

Prenatal listeriosis: Risk factors, education, and prevention

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Outline

- **Background**
 - Symptoms
 - Transmission
 - Diagnosis, Management, and Treatment
- Modifiable Risk Factors
- Education and Prevention

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What is *Listeria monocytogenes* (Listeria)?

- Bacterium found in soil, wood, and decaying matter in the environment (rod shaped, gram +)
- Thick cell wall, biofilm-producing
 - Allows it to better survive sanitation measures
- Many animals carry without appearing ill
- Most commonly transmitted to humans through contaminated foods
- Causes severe disease in select human populations (20-30% mortality rate)



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Epidemiology




- According to CDC estimates for the US:
 - Of 1,600 *Listeria*-related illnesses per year, ~14% in pregnant women
 - 260 deaths annually
 - Based on 2008-2016 data from the Foodborne Diseases Active Surveillance Network (FoodNet), invasive listeriosis annual incidence rate per 100,000 was 0.28 cases among the general population but 3.73 cases among pregnant women
 - Hispanic women 24 times more likely to become infected with *Listeria* than other women, likely attributable to cultural food preferences

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Contributing Physiological Factors




- Pregnant women more at risk for infection with *Listeria*
 - Downregulation of the cellular immune system during pregnancy, especially in the third trimester
 - Changes in T-helper and cytotoxic T-cell function in the recognition of foreign antigens, as well as a natural decrease in the amount of natural killer cells found during pregnancy
 - Bacterium's affinity for placental cell receptors



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Symptoms: Non-Invasive Listeriosis



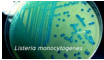
- Gastrointestinal (diarrhea)
- Fever
- Muscle aches
 - Usually resolve in 1-3 days but can occur up to 21 days post-infection
- Non-invasive listeriosis is often undiagnosed
- However, this presentation will focus on invasive listeriosis

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Symptoms: Invasive Listeriosis




- Invasive infection, defined as isolation of *Listeria* from a normally sterile site (typically blood or cerebrospinal fluid), is uncommon
- Usually occurs in pregnant women, elderly, young children, or immunocompromised populations
- Infection may be asymptomatic
- Symptoms can take days or weeks to appear
 - Nonspecific, flu-like illness with fever, chills, myalgia, backache, muscle and/or joint pain, headache, stiff neck, confusion, and loss of balance, often preceded by diarrhea or other gastrointestinal symptoms



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Perinatal Outcomes: Invasive Listeriosis




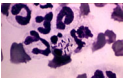
- Outcomes if not treated early enough
 - Miscarriages in first trimester of pregnancy
 - Premature labor, delivery of low birth weight infant, or infant death
 - Fetuses with late infection: seizures, blindness, paralysis, cognitive disability, or impairments of the brain, heart, or kidney
 - Newborns: sepsis, meningitis

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**Transmission:
Contaminated Food**







- Outbreaks have been linked to a wide variety of foods, including contaminated produce, ready-to-eat meats, poultry, seafood, dairy products
- *Listeria* characteristics of particular concern to food industry
 - Facultative anaerobe
 - Psychrotrophic
 - Ubiquitous in the environment
 - Motile
 - Can be an intracellular pathogen


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Select Outbreaks of Listeriosis

- Cantaloupes – 28 states in 2011
 - 147 ill (143 hospitalized), 33 deaths
- Ricotta salata cheese – 14 states in 2012
 - 22 ill (20 hospitalized), 4 deaths
- Caramel apples – 12 states in 2014
 - 35 ill (34 hospitalized), 7 deaths
- Ice cream – 4 states in 2015
 - 10 ill (all hospitalized), 3 deaths


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Transmission: Other Routes

- Nosocomial/hospital-acquired
 - Rare, but found to occur among healthy newborns
- Vertical/mother to child
 - *Listeria* can colonize the vagina of some women and infect babies, but this is rare
 - Infection of the mother can lead to infection of the baby
- Breast milk?
 - At this time, the CDC reports that there have been no documented cases of transmission of *Listeria* to infants directly from breast milk
 - There is evidence of bacterial shedding of *Listeria* in the breast milk of mice
 - However, research on human transmission of *Listeria* via breast milk is lacking


