



衛生防護中心  
Centre for Health Protection

## Scientific Committee on Enteric Infections and Foodborne Disease

### Epidemiology of Listeriosis and Prevention Strategies

#### Purpose

This paper provides an overview of listeriosis, the global and local epidemiology, and examines the public health measures for disease prevention and control.

#### The Pathogen and the Disease

##### The Bacteria

2. Listeriosis is a bacterial infection caused by a gram-positive, rod-shaped, motile bacterium, *Listeria monocytogenes*. It is classified in the Family Listeriaceae and there are six species of *Listeria* within this phylogeny. *Listeria monocytogenes* has been recognized as a human pathogen since 1929 but the route of transmission only became clear since the 1980s when a series of outbreaks were found to be related to food.<sup>1</sup> It is a facultative intracellular bacterium that has a propensity for central nervous system infection in humans and domesticated mammals. On the basis of somatic (O) and flagellar (H) antigens, 17 serovars have been described.<sup>2</sup> Human infection is usually (> 98%) caused by serovars 1/2a, 1/2b, 1/2c and 4b.<sup>3</sup>

3. *Listeria monocytogenes* has an unusual characteristic of surviving in temperatures from -7°C to 45°C.<sup>2,4</sup> Its optimum growing temperature is around 37°C and it is able to grow, albeit slowly, at temperature as low as 0°C. As a result, it can multiply in properly refrigerated food after contamination. Nevertheless, it can be easily



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destroyed under normal cooking temperatures. *Listeria monocytogenes* and grow over a wide range of environmental conditions such as low pH and high salt concentration.<sup>4</sup> It can form biofilms on solid surfaces, including food processing facilities, which are more resistant to disinfectants and sanitizing agents. The infective dose of *Listeria monocytogenes* is unknown and may vary with the strain and susceptibility of the host.<sup>5</sup>

### Reservoir and Routes of Transmission

4. *Listeria monocytogenes* is widely dispersed in the natural environment, including soil, water and decaying vegetation. Common animal reservoirs include domestic and wild mammals such as cattle, sheep and fowls. Humans may also act as reservoirs and asymptomatic faecal carriage has been reported in humans, particularly abattoir workers and laboratory workers exposed to *Listeria monocytogenes* culture.<sup>3</sup>

5. Transmission of *Listeria monocytogenes* is principally via the faecal-oral route through the consumption of contaminated food. Raw or contaminated milk, vegetables and ready-to-eat meat have been implicated in overseas outbreaks. Food may be contaminated by *Listeria monocytogenes* during preparation and it then multiplies during the storage process. Unlike some other foodborne pathogens, *Listeria monocytogenes* can multiply in contaminated refrigerated food.<sup>3</sup> For example, soft cheese is considered as a high risk product for listeriosis because the bacteria may grow to significant numbers during refrigeration.

6. In neonatal infection, the pathogen is transmitted from the infected mother to her fetus transplacentally following maternal bacteraemia. Some infections may also occur through ascending spread from vaginal colonization with the fetus acquiring infection during passage through the birth canal. Other routes of transmission, e.g. outbreaks attributed to contaminated equipment or materials in delivery room and hospital have also been reported.<sup>6,7</sup>

### Clinical Presentation and Course of the Disease

7. The incubation period is variable, ranging from 3 to 70 days following exposure to the contaminated source.<sup>3</sup> The average incubation period is 3 weeks. After ingestion of the contaminated food, the bacteria that survive the acidity of the stomach enter the small intestine, cross the epithelial barrier and then spread to the liver, spleen, central nervous system and the fetus in pregnant women.<sup>2</sup>

8. Most healthy people infected with listeriosis are asymptomatic or only have a mild febrile illness. Symptomatic infection most commonly occurs in pregnant women, infants, elderly and the immunosuppressed. The various

clinical presentations and predisposing conditions in different susceptible groups associated with *Listeria monocytogenes* infection are summarized in Table 1.

