

### A REVIEW ON LISTERIOSIS

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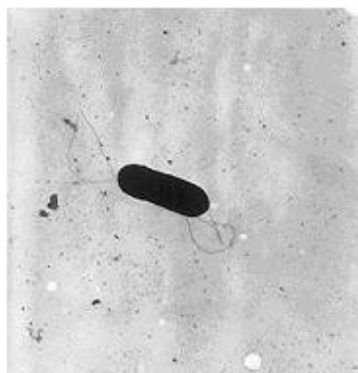
#### Summary

Listeriosis is a rare bacterial infection caused by *Listeria monocytogenes* a Gram-positive facultatively intracellular food borne pathogen occurs primarily in newborn infants, elderly patients and patients who are immunocompromised. It has shown to be of world-wide prevalence and is associated with serious disease in a wide variety of animals, including man. If the infection spreads to the nervous system it can cause meningitis. It has a very low incidence in humans. Pregnant women are at high risk than rest of the population to contract it. Infection in a pregnant woman can lead to early delivery, infection of the newborn and death of the baby. *Listeria* is also a common veterinary pathogen, being associated with abortion and encephalitis in sheep and cattle. It can be isolated from soil, water and decaying vegetation. Unless recognized and treated, *Listeria* infections can result in significant morbidity and mortality. This review offers an introduction to the organism, epidemiology, etiology, transmission with a description of the diagnosis, treatment and control of *Listeria*.

**Keywords:** Listeriosis; *Listeria*; Meningitis.

### Introduction

**Listeriosis** is a bacterial infection caused by a Gram-positive, non spore forming rods with tumbling motility, *Listeria monocytogenes*. Listeriosis is relatively rare and occurs primarily in newborn infants, elderly patients and patients who are immunocompromised. The symptoms of listeriosis usually last 7–10 days. The most common symptoms are fever and muscle aches and vomiting. Nausea and diarrhea are less common symptoms<sup>1</sup>. If the infection spreads to the nervous system it can cause meningitis, an infection of the covering of the brain and spinal cord. Symptoms of meningitis are headache, stiff neck, confusion, loss of balance and convulsions. Listeriosis has a very low incidence in humans. However, pregnant women are much more likely than the rest of the population to contract it. Infected pregnant women may have only mild, flulike symptoms. However, infection in a pregnant woman can lead to early delivery, infection of the newborn and death of the baby. In veterinary medicine, listeriosis can be a quite common condition in some farm outbreaks. It can also be found in wild animals<sup>2</sup>.



**Figure 1: Microscopic image of *Listeria monocytogenes***

### Epidemiology

Incidence in 2004–2005 was 2.5–3 cases per million populations a year in the United States, where pregnant women accounted for 30% of all cases. Of all nonperinatal infections, 70% occur in immunocompromised patients. Incidence in the U.S. has been falling since the 1990s, in contrast to Europe where changes in eating habits have led to an increase during the same time. In Sweden, it has stabilized at around 5 cases per annum per million populations, with pregnant women typically accounting for 1–2 of some 40 total yearly cases<sup>3</sup>.

### There Are Four Distinct Clinical Syndromes<sup>4,5</sup>

Infection in pregnancy	<i>Listeria</i> can proliferate asymptotically in the vagina and uterus. If the mother becomes symptomatic, it is usually in the third trimester. Symptoms include fever, myalgias, arthralgias and headache. Miscarriage, stillbirth and preterm labor are complications of this infection. Symptoms last 7–10 days.
Neonatal infection (granulomatosis infantisepticum)	There are two forms. One, an early-onset sepsis, with <i>Listeria</i> acquired in utero, results in premature birth. <i>Listeria</i> can be isolated in the placenta, blood, meconium, nose, ears and throat. Late-onset meningitis is acquired through vaginal transmission, although it also has been reported with caesarean deliveries.

