

# *Listeria* infection in pregnancy: A potentially serious foodborne illness

In pregnant women and immunocompromised individuals, listeriosis can be devastating, and it poses major danger to the developing fetus

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## **CASE Pregnant patient with concerning symptoms of infection**

A 28-year-old primigravid woman at 26 weeks' gestation requests evaluation because of a 3-day history of low-grade fever (38.3 °C), chills, malaise, myalgias, pain in her upper back, nausea, diarrhea, and intermittent uterine contractions. Her symptoms began 2 days after she and her husband dined at a local Mexican restaurant. She specifically recalls eating unpasteurized cheese (queso fresco). Her husband also is experiencing similar symptoms.

- What is the most likely diagnosis?
- What tests should be performed to confirm the diagnosis?
- Does this infection pose a risk to the fetus?
- How should this patient be treated?



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Listeriosis, a potentially serious foodborne illness, is an unusual infection in pregnancy. It can cause a number of adverse effects in both the pregnant woman and her fetus, including fetal death in utero. In this article, we review the microbiology and epidemiology of *Listeria* infection, consider the important steps in diagnosis, and discuss treatment options and prevention measures.

## **The causative organism in listeriosis**

Listeriosis is caused by *Listeria monocytogenes*, a gram-positive, non-spore-forming bacillus. The organism is catalase positive and oxidase negative, and it exhibits tumbling motility when grown in culture. It can grow at temperatures less than 4 °C, which facilitates foodborne transmission of the bacterium despite adequate refrigeration. Of the 13 serotypes of *L monocytogenes*, the 1/2a, 1/2b, and 4b are most likely to be associated with human infection. The major virulence factors of *L monocytogenes* are the internalin surface proteins and the pore-forming listeriolysin O (LLO) cytotoxin. These factors enable the organism to effectively invade host cells.<sup>1</sup>

The pathogen uses several mechanisms to evade gastrointestinal defenses prior to entry into the bloodstream. It avoids destruction

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in the stomach by using proton pump inhibitors to elevate the pH of gastric acid. In the duodenum, it survives the antibacterial properties of bile by secreting bile salt hydrolases, which catabolize bile salts. In addition, the cytotoxin listeriolysin S (LLS) disrupts the protective barrier created by the normal gut flora. Once the organism penetrates the gastrointestinal barriers, it disseminates through the blood and lymphatics and then infects other tissues, such as the brain and placenta.<sup>1,2</sup>

### Pathogenesis of infection

The primary reservoir of *Listeria* is soil and decaying vegetable matter. The organism also has been isolated from animal feed, water, sewage, and many animal species. With rare exceptions, most infections in adults result from inadvertent ingestion of the organism in contaminated food. In certain high-risk occupations, such as veterinary medicine, farming, and laboratory work, infection of the skin or eye can result from direct contact with an infected animal.<sup>3</sup>

Of note, foodborne illness caused by *Listeria* has the third highest mortality rate of any foodborne infection, 16% compared with 35% for *Vibrio vulnificus* and 17% for *Clostridium botulinum*.<sup>2,3</sup> The principal foods that have been linked to listeriosis include:

- soft cheeses, particularly those made from unpasteurized milk
- melon
- hot dogs
- lunch meat, such as bologna
- deli meat, especially chicken
- canned foods, such as smoked seafood, and pâté or meat spreads that are labeled “keep refrigerated”
- unpasteurized milk
- sprouts
- hummus.