Table 1. Clinical presentation of listeriosis infection

| Susceptible group   | Clinical Presentation  | Predisposing condition   |
|---------------------|--|--|
| Pregnant women      | Fever, flu-like illness, abortion  | -  |
| Newborns            | Sepsis, meningitis, pneumonia  | Prematurity  |
| Non-pregnant adults | Fever, gastroenteritis, sepsis, meningitis, focal infections such as liver abscesses | Advanced age, immunosuppression, alcoholics, cirrhosis, diabetes |
|                     | Endocarditis   | Underlying cardiac lesion  |

9. The onset of meningitis can be sudden, with fever, intense headache, nausea, vomiting and signs of meningeal irritation. Rhombencephalitis (brainstem encephalitis) occurs rarely and is characterized by progressive asymmetrical cranial nerve palsies, cerebellar signs, hemiparesis or hypesthesia and impairment of consciousness.<sup>8</sup> Focal infection rarely occurs, in which granulomatous lesions and abscesses can occur in the liver or other organs. Endocarditis occurs primarily in patients with underlying cardiac lesions.<sup>1</sup>

10. In pregnant women, meningitis rarely occurs. Instead, they often present with fever or flu-like illness. The infection may also result in abortion or is transmitted to the fetus to cause neonatal infection. It was reported in a recent review of listeriosis during pregnancy that fever was the most common symptom.<sup>9</sup> Twenty percent of the perinatal listeriosis cases resulted in spontaneous abortion or stillbirth and among the remaining neonates, 68.3% were infected by *Listeria*. Infected neonates were most commonly diagnosed with pneumonia, sepsis or meningitis. Meningitis alone, or in combination with sepsis or pneumonia, was associated with a worse prognosis. Less frequently, newborns may present with granulomatosis infantiseptica, which is characterized by disseminated abscesses or granulomas in multiple internal organs. Abortion can occur at any time during pregnancy but more commonly in the second half. Perinatal infection is acquired during the last trimester.

11. The case fatality rate is nearly 30% in those with underlying disease or receiving immunosuppressants and up to 70% in patients without adequate treatment.<sup>10,11</sup> The postpartum course for pregnant patients is usually uneventful, but the case-fatality rate in newborns may be as high as 30%.<sup>3</sup>

12. The disease can last from days to weeks and the infected person can shed the bacterium in their stools for several months. Mothers of infected

newborns can shed the bacteria in vaginal discharge and urine for 7-10 days after delivery.<sup>3</sup> There is little evidence of acquired immunity.

### Laboratory Diagnosis

13. Diagnosis can be confirmed by isolation of *Listeria monocytogenes* from clinical specimens obtained from normally sterile sites, e.g. blood, cerebrospinal fluid (CSF), or less commonly joint, pleural or pericardial fluid, placenta, amniotic fluid, meconium or fetal tissue. During a common source outbreak, isolation of *Listeria monocytogenes* from stool could also confirm the diagnosis. *Listeria monocytogenes* can be isolated readily from routine culture media, but it has to be distinguished from other gram-positive bacilli, e.g. diphtheroids. Isolation from contaminated specimens (e.g. stool) is more difficult because they contain large numbers of competing microorganisms. These specimens should be selectively enriched for *Listeria* spp. before being plated on *Listeria*-selective media. Typing of *Listeria monocytogenes* isolates from clinical specimens, e.g. by pulsed-field gel electrophoresis and serotyping, which is available in Public Health Laboratory Services Branch (PHLSB) of Centre for Health Protection (CHP), can help investigation for single source clusters of foodborne infection.<sup>12</sup>

14. For non-culture tests, microscopic examination of Gram-positive rods in the CSF permits a presumptive diagnosis. Use of PCR for direct molecular detection has been reported but is not widely available. Serological tests are unreliable.

### Patient management and infection control

15. Patients with listeriosis are often admitted to hospital for management. Antibiotics should be used to treat the infection. In the public hospitals in Hong Kong, the treatment of choice for listeriosis is intravenous ampicillin or penicillin, often in combination with an aminoglycoside for synergy.<sup>13</sup> Cephalosporin antibiotics are not recommended as *Listeria monocytogenes* is uniformly resistant. The optimal length of therapy has not been established but relapses have been reported in renal transplant patients after two weeks of penicillin therapy.<sup>14</sup> A prudent course of treatment is at least 2 weeks and should be longer for complicated infections such as abscesses and cerebritis in central nervous system infection and in immunocompromised patients.