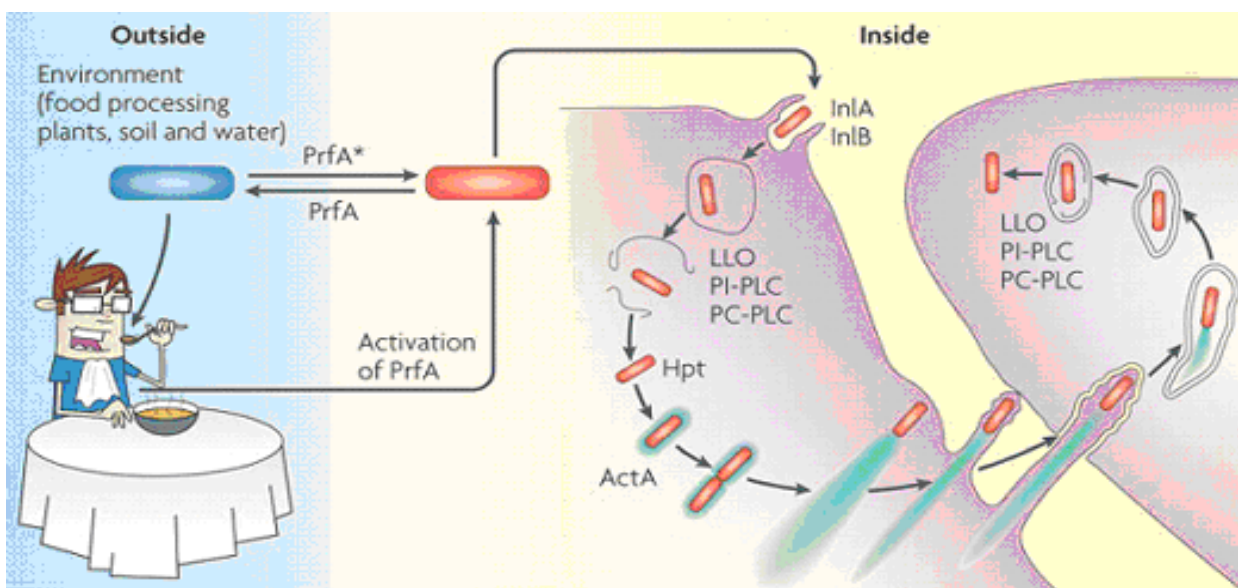
Central nervous system (CNS) infection	<i>Listeria</i> has a predilection for the brain parenchyma, especially the brain stem and the meninges. It can cause cranial nerve palsies, encephalitis, meningitis, meningoencephalitis and abscesses. Mental status changes are common. Seizures occur in at least 25% of patients.
Gastroenteritis	<i>L. monocytogenes</i> can produce food-borne diarrheal disease, which typically is noninvasive. The median incubation period is 21 days, with diarrhea lasting anywhere from 1–3 days. Patients present with fever, muscle aches, gastrointestinal nausea or diarrhea, headache, stiff neck, confusion, loss of balance or convulsions.

**Table 1: Clinical Syndromes Listeriosis**

### Etiology

*Listeria monocytogenes* is ubiquitous in the environment. The main route of acquisition of *Listeria* is through the ingestion of contaminated food products. *Listeria* has been isolated from raw meat, dairy products, vegetables and seafood. Soft cheeses, unpasteurized milk and unpasteurized pate are potential dangers; however, some outbreaks involving post-pasteurized milk have been reported. Rarely listeriosis may present as cutaneous listeriosis. This infection occurs after direct exposure to *L. monocytogenes* by intact skin and is largely confined to veterinarians who are handling diseased animals, most often after a listerial abortion. It can be more common in patients with hemochromatosis <sup>6</sup>.

### Life cycle of listeria monocytogenes <sup>5</sup>



**Figure 2: Life Cycle of Listeria monocytogenes**

*Listeria monocytogenes* survives in a diverse array of environments, in habitats that include soil and water as well as food processing facilities. Central to the switch between life outside and life inside mammalian hosts is the transcriptional activator PrfA, which regulates the expression of many gene products that are required for bacterial virulence.

Outside a host cell, PrfA exists in a low-activity state, with correspondingly low levels of virulence gene expression. Once inside the host, PrfA becomes activated (PrfA\*) and induces the expression of gene products that are needed for host cell invasion (internalins InlA and InlB), phagosome lysis (listeriolysin O (LLO), phosphatidylinositol-specific phospholipase C (PI-PLC) and phosphatidylcholine (PC)-PLC), intracellular growth (hexose-6-phosphate transporter (Hpt)) and cell-to-cell spread (actin assembly-inducing protein (ActA); actin polymerization is shown in turquoise). The intracellular life cycle is modified, with permission <sup>5</sup>.

