 33%, due to it being an intracellular germ and easily confused with diplococcus, diphtheroidsand Haemophilus. Stool culture and urogenital cultures have low clinical relevance. The isolation of the microorganism in the genital tract is exceptional and the isolation in the fecal sample does not mean a clinical infection (between 1 and 15% are healthy carriers).

4. TREATMENT

The objective of the treatment is to improve fetal and neonatal evolution. Early and appropriate treatment can improve the evolution and might reverse the process. In contrast to other causes of chorioamnionitis where induction of labour is indicated, infection by listeria can be treated to reach gestation at term without complications.

The antibiotic must act at the intracellular level and cross the placenta to be effective. For this reason, it should be given at a **high dose** and for a long period of time. **Ampicillin** is the elective treatment but amoxicillin and penicillin have also shown to be effective. The association with gentamicin has a synergic effect. *Listeria monocytogenes* is resistant to cephalosporin and clindamycin. In cases of penicillin allergy, the elective treatment during pregnancy is erythromycin.

4.1 HOSPITAL TREATMENT:

In the case of a pregnant woman with **fever, no other focus** and elevation of CRP (**≥ 5 mg/dl**), it is indicated to start empirical intravenous antibiotic therapy until blood culture and/or amniotic fluid culture results:

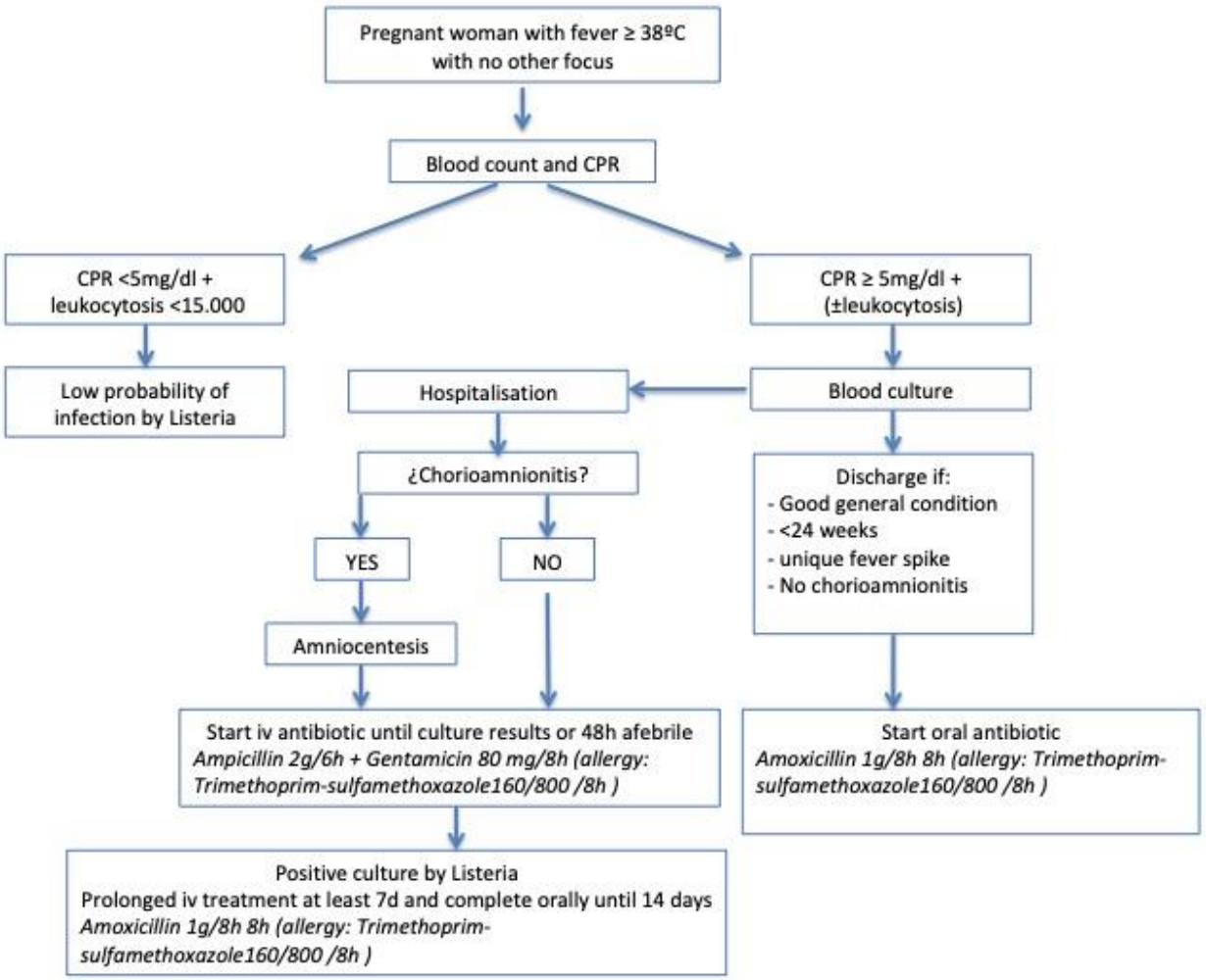
- **Ampicillin 2g/6h iv + Gentamicin 80mg/8h** iv (synergic effect and covers other possible germs)
- In cases of penicillin allergy the best alternative is **Trimethoprim-sulfamethoxazole 160/800mg/ 8h** iv
- When the infection is confirmed (positive culture) the therapy should be prolonged at least **7 days intravenously**, and in cases with fetal surveillance **at least 14 days**. From 7 days of treatment, and if the patient remains asymptomatic, intravenous therapy can be switch to oral therapy (**Amoxicillin 1g/8h; if allergy: Trimethoprim-sulfamethoxazole 160/800mg/ 8h)**. In cases of stillbirth or delivery, the maternal treatment should be prolonged until 14 days. Intravenous therapy can be switched to oral therapy after 48 hours afebrile.