16. Standard precautions should be performed in hospital when taking care of the patient.<sup>15</sup> Careful handling and disposal of body fluids and excretions, such as vaginal fluid, urine and faeces should be observed. Equipment and the environment around the patient should be properly decontaminated according to hospital policies.

## Global Epidemiology

17. Listeriosis is an emerging infection with major public health concern worldwide because of occurrence of associated foodborne outbreak and significant risk of mortality and morbidity. Large foodborne outbreaks of listeriosis have occurred during the last decade in Europe and the USA.<sup>12,16-20</sup> Between 1991-2002, 19 outbreaks of invasive listeriosis infection were reported in nine European countries, with a total of 526 related cases. In 1997, one large outbreak resulting in 1,566 cases of listeria gastroenteritis was reported in Italy and traced to the consumption of contaminated corn salad. A recent nationwide outbreak linked to contaminated packaged meat products occurred in Canada in 2008 resulting in 56 patients, including 20 deaths.<sup>18</sup>

18. In Europe, listeriosis surveillance data is available at the national level in 16 countries.<sup>19</sup> Recent reports based on these national surveillance systems indicate an increase in the incidence of listeriosis in many European countries including England and Wales, Denmark, Belgium, Germany, the Netherlands, Switzerland and Finland during 2000 to 2006.<sup>21</sup> In England and Wales the incidence of listeriosis has nearly doubled from an annual average of 110 cases in 1990s to 230 per year in 2007.<sup>22</sup> Increased risk of listeria infection is predominantly seen in patients aged 60 years or above.<sup>23</sup> Similar trends are also found in other European countries where the incidence of listeriosis is higher among older persons.<sup>20</sup>

19. In the United States, the CDC Foodborne Diseases Active Surveillance Network (FoodNet) monitors trends in listeriosis over time. In contrast to the EU countries, there has been a continued reduction in incidence in recent years. From 1996 through 2003, the incidence rate decreased significantly by 24%, from 4.1 cases per million people in 1996 to 3.1 cases per million people in 2003.<sup>24</sup> In 2007, listeriosis cases have decreased by 42% with rates reaching 0.27 per 100,000 compared to the baseline period (1996-1998).<sup>20</sup>

20. In the Asia-Pacific region, Australia's national notifiable disease surveillance system reported an annual number of listeriosis cases that ranged from 35 to 73 during the period 1991 to 2007.<sup>25</sup> In Singapore, the annual number of administratively-required (non-statutory) notifications to the Ministry of Health ranged from one to nine cases from 2001 to 2007.<sup>26</sup>

21. Recent developments in food processing and food distribution have increased the risks of listeriosis outbreaks. Epidemiological investigations have revealed that some outbreaks were associated with consumption of contaminated dairy products such as cheese and butter, processed meat and fish products and contaminated salad and ice cream cake.<sup>19</sup>

## Local Situation

22. The Department of Health (DH) had been conducting a case-based surveillance for listeriosis in the past years and encouraged doctors in Hong Kong to report cases of listeriosis voluntarily for epidemiological investigation and control. Since 14 July 2008, DH has made listeriosis notifiable under the Prevention and Control of Disease Ordinance (Cap. 599). All medical practitioners are required by law to report listeriosis cases to the CHP. From June 2004 to December 2008, a total of 52 cases of listeriosis were reported to CHP. A notable increase in the number of cases reported has been observed over the past five years, rising from 3 cases in 2004 to 17 cases in 2008 (Figure 1). This may be the result of increased awareness of this infection among health care professionals and enhanced surveillance for listeriosis. No obvious seasonal trend in disease occurrence is observed (Figure 2).

Figure 1. Number of Listeriosis cases reported to CHP (June 2004 to December 2008).