In healthy adults, listeriosis is usually a short-lived illness. However, in older adults, immunocompromised patients, and pregnant women, the infection can be devastating. Infection in the pregnant woman also poses major danger to the developing fetus because the organism has a special predilection for placental and fetal tissue.<sup>1,3,4</sup>

Immunity to *Listeria* infection depends primarily on T-cell lymphokine activation of macrophages. These latter cells are responsible for clearing the bacterium from the blood. As noted above, the principal virulence factor of *L monocytogenes* is listeriolysin O, a cholesterol-dependent cytolysin. This substance induces T-cell receptor unresponsiveness, thus interfering with the host immune response to the invading pathogen.<sup>1,3-5</sup>

### Clinical manifestations of listeriosis

*Listeria* infections may present with various manifestations, depending on the degree of exposure and the underlying immunocompetence of the host (FIGURE). In its most common and simplest form, listeriosis presents as a mild to moderate gastroenteritis following exposure to contaminated food. Symptoms typically develop within 24 hours of exposure and include fever, myalgias, abdominal or back pain, nausea, vomiting, and diarrhea.<sup>5</sup>

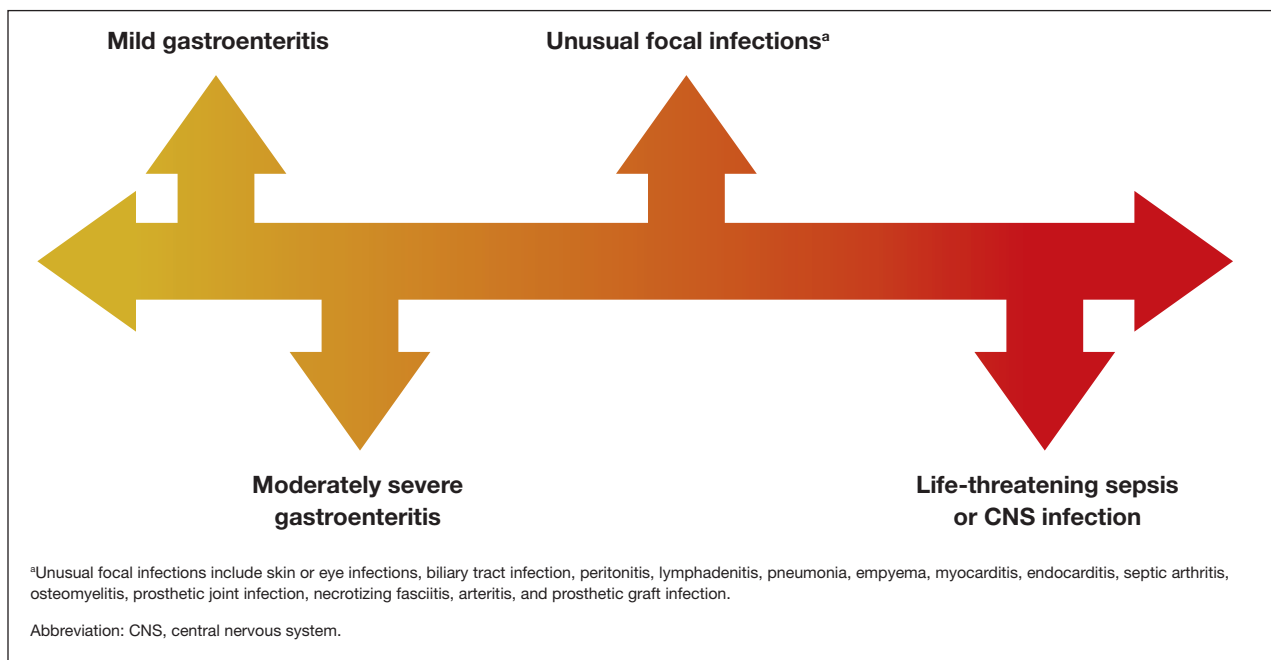
Conversely, in immunocompromised patients, including pregnant women, listeriosis can present as life-threatening sepsis and/or central nervous system (CNS) infection (invasive infection). In this clinical setting, the mean incubation period is 11 days. The manifestations of CNS infection include meningoenzephalitis, cerebritis, rhombencephalitis (infection and inflammation of the brain stem), brain abscess, and spinal cord abscess.<sup>5</sup>

