The Trouble with Listeria

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Listeria monocytogenes has recently been the subject of attention in Canada due to an outbreak of foodborne listeriosis. This outbreak caused by the consumption of contaminated deli meats has unfortunately resulted in significant morbidity and mortality. Although this bacteria has recently entered the limelight in Canada, it is a pathogen about which we have known much for decades and is therefore this month's **Bug of the Month**.

What is Listeria monocytogenes*?*

There are six species of *Listeria* (*L. monocytogenes*, *L. seeligeri*, *L. welshimeri*, *L. innocua*, *L. ivanovii*, *L. grayi*). However, only *L. monocytogenes* is pathogenic in humans. *L. monocytogenes* is a small, gram-positive bacillus that is a facultative anaerobe, as it is capable of growing either aerobically or anaerobically. It is motile at 25ºC and under the microscope it shows a characteristic "tumbling" motility. It derives its species name "monocytogenes" because it induces a "monocytosis" in experimentally infected rabbits. However, a monocytosis is only rarely observed in human disease.

Why is it such an effective pathogen?

One of its key characteristics is that although its ideal temperature range for growth is 30ºC to 37ºC, it actually grows very well at refrigerator temperatures (4ºC to 10ºC) where other competing microflora are inhibited. It is this feature of being able to thrive in cold environments which allows *L. monocytogenes* to grow to significant numbers that would enhance transmission to the host. There are also unique features of the organism that allow it to evade the immune system once ingested.

Where do we find it?

L. monocytogenes is ubiquitous in the environment (water, soil, vegetation) and has been recovered from many different foods such as coleslaw/cabbage, milk products such as cheeses and butter, hotdogs and deli meats. Globally, there have been numerous outbreaks of listeriosis. In Canada, apart from the recent deli meat associated outbreak, a large foodborne outbreak occurred in the Maritimes in 1980 to 1981 which was traced back to contaminated coleslaw. This outbreak occurred when cabbages contaminated with infected sheep manure were stored in the cold and subsequently used for manufacturing coleslaw. The finished product was then consumed by pregnant women and other adults.

Mode of infection

Most human infections occur through ingestion of the microorganism in food. The number of *Listeria* microorganisms required to cause human disease is unknown. As for any foodborne pathogen, any condition which raises the pH of the stomach will predispose humans to infection. The incubation period has a mean of approximately 31 days with a range of approximately 11 to 70, although a short incubation (24 to 48 hours) febrile gastroenteritis has been described. Once in the GI tract, the microorganism can cross the mucosal barrier by means of active endocytosis. Hematogenous dissemination then occurs, transporting the organism to various locations such as the central nervous system and the placenta, for which this pathogen appears to have a specific predilection. Immunity to this bacteria is provided primarily by innate immunity and the cell mediated immune system and therefore, any condition which impaires these protective responses will put humans at risk of infection.

What are the symptoms?

The initial manifestations of listeriosis can be quite non-specific as persons with infection may present with abdominal complaints such as nausea, vomiting, diarrhea, fever and a flu-like syndrome. In the majority of healthy persons, their symptoms may be mild and self-limited, while those in high-risk groups (Table 1), may present with a myriad of clinical manifestations ranging from bacteremia to brainstem encephalitis. These clinical manifestations are summarized as follows:

- Infection in pregnancy: A bacteremia may occur with the microorganism ultimately reaching and proliferating in the placenta. The bacteremia may result in amnionitis, still births and neonatal listeriosis
- Neonatal listeriosis: Neonatal infections can occur either from transplacental transfer (early onset listeriosis), leading to a sepsis syndrome (granulomatosis infantiseptica) which may be associated with prematurity, or a late-onset meningitis may occur within a few weeks after delivery due to the microorganism being acquired through the birth canal at the time of delivery
- Bacteremia: Bacteremias have been observed without an obvious focus for infection almost always in patients with impaired immunity
- Central nervous system infections: *L. monocytogenes* is a recognized cause of central nervous system infection, specifically, meningitis in infants as noted above where it is one of the three top causes along with group B *streptococcus* and *E. coli*. It may also cause meningitis in adults, primarily those who are > 60-years-of-age and who have impaired immune systems from many causes. A characteristic brainstem encephalitis (rhombencephalitis) may occur, which mimics a similar disease seen in ruminants such as sheep or cattle. It presents with cranial nerve deficits, hemiparesis and cerebellar signs
- Endocarditis: Although an unusual cause of endocarditis, *L. monocytogenes* can cause both native and prosthetic valve endocarditis
- Febrile gastroenteritis: For many persons who develop bloodstream and central nervous system infections with *L. monocytogenes*, GI symptoms, such as diarrhea, nausea, vomiting and fever may occur. In addition, a short incubation, self-limited febrile gastroenteritis similar to salmonellosis or *Campylobacter spp* infection has been described

