

## PUBLIC HEALTH

## Listeriosis: a primer

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Serious outbreaks of food-borne illness, whether regional or national, dramatically raise community anxiety about personal health and increase the workloads of front-line physicians. The drama further increases when the offending microbe is not well known. This primer on listeriosis hones in on the microbe, the incidence of infection, clinical presentations, diagnosis, treatment and prevention. The information is based on a MEDLINE search on listeriosis and discussion with experts.

## The microbe

*Listeria monocytogenes* is a small, gram-positive bacillus that can grow in anaerobic or aerobic conditions. It is found widely in the environment in soil, decaying vegetation and water and may be part of the fecal flora of many mammals, including healthy human adults.<sup>1</sup>

*L. monocytogenes* presents a particular concern with respect to food handling because it can grow at refrigerator temperatures (4°C to 10°C), temperatures commonly used to control pathogens in foods. Freezing also has little detrimental effect on the microbe. Although pasteurization is sufficient to kill *Listeria*, failure to reach the desired temperature in large packages can allow the organism to survive. Food can also be contaminated after processing by the introduction of unpasteurized material, as happens during the preparation of some cheeses. *Listeria* can also be spread by contact with contaminated hands, equipment and counter tops.

The centralized production of prepared ready-to-eat food products in Canada increases the risk of higher levels of contamination, since it requires that foods be stored for long periods at refrigerated temperatures that favour the growth of *Listeria*. During the preparation, transportation and storage of prepared foods, the organism can multiply to reach a threshold needed to cause infection.

The approximate infective dose of *L. monocytogenes* is es-

**Box 1: People at high risk of listeriosis****Pregnant women**

- The risk of listeriosis is about 20 times higher among pregnant women than among nonpregnant healthy adults
- About one-third of listeriosis cases are diagnosed in pregnant women
- Pregnant women with listeriosis are at increased risk of spontaneous abortion, preterm delivery or stillbirth

**Newborns**

- Whereas pregnant women may get a mild form of the infection, newborns are at greater risk of the serious effects of infection
- Newborns may present clinically with early-onset listeriosis (< 7 days) or late-onset infection (≥ 7 days)
- Early-onset listeriosis is typically diagnosed within the first 24 hours of life and is usually transmitted from the mother transplacentally
- Late-onset neonatal listeriosis is less common; the mode of acquisition is poorly understood, but in most cases there is no history of maternal infection
- Listeriosis is not felt to be spread through breast milk
- Mortality among infected newborns is high (50%)

**Elderly people (age ≥ 60 yr)**

- About 50% of cases occur in this age group

**Immunocompromised people**

- People with cancer, diabetes or kidney disease
- People with HIV/AIDS: listeriosis is up to 300 times more likely to occur in this group than in healthy adults
- Patients receiving immunosuppressive drug therapy (e.g., high-dose glucocorticosteroid, tumour necrosis factor inhibitor)
- Transplant patients receiving anti-rejection drug therapy

timated to be 10–100 million colony forming units (CFU) in healthy hosts, and only 0.1–10 million CFU in people at high risk of infection (Box 1).<sup>2</sup> Foods such as raw vegetables, raw (unpasteurized) milk and cheese, and meats (fresh and frozen) may become contaminated with *L. monocytogenes* because of where they come from and how they are processed. Ready-to-eat foods such as cold cuts or deli meats, cheeses and other dairy products are ideal sources for contamination.