In addition to these 2 clinical presentations, listeriosis can cause unusual focal infections as illustrated in the FIGURE. Some of these infections have unique clinical associations. For example, skin or eye infections may occur as a result of direct inoculation in veterinarians, farmers, and laboratory workers. *Listeria* peritonitis may occur in patients who are receiving peritoneal dialysis and in those who have cirrhosis. Prosthetic joint and graft infections, of course, may occur in patients who have had invasive procedures for implantation of grafts or prosthetic devices.<sup>5</sup>

### FAST TRACK

*With rare exceptions, most Listeria infections in adults result from inadvertent ingestion of the organism in contaminated food*

**FIGURE** Spectrum of clinical illness due to *Listeria monocytogenes*



Listeriosis is especially dangerous in pregnancy because it not only can cause serious injury to the mother and even death but it also may pose a major risk to fetal well-being. Possible perinatal complications include fetal death; preterm labor and delivery; and neonatal sepsis, meningitis, and death.<sup>5-8</sup>

### Making the diagnosis

Diagnosis begins with a thorough and focused history to assess for characteristic symptoms and possible *Listeria* exposure. Exposure should be presumed for patients who report consuming high-risk foods, especially foods recently recalled by the US Food and Drug Administration.

In the asymptomatic pregnant patient, diagnostic testing can be deferred, and the patient should be instructed to return for evaluation if symptoms develop within 2 months of exposure. However, symptomatic, febrile patients require testing. The most valuable testing modality is Gram stain and culture of blood. Gram stain typically will show gram-positive pleomorphic rods with rounded ends. Amniocentesis may be indicated if blood cultures are not definitive.

Meconium staining of the amniotic fluid and a positive Gram stain are highly indicative of fetal infection. Cultures of the cerebrospinal fluid are indicated in any individual with focal neurologic findings. Stool cultures are rarely indicated.

When obtaining any of the cultures noted above, the clinician should alert the microbiologist of the concern for listeriosis because *L. monocytogenes* can be confused with common contaminants, such as diphtheroids.<sup>5-9</sup>

### Treatment and follow-up

The treatment of listeriosis in pregnancy depends on the severity of the infection and the immune status of the mother. The **TABLE** (page 24) offers several different clinical scenarios and the appropriate treatment for each. As noted, several scenarios may require cultures of the blood, cerebrospinal fluid, and amniotic fluid.<sup>7,9,10</sup>

Following treatment of the mother, serial ultrasound examinations should be performed to monitor fetal growth, CNS anatomy, placental morphology, amniotic fluid volume, and umbilical artery Doppler velocimetry. In the presence of fetal growth

### FAST TRACK

*Diagnosis begins with a thorough and focused history to assess for characteristic symptoms and possible *Listeria* exposure*

**TABLE Management of listeriosis in pregnant women**<sup>7,9,10</sup>

| Clinical scenario                            | Management   |
|--|--|
| Presumptive exposure and asymptomatic        | <ul style="list-style-type: none"> <li>No cultures should be performed and no antibiotic treatment is indicated.</li> <li>Patient should be re-evaluated if symptoms develop.</li> </ul>   |
| Presumptive exposure, afebrile, mild illness | <ul style="list-style-type: none"> <li>Oral amoxicillin, 875 mg twice daily or 500 mg 3 times daily for 7 days.<sup>a</sup></li> </ul>   |
| Symptomatic febrile illness                  | <ul style="list-style-type: none"> <li>Perform blood cultures.</li> <li>If CNS symptoms are present, perform lumbar puncture.</li> <li>If mother appears septic, obtain amniotic fluid for Gram stain and culture.</li> <li>Hospitalize and treat with intravenous ampicillin 2 g every 4 hours.<sup>b</sup></li> <li>If cultures are negative, complete 7-day course of therapy with oral amoxicillin, 875 mg twice daily or 500 mg 3 times daily.</li> <li>If blood cultures are positive, continue intravenous treatment for 14 days.</li> <li>Patients with positive cultures of the CSF should be treated for a minimum of 3–4 weeks. If bacterial endocarditis is suspected or confirmed, treatment should be extended for 4–6 weeks.</li> </ul> |

<sup>a</sup>If patient is allergic to penicillin, administer trimethoprim-sulfamethoxazole double strength 1 tablet twice daily for 7 days.