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Table 1

High-risk groups for listeriosis

- **Pregnant women**
- **Those at the extremes of age:**
  - Newborns
  - Persons > 60-years-of-age
- **Immunocompromised:**
  - Infection with HIV/AIDS
  - Corticosteroid immunosuppression
  - Those receiving immunosuppressive therapy:
    - Transplant recipients
    - Cancer chemotherapy recipients
    - Those receiving tumour necrosis factor-α neutralizing agents
    - Congenital immunodeficiency syndromes
- **Other risk conditions:**
  - Alcoholism
  - Diabetes mellitus

How is it diagnosed?

The first step towards establishing a diagnosis is having a high index of suspicion based on the clinical syndrome such as typical rhombencephalitis or known listeriosis cases in the community. During the recent Canadian deli meat associated outbreak, a heightened level of suspicion was present amongst healthcare providers when persons, particularly those in high-risk groups, presented with fever and other manifestations such as those outlined above. The specimens used for diagnosis depend upon the patient's clinical manifestations at the time of presentation. All persons with fever and sepsis syndrome should have blood and urine cultures performed routinely. *L. monocytogenes* grow well in usual laboratory media. While individuals with GI symptoms should have stool obtained for the usual pathogens, stool cultures for *L. monocytogenes*, which require selective media, should only be obtained for research or epidemiologic purposes. Patients with central nervous system manifestations should have blood cultures and lumbar puncture (culture, cell count, total protein, glucose) as well as imaging of the brain with either a computed tomographic scan or a magnetic resonance scan (preferable) to exclude rhombencephalitis. In asymptomatic persons who may have been exposed

Table 2

How to prevent foodborne listeriosis*

The basics:

- Thoroughly cook all raw meat prior to eating
- Thoroughly wash all raw vegetables prior to eating
- Keep all uncooked meats refrigerated and separate from cooked and ready-to-eat food
- Avoid consuming unpasteurized milk and milk products
- Thoroughly wash hands, kitchen utensils and cutting surfaces after handling uncooked foods

Additional precautions for persons at high risk:

- Avoid soft cheeses
- Only consume hotdogs and ready-to-eat foods such as deli meats, once reheated to steaming hot
- Careful handwashing before and after handling hotdogs and ready-to-eat foods
- Avoid refrigerated smoked seafood or similar foods where reheating would make them unpalatable
- Shelf-stable seafood may be consumed

*Modified from:

1. Centres for Disease Control and Prevention. Diagnosis and Management of Food Borne Illnesses. A Primer for Physicians. MMWR 2001; 50(No. RR-2):1-69.
2. Public Health Agency of Canada: http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/food-aliment/listeria-eng.php.

to a potentially contaminated food, the collection of specimens (blood, urine, or stool) to screen for listeriosis is not indicated. Because listeriosis is a rare disorder, consultation with a clinical microbiologist or infectious diseases specialist may be prudent and all documented listeriosis cases should be reported to the local Medical Officer of Health. During outbreaks, always review the statements from the Public Health Agency of Canada (PHAC) and local Public Health Departments to ensure that the appropriate diagnostic and therapeutic interventions are being undertaken. The current PHAC recommendations for screening and treatment can be found at: http://www.phac-aspc.gc.ca/alert-alerte/listeria/archive/rec-hcp_rps-eng.php.

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How is it treated?

Treatment recommendations are based upon the clinical syndrome and whether empiric or specific treatment for listeriosis is warranted. For febrile gastroenteritis in the immunocompetent host, therapy is rarely indicated regardless of the pathogen isolated. For persons presenting with sepsis, who are in high-risk groups, conventional empiric therapy should be initiated and may include ampicillin to provide antibacterial coverage for *L. monocytogenes*. It should be noted that *L. monocytogenes* are always resistant to cephalosporins, which are frequently used for empiric treatment of many infections. For established listeriosis, gentamicin should be added for antibacterial synergy, as β-lactam antibiotics are often considered bacteriostatic for *Listeria spp.* For persons with meningitis, conventional therapy should be used and for those with risk factors for listeriosis, ampicillin should be added in appropriate doses.

In persons who have anaphylaxis to β-lactam antimicrobial agents, trimethoprim-sulfamethoxazole, or vancomycin may be used as alternatives.

How can foodborne listeriosis be prevented?

Table 2 demonstrates steps that can be taken to minimize the risk of acquiring listeriosis in all persons and those who are deemed to be at high risk.

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