Although *L. monocytogenes* was recognized as an animal pathogen over 80 years ago,<sup>3</sup> the first outbreak confirming an

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indirect transmission from animals to humans was reported only in 1983, in Canada's Maritime provinces.<sup>4</sup> In that outbreak, cabbages, stored in the cold over the winter, were contaminated with *Listeria* through exposure to infected sheep manure. A subsequent outbreak in California in 1985 confirmed the role of food in disseminating listeriosis. Since then *Listeria* has been implicated in many outbreaks of food-borne illness, most commonly from exposure to contaminated dairy products and prepared meat products, including turkey and deli meats, pâté, hot dogs and seafood and fish.<sup>5</sup>

## Incidence of infection

The incidence of listeriosis is difficult to establish, since symptoms may be mistaken for a flu-like illness or gastroenteritis and appropriate cultures not obtained. The Canadian Listeriosis Reference Service was created in 2001 to actively investigate cases and develop a molecular epidemiology database of isolates as a resource for outbreak investigations. In 2006, listeriosis was named as a nationally notifiable disease by the Public Health Agency of Canada. Between 1995 and 1999 (the most recent years for which data are available), 25–51 cases occurred annually in Canada.<sup>6</sup> However, passive surveillance programs such as this may suffer from under-reporting of cases.<sup>5</sup> Countries with surveillance programs have reported rates of infection from 0.6 to 6.2 cases per million, with countries having active surveillance programs reporting the highest incidence.<sup>5,7–11</sup> The case-fatality rates vary from country to country, but invariably the highest mortality is among newborns with infection acquired from their mothers (25%–50%). Mortality among those over 60 years of age is also high (10%–20%).

## Clinical presentations

Initial symptoms of infection include nonspecific flu-like symptoms, nausea, vomiting, cramps, diarrhea and fever. There are few clinical features that are unique to listeriosis. Therefore, clinicians must consider a variety of potential causes for infection, including viral infections (influenza) and other bacterial infections that may cause sepsis or meningitis. Symptoms can develop at any time from 2 to 70 days after eating contaminated food. Except for vertical mother–fetus transmission, most cases of listeriosis begin with ingestion of the organism from a food source.

Most healthy adults and children who consume contaminated food experience only mild to moderate symptoms. The infection is usually self-limited, since, in healthy hosts, exposure to *Listeria* stimulates the production of tumour necrosis factor and other cytokines, which activate monocytes and macrophages to eradicate the organism.<sup>12,13</sup> Few people with normal immune function go on to have more severe, life-threatening forms of listeriosis, characterized by septic shock, meningitis and encephalitis.

In contrast, people with poor immune function are at much higher risk of severe, life-threatening forms of listeriosis. High-risk groups include pregnant women, newborns, elderly people ( $\geq 60$  years of age) and people with a weakened im-

mune system (Box 1). Individuals taking tumour necrosis factor inhibitors and transplant recipients taking anti-rejection drugs are now included in this high-risk group.<sup>14</sup>

Pregnant women with listeriosis may have only mild symptoms of the infection. However, they are at increased risk of having a spontaneous abortion during the first trimester or of giving birth to a premature infant with acute sepsis if they are exposed later in the pregnancy.

Newborns may present clinically with early- (< 7 days) or late-onset forms of infection ( $\geq 7$  days). Those with the early-onset form are often diagnosed in the first 24 hours of life with sepsis. Early-onset listeriosis is most often acquired from the mother through transplacental transmission. Late-onset neonatal listeriosis is less common than the early-onset form. Clinical symptoms may be subtle and include irritability, fever and poor feeding.<sup>13</sup> The mode of acquisition of late-onset listeriosis is poorly understood, but acquisition of the organism after birth is implicated, since there is usually no maternal infection in such cases. The organism is not felt to be spread through breast-feeding.

Common clinical features among patients with nonperinatal forms of listeriosis include meningitis (about 33% of such cases) and septicemia (25%). Less commonly, patients may have inflammatory gastroenteritis, endocarditis or joint infections.<sup>8,13</sup>

## Diagnosis and management

Early diagnosis and treatment of listeriosis in high-risk patients is critical, since the outcome of untreated infection can be devastating. This is especially true for pregnant women because of the increased risk of spontaneous abortion and preterm delivery. Depending on the risk group, rates of death from listeriosis range from 10% to 50%, with the highest rate among newborns in the first week of life.