If the culture is not positive after 48 h of being afebrile (low probability of infection by listeria), intravenous therapy can be switched to oral treatment (**Amoxicillin 1g/8h; if allergy: Trimethoprim-sulfamethoxazole 160/800mg/ 8h)** until the definitive result.

4.2. OUTPATIENT TREATMENT

The pregnant woman should be **hospitalised** if infection by listeria is suspected (fever without other focus with CPR >5mg/dl) to start **intravenous antibiotic treatment** as soon as possible until the culture results or until 48h after being afebrile if the cultures are not available. However, in **selected cases** (maternal good general condition, gestational age <24 weeks, unique fever spike, clinical absence of chorioamnionitis), the **patient can be discharged from the hospital under treatment with Amoxicillin 1g/8h orally or Trimethoprim-sulfamethoxazole 160/800mg/ 8h in case of allergy** until the result of the blood culture. If the culture is positive, the treatment must be prolonged at least 14 days, evaluating the need for hospitalisation for intravenous therapy according to the symptoms. In those cases for which you cannot verify fever in the emergency room (with no other focus and CPR >5mg/dl) and it's not possible to obtain a blood culture sample, the patient can remain in observation or can be discharged under treatment (Amoxicillin 1g/8h orally) with clear instructions to attend to the emergency room in case of a new fever spike and a clinical check in 48-72 hours.

ANNEX 1: DIAGNOSTIC ALGORITHM IN CASE OF SUSPECTED INFECTION BY LISTERIA



ANNEX 2: HIGH RISK CONSUMER ADVICE (IMMUNOCOMPROMISED PREGNANT WOMEN)

Listeria is a heat- and cold-resistant microorganism that replicates at temperatures between 4ºC and 45ºC. Low temperatures slow down its growth, but it is not destroyed by freezing. Listeria is only destroyed by high temperatures >50ºC. It can survive in salty preserved foods.

AVOID EATING	YOU CAN EAT
Hot dogs and ready-to-eat luncheon meats	Hot dogs and ready-to-eat luncheon meats if they are heated until steaming hot just before serving
Unpasteurised milk and foods made with unpasteurised milk	Pasteurised milk and foods made with pasteurised milk
Soft cheeses (feta, brie, camembert, blue-veined cheese, Mexican-style cheese such as queso blanco fresco)	Hard cheese, semi-soft cheese (mozzarella), pasteurised processed cheeses such as slices and spreads; cream cheese; and cottage cheese.
Refrigerated pâté and meat spreads	Canned or shelf-stable pâtés and meat spreads.
Refrigerated smoked seafood	Canned or shelf-stable smoked seafood
Unwashed raw produce such as fruits and vegetables	Washed fruits and vegetables

RECOMMENDATIONS TO AVOID BACTERIAL FOOD CONTAMINATION

CLEAN:

Wash your hands before, during and after handling food.

Wash utensils, cutting boards, and any surfaces that food touches after each use.

Wash fruits and vegetables-but not meat, poultry, or eggs.

SEPARATE:

Use separate cutting boards, plates, and utensils for raw (uncooked) produce and for raw (uncooked) meat, poultry, seafood, and eggs.

Keep meat, poultry, seafood and eggs separate from all other foods while shopping and in the refrigerator.

COOK:

Make sure meat, poultry, fish and casseroles are cooked >145ºF (> 50 ºC)

CHILL:

Use appliance thermometers to be sure your refrigerator is at or below 40ºF (4ºC) and your freezer is 0ºF (-18ºC) or below.

Between 40ºF (4ºC) and 140ºF (60ºC) is the danger zone

Adapted from "Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration"

If you are pregnant and have symptoms compatible with infection by listeria, contact your medical centre.