

# 83 *Listeria Monocytogenes* (Including Listeriosis)

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## Definition/Classification

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Listeriosis is an infection caused by the bacterium *Listeria monocytogenes* with a spectrum of disease ranging from asymptomatic infections in the immunocompetent patient to severe sepsis and death in certain populations including neonates. It is one of the three major worldwide causes of neonatal meningitis.

## Etiology

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The genus *Listeria* was named after Sir Joseph Lister, father of antiseptic surgery, while *monocytogenes* refers to the monocytosis often seen in animals infected with the bacteria. *Listeria* spp. are ubiquitous, gram-positive, facultatively anaerobic, intracellular, motile bacilli found in many environments including soil, water, and refrigerated foods. The organisms can survive in acidic, salty, and cold conditions. *Listeria* spp. can infect multiple animal species but, apart from scattered case reports involving *Listeria ivanovii*, *L. monocytogenes* is the main species to cause disease in humans. Furthermore, of the *Listeria monocytogenes* serotypes, three are responsible for 95% of infections in humans: 1/2a, 1/2b, and 4b. Serotype 4b appears to be more virulent than the others.

## Epidemiology

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Listeriosis is an uncommon cause of infection in the general population but it can lead to serious infections in pregnant women and their fetus, neonates, the elderly, and immunocompromised patients. While *Listeria* spp. are found throughout the world, listeriosis is more common in industrialized countries. Cases are mostly sporadic but can occur as part of an outbreak. The incidence varies from 0.1 to 11.3 per million in different countries. Infection rates also vary by age (● Fig. 83.1) and are inversely proportional to gestational age. Males and females are

affected equally. Women are 20 times more likely to develop a listerial infection during pregnancy, mostly in the third trimester. This is likely due to impaired cell-mediated immunity during the third trimester of pregnancy.

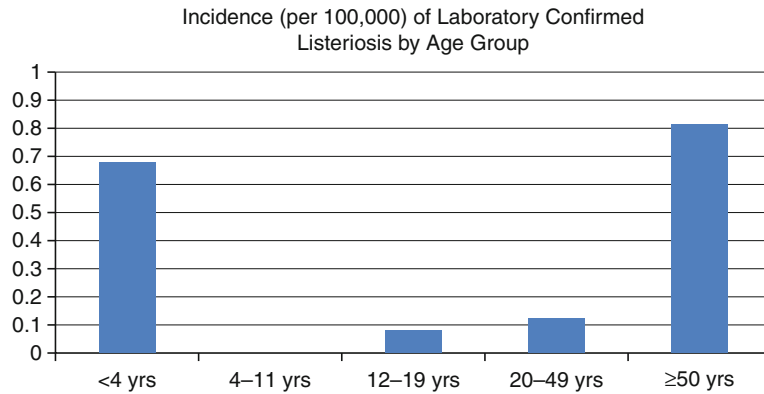
Several nations have seen decreases in incidence in the last 2 decades following public health and food industry initiatives in response to foodborne outbreaks. For example, France saw a 68% reduction in listeriosis from 1987 to 1997 while the United States of America saw a 40% decline from 1996 to 2004. Still, outbreaks have been reported in several countries in the past 10 years linked to dairy and ready-to-eat products. *Listeria* is also found in the stool of 5% of healthy adults.

## Pathogenesis

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Both early-onset and late-onset neonatal infections can be caused by transplacental transmission. The pregnant woman ingests *Listeria*. The bacterium then crosses the intestinal mucosa into the bloodstream where it travels to the placenta and infects the fetus. Ascending infection during pregnancy can also lead to early-onset listeriosis while late-onset infection can be acquired by exposure of the neonate to *Listeria* while passing through the contaminated birth canal. Infections after the neonatal period are all thought to be foodborne or via exposure to an extrinsic source.

The mechanism by which *Listeria* becomes pathogenic and invades cells continues to be studied. First, the bacteria gain access to the blood stream and other cells, including macrophages and placental trophoblasts, via the interaction of surface proteins such as internalin A and internalin B with cell-surface proteins like E-cadherin. One hypothesis explaining *Listeria's* tropism for tissues like the central nervous system and the placental unit is that E-cadherin, for example, is found specifically on the cell surface of trophoblasts. Once endocytosed, the bacteria lyse the vacuoles which house them via the action of



■ **Figure 83.1**

From preliminary FoodNet data on the incidence of infection in the USA with pathogens transmitted commonly through food – 10 states, 2009

proteins like listeriolysin O and become motile within the cytoplasm by acquiring an actin-rich “comet-tail.” *Listeria* then migrates to the cell periphery where it spreads to neighboring or immune cells like macrophages via cell wall protrusions that are endocytosed. The bacteria can therefore hijack the very cells, macrophages, which otherwise help clear intracellular infections.

