

# *Listeria*

*Listeria* is a bacterial genus that contains six species.<sup>[1]</sup> Named after the English pioneer of sterile surgery Joseph Lister, the genus received its current name in 1940. *Listeria* species are Gram-positive bacilli and are typified by *L. monocytogenes*, the causative agent of listeriosis.

*Listeria ivanovii* is a pathogen of ruminants, and can infect mice in the laboratory, although it is only rarely the cause of human disease.

## *Listeria monocytogenes*

*Listeria monocytogenes* is commonly found in soil, stream water, sewage, plants, and food.<sup>[2]</sup> *Listeria* are responsible for listeriosis, a rare but potentially lethal food-borne infection. The case fatality rate for those with a severe form of infection may approach 25%.<sup>[3]</sup> (*Salmonella*, in comparison, has a mortality rate estimated at less than 1%<sup>[4]</sup>). Although listeria has low infectivity, it is hardy and can grow in temperatures from 4 °C (39.2 °F) (the temperature of a refrigerator), to 37 °C (98.6 °F), (the body's internal temperature).<sup>[2]</sup> Listeriosis is a serious illness, and the disease may manifest as meningitis, or affect newborns due to its ability to penetrate the endothelial layer of the placenta.<sup>[3]</sup> Vegetables can become contaminated from the soil, and animals can also be carriers. *Listeria* has been found in uncooked meats, uncooked vegetables, fruit such as cantaloupes,<sup>[5]</sup> unpasteurized milk, foods made from unpasteurized milk, and processed foods. Pasteurization and sufficient cooking kill listeria; however, contamination may occur after cooking and before packaging. For example, meat-processing plants producing ready-to-eat foods, such as hot dogs and deli meats, must follow extensive sanitation policies and procedures to prevent listeria contamination.<sup>[6]</sup>

## Pathogenesis

*Listeria* uses the cellular machinery to move around inside the host cell: It induces directed polymerization of actin by the ActA transmembrane protein, thus pushing the bacterial cell around.<sup>[citation needed]</sup>

*Listeria monocytogenes*, for example, encodes virulence genes that are thermoregulated. The expression of virulence factor is optimal at 37 degrees Celsius and is controlled by a transcriptional activator, PrfA, whose expression is thermoregulated by the PrfA thermoregulator UTR element. At low temperatures, the PrfA transcript is not translated due to structural elements near the ribosome binding site. As the bacteria infect the host, the temperature of the host melts the structure and allows translation initiation for the virulent genes.

*Listeria monocytogenes* is a Gram-positive, rod-shaped bacterium. It is the agent of listeriosis, a serious infection caused by eating food contaminated with the bacteria. The

disease affects primarily pregnant women, newborns, and adults with weakened immune systems. Listeriosis is a serious disease for humans; the overt form of the disease has a mortality greater than 25 percent. The two main clinical manifestations are sepsis and meningitis. Meningitis is often complicated by encephalitis, a pathology that is unusual for bacterial infections.

Under the microscope, *Listeria* species appear as small, Gram-positive rods, which are sometimes arranged in short chains. In direct smears, they may be coccoid, so they can be mistaken for streptococci. Longer cells may resemble corynebacteria. Flagella are produced at room temperature, but not at 37 °C. Hemolytic activity on blood agar has been used as a marker to distinguish *L. monocytogenes* among other *Listeria* species, but it is not an absolutely definitive criterion. Further biochemical characterization may be necessary to distinguish between the different *Listeria* species.

As Gram-positive, nonsporeforming, catalase-positive rods, the genus *Listeria* was classified in the family Corynebacteriaceae through the seventh edition of Bergey's Manual. The 16S rRNA cataloging studies of Stackebrandt, et al. demonstrated that *L. monocytogenes* is a distinct taxon within the Lactobacillus-Bacillus branch of the bacterial phylogeny constructed by Woese. In 2001, the Family Listeriaceae was created within the expanding Order Bacillales, which also includes Staphylococcaceae, Bacillaceae and others. Within this phylogeny, there are six species of *Listeria*. The only other genus in the family is *Brochothrix*.