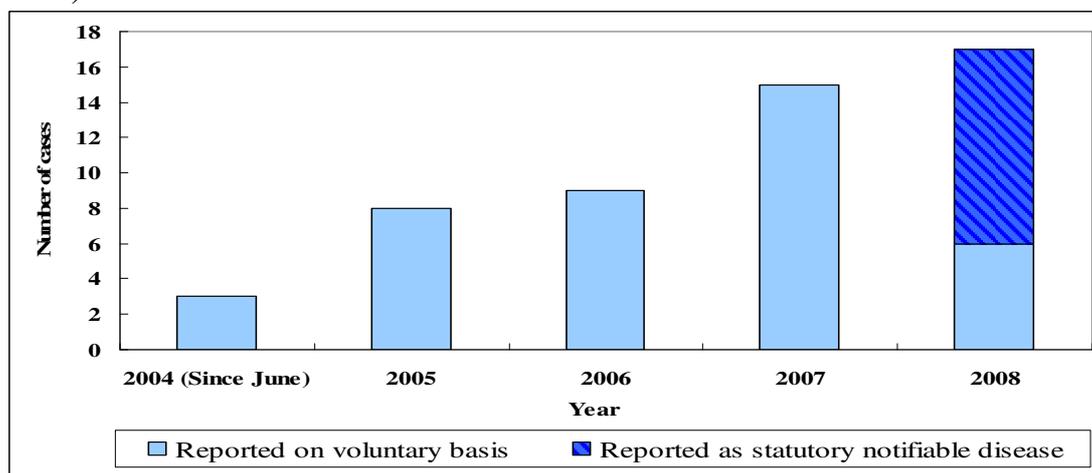
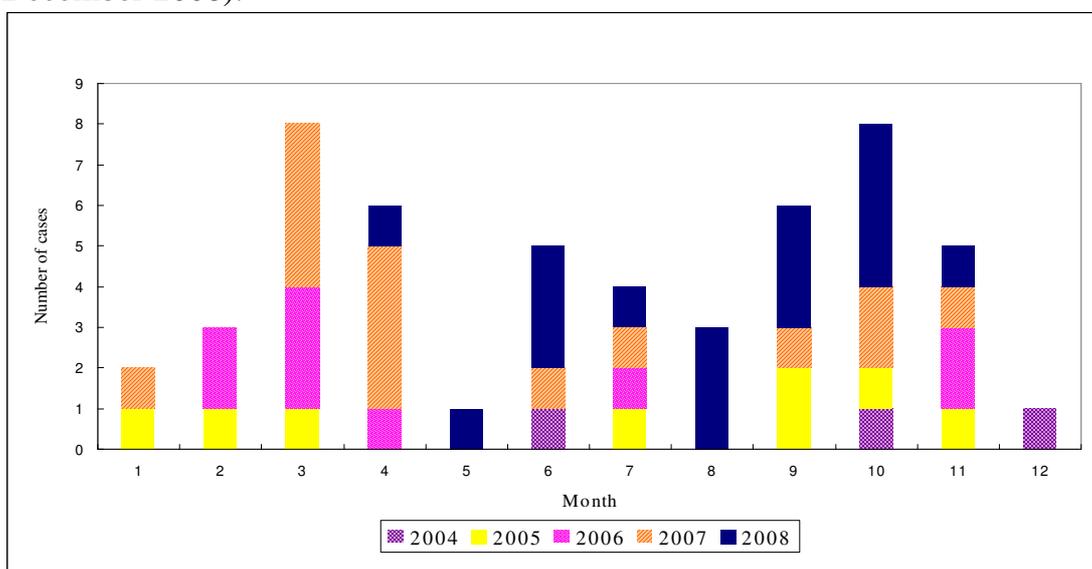


Figure 2. Number of Listeriosis reported to CHP by year (June 2004 to December 2008).



23. All reported cases occurred sporadically and no outbreaks were noted. Both sexes and all ages have been affected with the male-to-female ratio being 1:0.9 and the age range from 1 day to 91 years (median = 61 years). Figure 3 shows the age distribution of the cases. Two-third of the cases had underlying chronic illnesses such as diabetes mellitus and heart failure, or were suffering from one or more immunocompromising conditions such as systemic lupus erythematosus, renal failure, cirrhosis, leukaemia, multiple myeloma, nephrotic syndrome and cancer. Most of the patients presented with non-specific symptoms including fever, chills and headache and the majority of patients had a mild course of illness and recovered fully. There were two deaths due to listeriosis among these 52 cases: a 63-year-old woman with history of end stage renal failure on continuous ambulatory peritoneal dialysis; and a 59-year-old man who presented with meningitis complicated by septicaemic shock.