## Pathology

Placental pathology demonstrates multiple, well-defined macroabscesses while severe fetal infection is characterized by disseminated granulomatous lesions with microabscesses found throughout the body, including the skin.

## Clinical Manifestations

Pregnant women infected with *Listeria* may be asymptomatic or have a flu-like illness. Fetal infection leads to premature birth or neonatal death in 22% of cases. While there are no pathognomic clinical features of listeriosis in the neonate, early-onset neonatal listeriosis presents on average at 1.5 days of life with signs and symptoms of sepsis. Other clinical manifestations include chorioamnionitis, meningitis, and pneumonia. In severe disease, granulomas and abscesses can be found disseminated throughout the body and skin, termed granulomatosis infantisepticum. The associated rash is characterized by lesions found mainly on the trunk or extremities which are maculopapular or papulovesicular in nature.

Late-onset listeriosis is less common than early-onset disease and presents around 2 weeks of life with nonspecific signs and symptoms of illness like fever, lethargy, and decreased feeding. It most frequently presents with meningitis and is associated with serotype 4b.

Non-neonatal pediatric listeriosis is rare even in the immunocompromised patient and has a variety of presentations ranging from self-limited gastroenteritis accompanied by fever and diarrhea to meningoencephalitis.

## Diagnosis

The diagnosis of listeriosis is difficult to make on clinical presentation alone and therefore requires isolation of the bacteria from otherwise sterile sites such as the blood and cerebrospinal fluid (CSF). Identification can be challenging, however, as *Listeria* can look like cocci, diplococci, or diphtheroids under the microscope, often misleading the laboratory technician. Gram staining is only positive in approximately 30% patients. The organisms can be grown on selective media or using the cold enrichment technique and show a narrow zone of hemolysis. Rapid detection monoclonal antibody tests are available.

Unlike the name implies, infection in humans rarely leads to monocytosis. Instead, leukocytosis is more common with a predominance of polymorphonuclear cells. When meningitis is present, the CSF will usually be purulent with white blood cell counts ranging from 100 to 10,000 cells per mL. The glucose levels are low in only 40% of the cases while protein levels are usually elevated.

## Differential Diagnosis

Other neonatal sources of infection should be considered such as bacterial infections including group B streptococcus, *Escherichia coli*, and *Haemophilus influenzae*. Other diagnoses may include disseminated herpes simplex virus, cytomegalovirus, rubella, or toxoplasmosis.

## Treatment

While the diagnosis of maternofetal listeriosis is often missed due to the nonspecific symptoms associated with maternal infection, antimicrobial treatment of the mother during pregnancy can also treat the fetus and lead to a healthy newborn. Treatment of the neonate consists of supportive care in combination with antimicrobial therapy. High dose intravenous aminopenicillins such as ampicillin in combination with an aminoglycoside like gentamicin for synergy is the recommended treatment. Ampicillin alone is only weakly bactericidal and *Listeria* is resistant to all cephalosporins. An alternative in penicillin allergic patients is sulfamethazole-trimethoprim. Although there have been no randomized, controlled trials for the duration of therapy for listeriosis, the current recommendation is 10–14 days of IV therapy for invasive disease and 14–21 days for meningitis.

## Prognosis

Twenty percent of *Listeria* infections during pregnancy will lead to stillbirth or spontaneous abortion while 68% of the surviving newborns will develop neonatal sepsis. Listeriosis has a 20–30% case fatality rate despite antimicrobial therapy. Non-neonatal cases who survive will have neurological sequelae in 30% of patients.

## Prevention

There is no vaccine for *Listeria*. Avoidance of foods that are at high risk of being contaminated such as refrigerated deli

meats, hot dogs/frankfurters, unpasteurized dairy products, and smoked fish is recommended in patients who are immunocompromised or pregnant. Other measures which may reduce the incidence of listeriosis include washing vegetables prior to consumption, keeping refrigerator temperature at 4.4°C or lower and freezer temperatures at –17.8°C or lower, and thoroughly heating all foods prior to consumption.

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