<sup>b</sup>If patient is allergic to penicillin, administer intravenous trimethoprim-sulfamethoxazole 10–20 mg/kg per day (based on the trimethoprim component). Divide into 2–4 doses. Use the higher end of the dosing range for the more severely ill patient. If the patient is also allergic to sulfonamide antibiotics, the recommended alternative is meropenem 2 g intravenously every 8 hours.

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid.

**FAST TRACK**

*Conservative measures to prevent Listeria infection in pregnant women include avoiding all products made from unpasteurized milk and soft cheeses*

restriction, oligohydramnios, or abnormal Doppler velocimetry, biophysical profile testing should be performed. After delivery, the placenta should be examined carefully for histologic evidence of *Listeria* infection, such as miliary abscesses, and cultured for the bacterium.<sup>7-9</sup>

**Prevention measures**

Conservative measures for prevention of *Listeria* infection in pregnant women include the following<sup>7,10-12</sup>:

- Refrigerate milk and milk products at 40 °F (4.4 °C).
- Thoroughly cook raw food from animal sources.
- Wash raw vegetables carefully before eating.
- Keep uncooked meats separate from cooked meats and vegetables.
- Do not consume any beverages or foods made from unpasteurized milk.
- After handling uncooked foods, carefully wash all utensils and hands.
- Avoid all soft cheeses, such as Mexican-style feta, Brie, Camembert, and blue cheese, even if they are supposedly made from pasteurized milk.
- Reheat until steaming hot all leftover foods

- or ready-to-eat foods, such as hot dogs.
- Do not let juice from hot dogs or lunch meat packages drip onto other foods, utensils, or food preparation surfaces.
- Do not store opened hot dog packages in the refrigerator for more than 1 week. Do not store unopened packages for longer than 2 weeks.
- Do not store unopened lunch and deli meat packages in the refrigerator for longer than 2 weeks. Do not store opened packages for longer than 3 to 5 days.
- If other immunosuppressive conditions are present in combination with pregnancy, thoroughly heat cold cuts before eating.
- Do not eat raw or even lightly cooked sprouts of any kind. Cook sprouts thoroughly. Rinsing sprouts will not remove *Listeria* organisms.
- Do not eat refrigerated pâté or meat spreads from a deli counter or the refrigerated section of a grocery store.
- Canned or shelf-stable pâté and meat spreads are safe to eat, but be sure to refrigerate them after opening the packages.
- Do not eat refrigerated smoked seafood. Canned or shelf-stable seafood, particularly when incorporated into a casserole, is safe to eat.

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## Key points on listeriosis

- Listeriosis is primarily a foodborne illness caused by *Listeria monocytogenes*, a gram-positive bacillus.
- Pregnant women, particularly those who are immunocompromised, are especially susceptible to *Listeria* infection.
- Foods that pose particular risk of transmitting infection include fresh unpasteurized cheeses, processed meats such as hot dogs, refrigerated pâté and meat spreads, refrigerated smoked seafood, unpasteurized milk, and unwashed raw produce.
- The infection may range from a mild gastroenteritis to life-threatening sepsis and meningitis.
- Listeriosis may cause early and late-onset neonatal infection that presents as either meningitis or sepsis.
- Blood and amniotic fluid cultures are essential to diagnose maternal infection. Stool cultures usually are not indicated.
- Mildly symptomatic but afebrile patients do not require treatment.
- Febrile symptomatic patients should be treated with either intravenous ampicillin or trimethoprim-sulfamethoxazole.

- Eat cut melon immediately. Refrigerate uneaten melon quickly if not eaten. Discard cut melon that is left at room temperature for more than 4 hours.