## Mechanism of infection

The majority of *Listeria* bacteria are targeted by the immune system before they are able to cause infection. Those that escape the immune system's initial response, however, spread through intracellular mechanisms and are, therefore, guarded against circulating immune factors (AMI).<sup>[3]</sup>

To invade, *Listeria* induces macrophage phagocytic uptake by displaying D-galactose in their teichoic acids that are then bound by the macrophage's polysaccharide receptors. Other important adhesins are the internalins.<sup>[4]</sup> Once phagocytosed, the bacterium is encapsulated by the host cell's acidic phagolysosome organelle.<sup>[2]</sup> *Listeria*, however, escapes the phagolysosome by lysing the vacuole's entire membrane with secreted hemolysin,<sup>[7]</sup> now characterized as the exotoxin listeriolysin O.<sup>[2]</sup> The bacteria then replicate inside the host cell's cytoplasm.<sup>[3]</sup>

*Listeria* must then navigate to the cell's periphery to spread the infection to other cells. Outside the body, *Listeria* has flagellar-driven motility, sometimes described as a "tumbling motility." However, at 37 °C, flagella cease to develop and the bacterium instead usurps the host cell's cytoskeleton to move.<sup>[3]</sup> *Listeria*, inventively, polymerizes an actin tail or "comet",<sup>[7]</sup> from actin monomers in the host's cytoplasm<sup>[6]</sup> with the promotion of virulence factor ActA.<sup>[3]</sup> The comet forms in a polar manner<sup>[8]</sup> and aids the bacteria's migration to the host cell's outer membrane. Gelsolin, an actin filament severing protein, localizes at the tail of *Listeria* and accelerates the bacterium's motility.<sup>[8]</sup>

Once at the cell surface, the actin-propelled listeria pushes against the cell's membrane to form protrusions called filopods<sup>[2]</sup> or "rockets". The protrusions are guided by the cell's leading edge<sup>[9]</sup> to contact adjacent cells, which then engulf the listeria rocket and the process is repeated, perpetuating the infection.<sup>[3]</sup> Once phagocytosed, the listeria is never again extracellular: it is an intracytoplasmic parasite<sup>[7]</sup> like *Shigella flexneri* and *Rickettsia*.<sup>[3]</sup>

## Epidemiology

The Center for Science in the Public Interest has published a list of foods that have sometimes caused outbreaks of listeria: hot dogs, deli meats, raw milk, cheeses (particularly soft-ripened cheeses like feta, Brie, Camembert, blue-veined, or Mexican-style "queso blanco"), raw and cooked poultry, raw meats, ice cream, raw vegetables, some fruit such as cantaloupe, raw and smoked fish, and the green lip mussel.<sup>[10]</sup>

## Clinical features/signs and symptoms

The disease primarily affects older adults, persons with weakened immune systems, pregnant women, and newborns. Rarely, persons without these risk factors can also be affected. A person with listeriosis usually has fever and muscle aches, often preceded by diarrhea or other gastrointestinal symptoms. Almost everyone who is diagnosed with listeriosis has invasive infection (meaning that the bacteria spread from their intestines to their blood stream or other body sites). Disease may occur as much as two months after eating contaminated food.

The symptoms vary with the infected person:

- High-risk persons other than pregnant women: Symptoms can include fever, muscle aches, headache, stiff neck, confusion, loss of balance, and convulsions.
- Pregnant women: Pregnant women typically experience only a mild, flu-like illness. However, infections during pregnancy can lead to miscarriage, stillbirth, premature delivery, or life-threatening infection of the newborn.
- Previously healthy persons: People who were previously healthy but were exposed to a very large dose of Listeria can develop a non-invasive illness (meaning that the bacteria have not spread into their blood stream or other body sites). Symptoms can include diarrhea and fever.

If a person has eaten food contaminated with Listeria and does not have any symptoms, most experts believe that no tests or treatment are needed, even for persons at high risk for listeriosis.<sup>[11]</sup>

## September 2011 outbreak

As many as 16 people have died from possible listeria illnesses traced to cantaloupes from Jensen Farms in Colorado. This is the deadliest food outbreak in more than a

decade. The Centers for Disease Control and Prevention said on 27 September, 2011 that 72 illnesses, including 13 deaths, are linked to the tainted fruit.<sup>[12]</sup>

## **Prevention**

Preventing listeria as a food illness requires effective sanitation of food contact surfaces. Alcohol is an effective topical sanitizer against listeria. Quaternary ammonium can be used in conjunction with alcohol as a food contact safe sanitizer with increased duration of the sanitizing action. Refrigerated foods in the home should be kept below 4 °C (39.2 °F) to discourage bacterial growth. Preventing listeriosis also can be done by carrying out an effective sanitation of food contact surfaces.<sup>[13]</sup>

## **Modern relevance/future research**

Listeria is an opportunistic pathogen: It is most prevalent in the elderly, pregnant mothers, and AIDS patients. With improved healthcare leading to a growing elderly population and extended life expectancies for AIDS patients, physicians are more likely to encounter this otherwise-rare infection (only 7 per 1,000,000 healthy people are infected with virulent listeria each year).<sup>[2]</sup> Better understanding the cell biology of listeria infections, including relevant virulence factors, may help us better treat Listeriosis and other intracytoplasmic parasites. Researchers are now investigating the use of listeria as a cancer vaccine, taking advantage of its "ability to induce potent innate and adaptive immunity."<sup>[6][14]</sup>