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Diagnosis, Management, and Treatment


- Committee on Obstetric Practice, American College of Obstetricians and Gynecologists (ACOG), published [“Management of Pregnant Women With Presumptive Exposure to *Listeria monocytogenes*”](#) in 2014 and reaffirmed in 2016 to provide guidance for three categories of patients:
 - Asymptomatic
 - Mildly symptomatic but afebrile
 - Febrile with or without other symptoms of listeriosis

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ACOG Recommendations for Asymptomatic 


- No testing, including blood and stool cultures, or treatment indicated for asymptomatic pregnant woman who reports consumption of a product recalled or implicated during an outbreak of *Listeria* contamination.
- An asymptomatic patient should be instructed to return if she develops symptoms of listeriosis within 2 months of eating the recalled or implicated product.
- There is no reason to alter or begin fetal surveillance in asymptomatic women with known or presumptive exposure to *Listeria*.

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ACOG Recommendations for Mildly Symptomatic But Afebrile 

- A pregnant woman who ate a product that was recalled because of *Listeria* contamination and who is afebrile but has signs and symptoms consistent with a minor gastrointestinal or flu-like illness (such as mild myalgia, mild nausea, vomiting, or diarrhea) can be managed expectantly (i.e., the same as for an exposed, asymptomatic pregnant woman). This is a reasonable approach that limits low-yield testing.
- Alternatively, such a patient could be tested with blood culture for *Listeria*, but if such a course is elected, specific instruction should be given to the microbiology laboratory.
- Because the morphology of *Listeria* resembles that of diphtheroids, it may be mistaken for a contaminant. Therefore, the laboratory should be alerted to the clinical suspicion of listeriosis.

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ACOG Recommendations for Mildly Symptomatic But Afebrile
(continued) 

- If such diagnostic testing is performed, some experts would withhold antibiotic therapy unless the culture yielded *Listeria*.
- Others would initiate antibiotic therapy, although no effectiveness data exist to help clinicians and patients evaluate the risks and benefits of such a treatment choice.
- If testing is undertaken and the blood culture yields *Listeria*, standard antimicrobial treatment for listeriosis would be indicated (covered in slides to come).
- Assessments of fetal well-being should be addressed on an individualized basis with consideration given to the degree of concern for infection and the patient's clinical status.

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**ACOG Recommendations for
Febrile with or without other symptoms
of listeriosis**

FDA

- An exposed pregnant woman with a fever higher than 38.1°C (100.6°F) and signs and symptoms consistent with listeriosis for whom no other cause of illness is known should be simultaneously tested and treated for presumptive listeriosis.

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ACOG Committee on Obstetric Practice Opinion

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graph TD
    A[Presumptive exposure to listeria  
(Listeria monocytogenes)] --> B{Is patient symptomatic?}
    B -- No --> C[No testing or treatment]
    B -- Yes --> D{Is patient febrile?}
    D -- No --> E[Expectant management  
May consider obtaining blood cultures]
    D -- Yes --> F[Simultaneous testing with blood cultures and treatment with IV ampicillin*  
Obtain placental culture if delivered]
  
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Fig. 1. Management of pregnant women with presumptive exposure to listeria.
Abbreviation: IV, intravenous.
*Symptoms include flu-like symptoms, such as myalgia, abdominal or back pain, nausea, vomiting, or diarrhea.
†Trimethoprim with sulfamethoxazole should be used if patient is allergic to penicillin. ◀


Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. Committee Opinion No. 614: Management of pregnant women with presumptive exposure to *Listeria monocytogenes*. *Obstet Gynecol.* 2014 Dec;124(6):1241-4 (Reaffirmed 2016).