### CASE Diagnosis made and prompt treatment initiated

The most likely diagnosis in this patient is listeriosis. Because the patient is moderately ill and experiencing uterine contractions, she should be hospitalized and monitored for progressive cervical dilation. Blood cultures should be

obtained to identify *L. monocytogenes*. In addition, an amniocentesis should be performed, and the amniotic fluid should be cultured for this microorganism. Stool culture and culture of the cerebrospinal fluid are not indicated. The patient should be treated with intravenous ampicillin, 2 g every 4 hours for 14 days. If she is allergic to penicillin, the alternative drug is trimethoprim-sulfamethoxazole, 8 to 10 mg/kg per day in 2 divided doses, for 14 days. Prompt and effective treatment of the mother should prevent infection in the fetus and newborn. ●

### References

1. Radoshevich L, Cossart P. *Listeria monocytogenes*: towards a complete picture of its physiology and pathogenesis. *Nat Rev Microbiol.* 2018;16:32-46. doi:10.1038/nrmicro.2017.126.
2. Johnson JE, Mylonakis E. *Listeria monocytogenes*. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020:2543-2549.
3. Gelfand MS, Swamy GK, Thompson JL. Epidemiology and pathogenesis of *Listeria monocytogenes* infection. UpToDate. Updated August 23, 2022. Accessed November 9, 2022. [https://www.uptodate.com/contents/epidemiology-and-pathogenesis-of-listeria-monocytogenes-infection?sectionName=CLINICAL%20EPIDEMIOLOGY&topicRef=1277&anchor=H4&source=see\\_link#H4](https://www.uptodate.com/contents/epidemiology-and-pathogenesis-of-listeria-monocytogenes-infection?sectionName=CLINICAL%20EPIDEMIOLOGY&topicRef=1277&anchor=H4&source=see_link#H4)
4. Cherubin CE, Appleman MD, Heseltine PN, et al. Epidemiological spectrum and current treatment of listeriosis. *Rev Infect Dis.* 1991;13:1108-1114.
5. Gelfand MS, Swamy GK, Thompson JL. Clinical manifestations and diagnosis of *Listeria monocytogenes* infection. UpToDate. Updated August 23, 2022. Accessed November 7, 2022. <https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-listeria-monocytogenes-infection>
6. Boucher M, Yonekura ML. Perinatal listeriosis (early-onset): correlation of antenatal manifestations and neonatal outcome. *Obstet Gynecol.* 1986;68:593-597.
7. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 614: management of pregnant women with presumptive exposure to *Listeria monocytogenes*. *Obstet Gynecol.* 2014;124:1241-1244.
8. Rouse DJ, Keimig TW, Riley LE, et al. Case 16-2016. A 31-year-old pregnant woman with fever. *N Engl J Med.* 2016;374:2076-2083.
9. Craig AM, Dotters-Katz S, Kuller JA, et al. Listeriosis in pregnancy: a review. *Obstet Gynecol Surv.* 2019;74:362-368.
10. Gelfand MS, Thompson JL, Swamy GK. Treatment and prevention of *Listeria monocytogenes* infection. UpToDate. Updated August 23, 2022. Accessed November 9, 2022. [https://www.uptodate.com/contents/treatment-and-prevention-of-listeria-monocytogenes-infection?topicRef=1280&source=see\\_link](https://www.uptodate.com/contents/treatment-and-prevention-of-listeria-monocytogenes-infection?topicRef=1280&source=see_link)
11. Voetsch AC, Angulo FJ, Jones TE, et al; Centers for Disease Control and Prevention Emerging Infections Program Foodborne Diseases Active Surveillance Networking Group. Reduction in the incidence of invasive listeriosis in Foodborne Diseases Active Surveillance Network sites, 1996-2003. *Clin Infect Dis.* 2007;44:513-520.
12. MacDonald PDM, Whitwan RE, Boggs JD, et al. Outbreak of listeriosis among Mexican immigrants as a result of consumption of illicitly produced Mexican-style cheese. *Clin Infect Dis.* 2005;40:677-682.