Figure 3. Age distribution of listeriosis cases reported to CHP (June 2004 to December 2008).



24. Five pregnant women, aged 26 to 39, were reported with listeriosis since July 2004. Two of them experienced pre-term deliveries with uneventful outcome, one experienced an intra-uterine death of undetermined cause and the remaining two babies tested negative for listeriosis.

25. In addition, there were two babies diagnosed to have listeriosis but their mothers were not diagnosed with listeriosis. One of these babies died of severe meconium aspiration syndrome and bilateral pneumothoraces after emergency caesarean section on Day 1, while the other baby was delivered at 25 weeks gestation and was discharged after intensive medical care.

26. Among the 52 reported cases, half recalled consuming dairy products or other high risk foods such as raw food and sandwiches, during the incubation periods. However no specific food items and food premises were identified as the source of infection. Laboratory test results on the food samples and environmental swabs collected from patients' homes were all negative for *Listeria monocytogenes*.

## Prevention and control for listeriosis in Hong Kong

27. As most cases of the human listeriosis are foodborne, various measures targeting food safety should be implemented to reduce the incidence of listeriosis. Important control strategies include an effective disease surveillance programme and prompt investigation of reported cases and clusters, enforcement of regulations designed to minimize *Listeria monocytogenes* in foods, and increasing awareness of the disease in the trade and the public. The following, examines the existing prevention and control measures and discusses potential areas for improvement.

### Disease Surveillance and Control

28. To enhance disease surveillance, listeriosis has been listed as a notifiable disease since July 2008 in Hong Kong. All registered medical practitioners are required by law to report suspected or confirmed cases to the CHP for investigation and disease control. Cases are defined as persons with compatible clinical features together with laboratory confirmation. Detailed epidemiological information including exposure history of food, travel and risk factors are elicited to identify the source and mode of transmission. Household contacts are actively traced and put under medical surveillance.

29. If a common food source is suspected or a food premises is involved, the Food and Environmental Hygiene Department (FEHD) would be informed for further investigation of the food source and control measures would be implemented. FEHD inspects the environment and reviews the food preparatory process, conducts source tracing, collects food and environmental specimens for laboratory investigation, provides specific advice on food hygiene and takes actions against any irregularities detected. The sale and distribution of incriminated food may be suspended if necessary.

### Food Surveillance and Control

30. General preventive measures such as Good Hygiene Practices and Good Manufacturing Practices will help limit the risk of spreading the bacteria. The food industry also has to understand how contamination occurs in the food chain and to implement Hazard Analysis Critical Control Point (HACCP) programmes to minimize the presence of *Listeria monocytogenes* at important points in the production, processing, distribution and marketing of food. For instance, pasteurization (heating the milk to not less than 71.7°C for 15 seconds) at the dairy plant is a critical control point to reduce the hazard of infecting milk with listeria to an acceptable level.<sup>27</sup> The limits can be monitored by measuring the temperature and flow rate of the milk. If a deviation from the required parameters occurs, corrective actions like diverting the milk for further heat treatment, can be undertaken. Milk safety can be verified by reviewing the processing records to ensure that the critical limits have been met.

31. The Centre for Food Safety (CFS) conducts regular food surveillance at import, wholesale and retail levels to ensure food safety. In the first five months of 2007, CFS tested some 70 samples of ready-to-eat food for *Listeria monocytogenes* and identified no positive isolates.<sup>30</sup> Risk assessment studies for specific food items have also been done, e.g. of 1023 sandwich samples collected from 1997 to 1999, two positive samples of *Listeria monocytogenes* were detected and 88 samples (8.6%) were unsatisfactory in one or more microbiological tests.<sup>28</sup> Both the trade and consumers were advised to take precautions to enhance food safety. In addition, CFS monitors the food incidents involving *Listeria monocytogenes* contamination in other countries and takes appropriate action, e.g. asks retailers to stop selling the food items and warns the public not to consume affected products.

