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Listeria monocytogenes **A Clinical Practice Guideline**

Background: Listeriosis is a foodborne illness that usually presents as a self-limited syndrome with malaise, fever, and diarrhea with no further untoward outcome. In a minority of cases, particularly in immunocompromised, patients at the extremes of age (neonates and elderly) and pregnant women, septicaemia and meningitis can occur, accompanied by fetal loss in the pregnant woman.

Epidemiology: *Listeria monocytogenes* is widespread in nature, and commonly found in soil, decaying vegetation, and water.¹ **It is also commonly found in humans:** it has been isolated from the stools of 1-5% of healthy adults. It is not uncommon for foods such as raw vegetables, raw milk, unpasteurized cheese (especially soft cheeses), and meats (especially pâté) to be contaminated – ingestion of *L. monocytogenes* is likely a common occurrence.^{2,3} Ingestion of suspect food does not necessarily result in infection with *Listeria*.

Mother to child transmission (transplacentally or via the birth canal) may occur, and transmission has been described from ill infants in nurseries,⁴ but human to human transmission has otherwise not been described.

Pregnant women and their babies account for 30% of cases of listeriosis; almost all remaining cases occur in immunosuppressed patients (such as hematologic malignancy, AIDS, organ transplantation, persons receiving chemotherapy or corticosteroid therapy). Occasionally previously healthy persons can develop invasive disease, particularly if over 60 years of age. The organism has a predilection for the central nervous system and the placenta.

Mean **incubation period** is not well established. It likely varies depending on the concentration of *Listeria* in the food. In the largest outbreak of *Listeria* described the median incubation period was 31 days (range 11 to 70 days).⁵ In other *Listeria* outbreaks the incubation period ranged from 3 to 70 days.

Non-invasive Clinical Syndromes:

- **Febrile Gastroenteritis:** Ingestion of contaminated food can result in a febrile, self-limited gastroenteritis. The incubation period is usually

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short(range 6 hours to 10 days).⁶ **This non-invasive illness is self limiting and requires no therapy in persons in low risk groups.**

- **No testing is recommended for asymptomatic persons**, whether or not they are in a high risk group or there is a history of ingestion of foods known to be contaminated with *L. monocytogenes*.
- No stool testing is recommended for cases of isolated gastroenteritis in healthy adults unless they are in a specific high risk group as detailed above (pregnant, immunocompromised, neonates).
- **Isolated gastroenteritis:** Otherwise healthy persons with suspected listeria gastroenteritis require supportive therapy alone for this self-limiting illness, with no indication for antimicrobial therapy. There is no clear data to guide therapy of isolated gastroenteritis in high risk patients (pregnant, immunocompromised, neonates). If treatment is considered, it should be done in consultation with an infectious diseases physician.
- Patients presenting with minor or no symptoms with a history of consumption of recalled meat should be presented with the Listeria fact sheet presented at <http://www.inspection.gc.ca/english/fssa/concen/cause/listeriae.shtml> and cautioned about the signs of invasive disease.

Invasive Clinical Syndromes

- **Infection in pregnancy:** The highest risk period for invasive listeriosis is during the third trimester, associated with depressed cell mediated immunity which occurs at the end of gestation. Bacteremia manifests clinically as acute febrile illness, often accompanied by myalgias, arthralgias, headache, and backache. However, severe neonatal listeria infection or fetal loss may also follow when the mother experiences only a mild or flu-like illness. Twenty-two percent of human perinatal infections result in stillbirth or neonatal death; two thirds of surviving infants develop clinical neonatal listeriosis.⁷ There is no clear evidence that listeria is a cause of recurrent abortion.
- **Neonatal infection:** Neonatal infection may cause an early onset sepsis syndrome usually associated with prematurity. It may also cause a late-onset meningitis or sepsis occurring about 2 weeks post-partum.
- **Bacteremia:** Bacteremia without focus is the most common manifestation of listeriosis in immunocompromised persons. Clinical manifestations are

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similar to other forms of bacteremia, and typically include myalgias and fever. A prodromal illness of diarrhea and nausea may occur.