The Public Health Agency of Canada convened an expert panel in August 2008 to provide information to health care professionals and the general public on the diagnosis and management of listeriosis during the recent outbreak. The following information is based on the panel's discussion and addresses what should be done for patients who have eaten food items that are suspected of being contaminated with *Listeria* and who have symptoms of diarrhea with or without fever.

- For healthy adults and children with a normal immune system, no *Listeria*-specific investigation is required. Gastroenteritis due to *Listeria* infection has a short duration and is self-limited in this population. Culture of a stool specimen for common bacterial enteric pathogens may be warranted if indicated by the person's history and clinical condition.
- For high-risk patients (Box 1), more aggressive investigation and management strategies should be followed. If the patient has diarrhea only, culture of a stool specimen for common bacterial enteric pathogens may be indicated. If the patient has a fever, bacteremia must be suspected. Two blood samples for aerobic culture should be drawn. *Listeria* is only one of many bacteria that may cause infections in such patients; thus, investigations and treatment should be directed to cover common causes in addition to *Listeria*.

**Box 2: Recommendations for reducing the risk of listeriosis****General recommendations**

- Thoroughly cook raw food from animal sources, such as beef, pork and poultry
- Wash raw vegetables thoroughly before eating
- Keep uncooked meats separate from vegetables and from cooked foods and ready-to-eat foods
- Avoid raw (unpasteurized) milk or foods made from unpasteurized milk
- Wash hands, knives and cutting boards after handling uncooked foods
- Consume perishable and ready-to-eat foods as soon as possible

**Additional recommendations for high-risk groups**

- Do not eat hot dogs or ready-to-eat foods such as deli meats unless they are reheated until steaming hot
- Wash hands after handling hot dogs and ready-to-eat foods
- Do not eat soft cheeses (e.g., feta, brie and camembert) or blue-veined cheeses unless they have labels that clearly state they are made from pasteurized milk
- Do not eat refrigerated pâtés or meat spreads; canned or "shelf-stable" (pasteurized) pâtés and meat spreads may be eaten
- Do not eat refrigerated smoked seafood unless it is contained in a cooked dish, such as a casserole; canned or shelf-stable smoked seafood may be eaten

- For pregnant women with a fever or signs of sepsis, blood and urine samples should be obtained for culture. Empiric therapy, including ampicillin, should be started for coverage of *Listeria*.
- For infants born to women suspected of having listeriosis, blood cultures should be taken and antibiotic therapy started.

*Listeria* is susceptible to ampicillin, which should be given with gentamicin to patients with sepsis. If further advice on the management of patients with listeriosis is needed, it should be obtained in consultation with the appropriate specialist such as an obstetrician, a neonatologist or infectious disease specialist.

**Prevention of infection**

Given the characteristics of *Listeria* and the risk of infection, what can be done to minimize and prevent infection? The Canadian Food Inspection Agency and the US Centers for Disease Control and Prevention have made recommendations to protect against listeriosis in the home. People with a poor immune system and pregnant women are advised to take even more rigorous precautions by avoiding foods that may become contaminated with *Listeria* (Box 2).<sup>5,7</sup>

**Summary**

Although food-borne outbreaks of listeriosis are uncommon, they remain a major public health problem. In the United States, about 20%–65% of deaths from all food-borne infections are due to *Listeria*.<sup>5</sup> Therefore, detecting an outbreak early and identifying its source is a priority. Prompt reporting of all cases of *Listeria* infection to public health authorities is important to assist them in early detection of an outbreak.

During an outbreak of listeriosis, vigilance in the preparation of food is especially important for immunocompromised patients and pregnant women. Initial manifestations of infection are nonspecific and include flu-like symptoms. Such symptoms should be thoroughly investigated if they develop in patients at high risk of listeriosis (Box 1). In contrast, in patients with normal immune function, symptoms are usually milder and the infection self-limited; such patients do not need tests or treatment. Proper preparation, storage and handling of food by industry and in the home can minimize the risk of a widespread outbreak.

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