32. Criteria or recommendations for tolerable levels of *Listeria monocytogenes* varies among different countries, e.g. US practices “zero tolerance” (i.e. no organisms found in 25 g of a food product), while Canada and France apply different criteria to different foodstuffs, as complete absence of the bacteria in certain foods is unrealistic and unattainable and also does not have a positive impact on public health.<sup>29</sup> In February 2008, the US Food and Drug Administration revised its compliance standard to a tolerance of up to 100 colony-forming units per gram (cfu/g) *Listeria monocytogenes* in ready-to-eat foods that do support the growth of the bacterium.<sup>30</sup> <sup>Note</sup> In the European Union, a concentration of up to 100 CFU/g of food is tolerated in certain ready-to-eat foodstuffs. In Hong Kong, CFS developed a set of Microbiological Guidelines for Ready-to-eat Food in 2002 and revised this in 2007.<sup>31</sup> These guidelines stipulate that the *Listeria monocytogenes* limit for all ready-to-eat food be less than 100 cfu/g except for (i) food under refrigeration (excluding frozen food) and (ii) food intended for infants, where a “not detected in 25g” limit is set. This approach has a more stringent requirement towards high risk foods resulting in better resource allocation.

### Health Promotion to Trade and Public

33. Both CHP and CFS have produced a wide variety of health education materials and pamphlets for the food trade and the general public to heighten their awareness of this infection. CFS has also organized various publicity activities and seminars targeting food industry operators and food handlers about safe food handling practices, e.g. avoid post-cooking contamination of ready-to-eat foods, particularly those with long shelf lives. As

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<sup>Note</sup> According to the FDA Compliance Policy Guide Manual, a ready-to-eat food does not support the growth of *L. monocytogenes* if the food:

- has a pH that is less than or equal to 4.4; or
- is customarily held and consumed in a frozen state; or
- has a water activity that is less than 0.92; or
- is processed using an effective listeristatic control measure (e.g. antimicrobial substance or a combination of factors such as pH, water activity, and antimicrobial substance)

*Listeria monocytogenes* is commonly found in the natural environment, hygienic food manufacturing process must be ensured. FEHD has collaborated with the food trade to establish the HACCP to identify and control hazards.

34. Consumers are believed to benefit from clear recommendations on good food hygiene practice.<sup>32</sup> For persons who are at increased risk for listeriosis, including pregnant women and the immunocompromised, specific dietary measures should be taken to reduce the risk e.g. they should avoid eating high risk food including unpasteurized milk, soft cheese, prepared or stored salads and cold meats. They should also be encouraged to take careful note of the shelf-life of food in their refrigerators. Other dietary and food preparation measures include thorough cooking of raw food from animal sources, washing raw vegetables thoroughly before ingestion, keeping ready-to-eat foods away from raw foods and consuming perishable foods as soon as possible. These measures do not only reduce the risk of listeriosis, but also prevent other common foodborne diseases, e.g. salmonellosis and campylobacteriosis.

## **Summary and Recommendations**

35. Given the significant morbidity and potential for outbreaks of listeriosis, this infection requires refinement of public health strategies. Successful prevention for listeriosis rests on effective surveillance and control measures of both disease and food aspects. Prevention at source is probably the most effective means to reduce the impact of this infection. To further enhance the preventive and control measures of listeriosis, the following strategies are proposed:

### *Disease Surveillance and Control*

- Medical practitioners should be reminded that listeriosis was added to the list of statutory notifiable disease in July 2008. They should keep high index of suspicion for patients with compatible symptoms, especially among pregnant patients, and report cases to CHP for epidemiological investigation and control.
- Close collaboration between the CHP (including PHLSB) and FEHD should be maintained to initiate prompt investigation and control of any outbreak.

### *Food Surveillance and Control*

- Maintain a regular food surveillance programme at the import, wholesale and retail levels to ensure food safety.
- Enhance further collaboration with overseas authorities for rapid information exchange and prompt control measures like recall of contaminated food products.

*Health Promotion to Trade and Public*

- Continue health education to the trade and members of the general public for food safety measures against listeriosis.
- Specific health advice should be targeted at the high risk groups (e.g. pregnant women) based on scientific evidence and local dietary practices.

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