### Listeriosis Transmission

Listeria bacteria live in the intestines of infected people and animals (particularly cattle, pigs and poultry) and are found in feces. The bacteria may be found in soil, food, water, or surfaces that have been contaminated with infected feces. The disease is spread when a person swallows, or puts in his or her mouth, food or an object contaminated with the bacteria. For example, water can be contaminated with sewage or animal feces. Meat can be contaminated with feces during the slaughter process<sup>7</sup>. Food and surfaces can be contaminated by contact with infected feces from a person's hands. Most cases of Listeriosis are associated with eating food contaminated with the bacteria. Contaminated food looks and smells normal. The bacteria can be found in a variety of foods like raw meats, uncooked vegetables, processed meats, as well as unpasteurized dairy products (milk and soft cheeses)<sup>8</sup>.

### Pathogenesis of Cellular Listeria Monocytogenes Infection

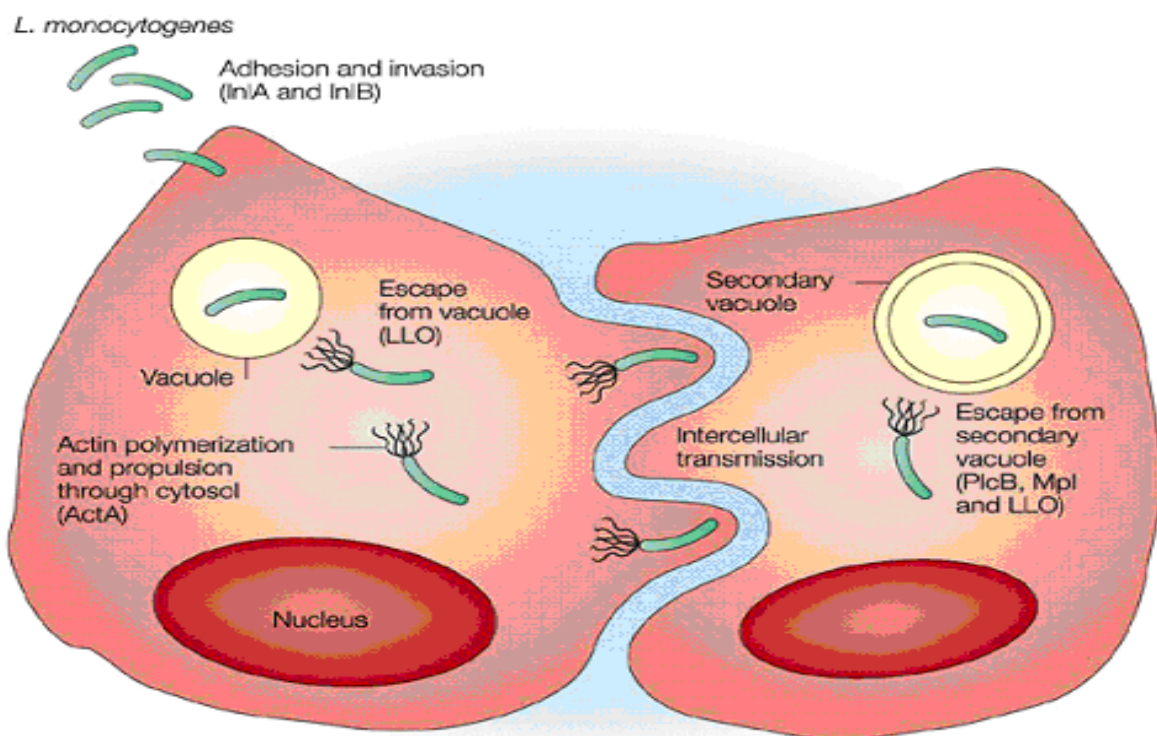
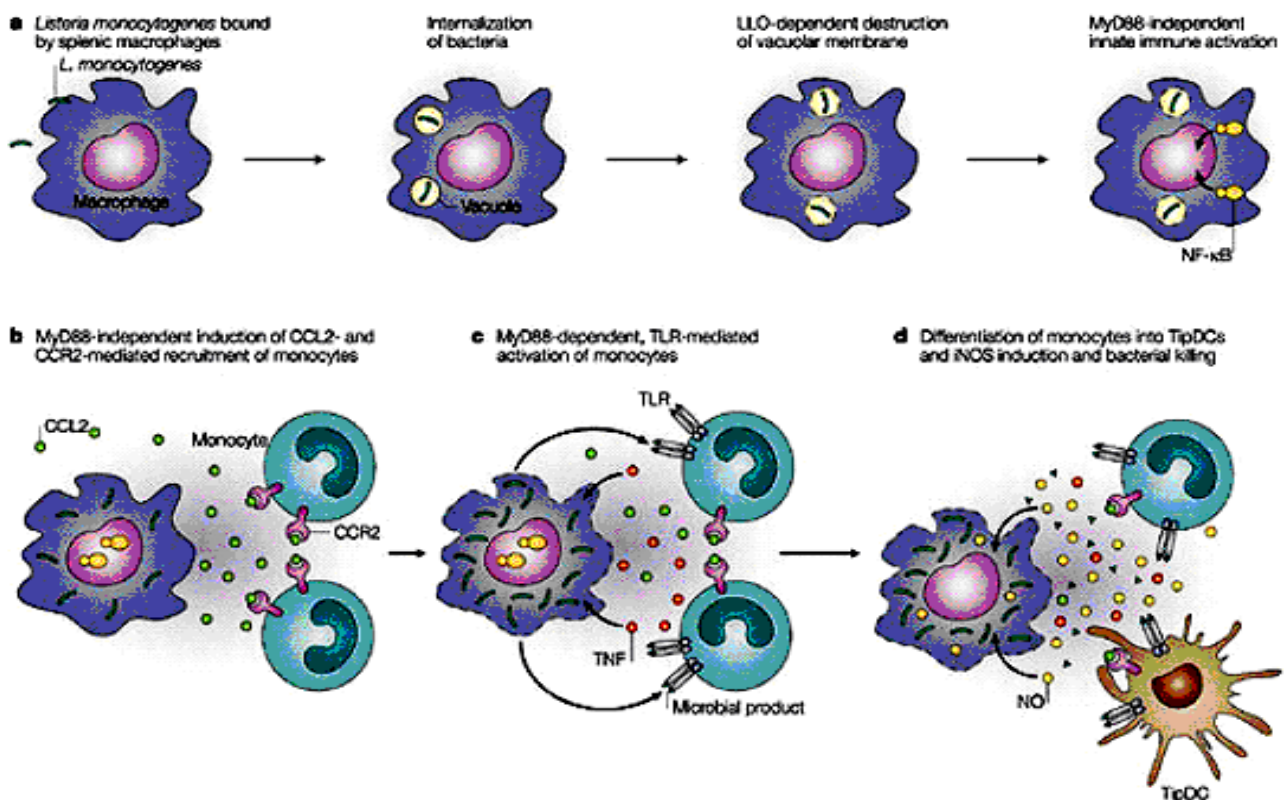