- **Central Nervous System Infection:** CNS infection is most common in neonates and persons over 60 years of age.⁸ *L. monocytogenes* has tropism for brain tissue, particularly the brainstem, as well as the meninges. Many with meningitis have true meningoencephalitis with altered consciousness, seizures, or movement disorders. Isolated meningitis is clinically similar to that by other causes, and brain abscess occurs in 10% of CNS listeria infections. Listeria is a cause of bacterial (nontuberculous) meningitis in which substantial lymphocytosis can be seen in the CSF differential.
- **Other Clinical Syndromes:** Endocarditis can occur as a manifestation of invasive listeriosis. *L. monocytogenes* can infect both native and prosthetic cardiac valves. There are rare reports of other focal infections complicating bacteremia.

Diagnosis and treatment of invasive disease: please refer to the recent Labstract on *L. monocytogenes* diagnostic testing:

<http://www.oahpp.ca/resources/labstracts.html>

- **Invasive Disease:** Advice from an infectious diseases physician should be sought when managing a suspected case of invasive listeriosis.
- Diagnosis of invasive disease requires isolation from normally sterile clinical specimens (blood, CSF, joint fluid, sterile tissue). Blood cultures should always be collected (as outlined in the Labstract), and other specimens according to the clinical syndrome.
- Antibody testing (serology) is not recommended as it has not proved useful for the diagnosis of acute listeriosis.⁹
- High dose antimicrobial therapy should be used in all cases of bacteraemia/possible bacteraemia. (**see Table 1 for antimicrobial dosing guidelines**)
 - Ampicillin is the preferred agent, although penicillin is likely to be as effective. Resistance to these two antibiotics has not been observed.
 - Most experts recommend adding gentamicin to ampicillin therapy for the treatment of bacteraemia in persons with impaired immunity (including neonates), and all cases of meningitis and endocarditis. Gentamicin is discontinued once the patient improves. Ampicillin alone can be used in pregnant women with isolated listerial bacteraemia.

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- Trimethoprim-sulfamethoxazole as a single agent is a suitable alternative in persons allergic to penicillins. Vancomycin can be used in penicillin allergic patients when sulfonamides are contraindicated (first trimester and last month of pregnancy, and infants less than 8 weeks of age).
- Cephalosporins must **not** be used to treat listeriosis, as they are ineffective against *L. monocytogenes*.
- Decisions about empiric therapy in patients with suspected listeriosis should be made in conjunction with an infectious diseases physician.
- **Duration of Therapy:** Bacteremic patients without CSF abnormalities can be treated for 2 weeks; meningitis should be treated for 3 weeks; relapses have been documented with shorter durations of therapy.¹⁰
- Longer durations of therapy are needed for encephalitis, brain abscess and endocarditis, and should be considered in any invasive infection in an immunocompromised person.
- Patients with invasive listeriosis do not need to be isolated.

Recommendations During an Outbreak

During an outbreak of listeriosis, the following changes to routine clinical practice are recommended:

- Any person (regardless of risk status) with meningitis, and any person in a high risk group with suspected sepsis should be treated empirically for listeriosis in addition to other possible causes of the clinical syndrome.
- Empiric therapy for listeriosis (in addition to empiric therapy for other causes of sepsis) should be strongly considered in any immunocompetent person with suspected sepsis of unknown cause. This can be discontinued if *L. monocytogenes* infection is not confirmed within 48 hours of blood culture collection.
- Empiric therapy for listeriosis should be strongly considered in any pregnant women with fever associated with labour or threatened labour.
- Blood cultures should be considered in any person in a high risk group with febrile gastroenteritis.
- Stool cultures may be useful in pregnant women, immunocompromised patients, and neonates with gastroenteritis without fever.

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Table1: Antibiotic Dosing Guidelines for Invasive Listeriosis

Antibiotic	Adult Dose	Paediatric Dose
Ampicillin	2 grams/dose IV, 4-hourly	100mg/kg/dose IV (max 3 grams), 6-hourly
Gentamicin	1-2mg/kg/dose IV, 8-hourly (monitor plasma levels)	2mg/kg/dose IV 8-hourly (monitor plasma levels)
Trimethoprim-Sulfamethoxazole (TMP-SMX) [‡]	5mg TMP/kg/dose IV (max 160mg TMP), 6-hourly	5mg TMP/kg/dose (max 160mg) IV, 6-hourly
Penicillin G	4 million units IV, 4-hourly	65,000 Units/kg/dose (max 4 million units) IV, 4-hourly

* Neonatal dosing is not addressed in this guideline.

‡ TMP-SMX is contraindicated in the first trimester and final month of pregnancy, and in neonates/infants below 8 weeks of age.

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