Diagnosis

FDA


- Work up indicated by high risk food consumption
- Blood, lumbar puncture, placental cultures diagnostic
- Care must be taken to distinguish this organism from other Gram-positive rods, particularly diphtheroids.
- Upon confirming diagnosis, health care providers should contact their state public health departments to comply with reporting requirements

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Treatment 


- For nonallergic
 - High-dose intravenous penicillin or ampicillin (at least 6 g/day) for at least 14 days
 - Note: gentamicin frequently added because of synergism with ampicillin, but disagreement on whether this adds to the effectiveness of the regimen, especially given the toxicity of gentamicin
- For those allergic to penicillin, ampicillin, or both
 - Trimethoprim with sulfamethoxazole or erythromycin preferred
- Gram-stain smear of meconium from clinically suspected newborns should be examined for short Gram-positive rods; if positive, prophylactic antibiotics should be administered as precaution
- If blood cultures negative after completion of recommended antibiotic regimen, decision on continuing or stopping antibiotics recommended to be made using clinical judgment in consultation with an infectious disease specialist, a maternal–fetal medicine specialist, or both

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Challenges 


- Symptoms of infection may not occur until 2 months after ingestion of contaminated food, making the diagnosis of listeriosis in pregnancy even more difficult
- This also makes cases difficult to attribute to a specific food source and challenging for FDA to develop appropriate regulatory or preventive policy

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Modifiable Risk Factors:
Exposures To Contaminated Foods 






- *Listeria* can survive and grow at refrigerator temperatures, unlike most other foodborne bacteria
- Most frequently linked to *Listeria* contamination:
 - Unpasteurized or “raw” dairy products
 - Soft cheeses
 - Blue-veined cheese
 - Feta
 - Brie
 - Camembert
 - Queso fresco/queso blanco
 - Deli meats
 - Hot dogs
 - Meat spreads (chicken salad/ham salad)
 - Unwashed raw vegetables, including lettuce
 - Refrigerated smoked seafood




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Modifiable Risk Factors:
Food Handling and Storage 


- **CLEAN: Wash hands and surfaces often**
 - Proper handwashing before preparing/eating food
 - Proper washing and drying of produce
- **SEPARATE: Separate raw meats from other foods**
 - Separating cooked from raw foods
- **COOK: Cook to the right temperature**
 - Thorough cooking
- **CHILL: Refrigerate foods promptly**
 - Use an appliance thermometer to be sure the temperature is consistently 40° F or below and the freezer temperature is 0° F or below.
 - Refrigerate or freeze meat, poultry, eggs, seafood, and other perishables within 2 hours of cooking or purchasing. Refrigerate within 1 hour if the temperature outside is above 90° F.
- **USE/DISPOSE**
 - Prompt use of perishables, prepared foods, and leftovers
 - Disposal of foods left at room temperature after 2 hours
 - Disposal if temperatures exceed 90° F (32° C) after 1 hour
 - Weekly checks of food supplies and disposal of those past expiration dates or recommended storage times



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Modifiable Risk Factors:
Hand Hygiene and Cleaning 

- To prevent hospital-acquired *Listeria* infections in healthy newborns
 - Proper handwashing in the hospital environment
 - Sufficient facility surface cleaning



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Education and Prevention




- While good agricultural and manufacturing practices are key to reducing burden, physicians and other healthcare providers play a major role in prevention of prenatal listeriosis by providing information on risk factors and healthy behaviors
- Share FDA recommendations for safe washing and handling of foods
- Provide advice to avoid high risk foods



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FDA's Advice: To Eat or Not to Eat?



Don't eat:

- Ready-to-eat meats: Hot dogs, deli meats, and luncheon meats - *unless they're reheated until steaming hot.*
- Soft cheeses like Feta, Brie, and Camembert, "blue-veined cheeses," or "queso blanco " queso fresco," or Panela – *unless they're made with pasteurized milk. Make sure the label says, "made with pasteurized milk."*
- Refrigerated pâtés or meat spreads.
- Refrigerated smoked seafood - unless it's in a cooked dish, such as a casserole.
 - Refrigerated smoked seafood, such as salmon, trout, whitefish, cod, tuna, or mackerel is most often labeled as "nova-style," "lox," "kippered," "smoked," or "jerky." These types of fish are found in the refrigerator section or sold at deli counters of grocery stores and delicatessens.
- Raw (unpasteurized) milk or foods that contain unpasteurized milk.

It's okay to eat:

- Canned or shelf-stable (able to be stored unrefrigerated on the shelf) pâtés and meat spreads.
- Canned or shelf-stable smoked seafood.
- Pasteurized milk or foods that contain pasteurized milk.

<https://www.fda.gov/Food/ResourcesForYou/HealthEducators/ucm083320.htm>

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