Figure 3: Pathogenesis of Listeria Monocytogenes

*Listeria monocytogenes* expresses cell-surface and secreted proteins that enable attachment to host cells, escape from the phagocytic vacuole and locomotion in the cytosol of the invaded cell. Internalin A (InlA) and InlB mediate the attachment of *L. monocytogenes* to the surface of host cells and listeriolysin O (LLO) lyses the phagosomal membrane. The actin-assembly-inducing protein (ActA) is expressed in a polarized manner and catalyses actin polymerization, which propels bacteria through the cell and into neighbouring cells. To escape the secondary vacuole in the newly invaded cell, *L. monocytogenes* expresses the phosphatidylcholine-specific phospholipase PlcB, a secreted zinc metalloproteinase (Mpl) and LLO.

### Innate Immune Activation by Virulent *Listeria monocytogenes* Is a Multistep Process



**Figure 3: Innate Immune Activation by Virulent *Listeria monocytogenes***

Bacteria in the bloodstream are bound by macrophages and internalized. In the macrophage vacuoles, bacteria secrete listeriolysin O (LLO), which lyses the vacuolar membrane and activates nuclear factor- $\kappa$ B (NF- $\kappa$ B)-mediated transcription of innate immune-response genes, such as CC-chemokine ligand 2 (CCL2). **b** | The CCL2 that is produced then induces the recruitment of circulating monocytes that express CC-chemokine receptor 2 (CCR2). **c** | Microbial products are released by infected macrophages and these activate recruited monocytes through Toll-like receptors (TLRs) in a MyD88 (myeloid differentiation primary-response protein 88)-dependent manner. **d** | Monocytes differentiate into tumour-necrosis factor (TNF)- and inducible nitric-oxide (iNOS)-producing dendritic cells (TipDCs), which promote bacterial killing<sup>10</sup>.

**Pregnant Women Need To Know**<sup>11, 12</sup>

Hormonal changes during pregnancy have an effect on the mother's immune system that lead to an increased susceptibility to listeriosis in the mother. Pregnant women are about 20 times more likely to get listeriosis than other healthy adults. Listeriosis can be transmitted to the fetus through the placenta even if the mother is not showing signs of illness. If a pregnant woman develops listeriosis during the first three months of her pregnancy, she may miscarry. Up to two weeks before a miscarriage, pregnant women may experience a mild flu-like illness with chills, fatigue, headache as well as muscular and joint pain. Listeriosis later on in the pregnancy can result in a stillbirth or the birth of an acutely-ill child. Pregnant women are, therefore, recommended to avoid the following foods due to their increased susceptibility to Listeriosis:

- Hot Dogs, especially eaten right from the package (minimize risk by cooking until steaming hot).
- Non-dried deli meats (dried and salted deli meats such as salami and pepperoni are safer alternatives, heating deli- meats until steaming hot will reduce risk).
- Unpasteurized soft and semi soft chesses such as feta, Brie, Camembert and blue cheese (choose cheeses made from pasteurized milk instead).
- Refrigerated pate and meat spreads.
- Refrigerated smoked seafood and fish (choose canned or shelf-stable smoked seafood and fish).
- Raw or undercooked meat, poultry and fish (be sure to cook thoroughly to reduce risk).

**Signs and Symptoms**<sup>13</sup>

- Mild symptoms
- Flu-like illness
- Fever
- Muscle aches
- Chills
- Tiredness
- Gastrointestinal symptoms
- Nausea
- Diarrhea
- Eye inflammation
- Enlarged lymph nodes

**Symptoms of Nervous System Involvement**

- Meningitis
- Headache
- Stiff neck
- Confusion
- Loss of balance
- Convulsions

### Diagnosis and Treatment

In CNS infection cases, *L. monocytogenes* can often be cultured from the blood and always cultured from the CSF<sup>9</sup>. There are no reliable serological or stool tests. Bacteremia should be treated for 2 weeks, meningitis for 3 weeks and brain abscess for at least 6 weeks. Ampicillin generally is considered antibiotic of choice; gentamicin is added frequently for its synergistic effects. Overall mortality rate is 20–30%; of all pregnancy-related cases, 22% resulted in fetal loss or neonatal death, but mothers usually survive<sup>14</sup>.

### Complications<sup>15</sup>

- Premature delivery
- Fetal loss
- Infection of the newborn
- Stillbirth
- Endocarditis
- Intrauterine growth retardation
- Pneumonia
- Miscarriage
- Bacteremia

### Prevention<sup>16, 17</sup>

- The most sensible thing is to avoid the foods such as raw fish, unpasteurised milk, soft cheese, undercooked poultry, raw vegetables and pre-cooked chilled foods. and to take extra care when handling food at home.
- Wash your hands before and after preparing meals and check that your fridge and freezer are set at the manufacturer's recommended temperature.
- Freezing temperatures don't kill the bacteria that cause listeriosis, but only slow it down. After a long power cut it may be a good idea to throw away any poultry or unpasteurised milk products in your fridge.
- Wash vegetables and fruits well before consuming.
- Avoid cross contamination by ensuring that your chopping boards, knives and cutlery are washed and dried well.
- The bacteria are killed by pasteurisation and cooking. If you are cooking meat, ensure that it is well cooked.
- Avoid cold cuts or food that has only been marinated.
- When eating pre-cooked meals and leftovers, do ensure that they are heated to a boiling temperature and are piping hot.

### Conclusion

Listeriosis even though a rare disease in humans still if not diagnosed and treated can lead to serious complications such as meningitis, myalgia, miscarriage, premature delivery, convulsions etc. Monitoring of *L. monocytogenes* over many decades has demonstrated that this once-mainly animal-related pathogen has become a major contributor to human foodborne disease because of its high hospitalization and death rates associated with the organisms invasive qualities. Studies have revealed the presence of this microorganism in several products like raw fish, unpasteurised milk, soft cheese, undercooked poultry, raw vegetables and pre-cooked chilled foods. Hence hygienic measures at home and in the food processing industry need to be improved. From the present review simple preventive measures can keep us far away from this infection.

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