衞生防護中心
Centre for Health Protection

Scientific Committee on Enteric Infections and Foodborne Diseases

Update on Epidemiology of Listeriosis in Hong Kong

Purpose

This paper provides an update on the global and local epidemiology of listeriosis and reviews the public health measures for prevention and control of the disease in Hong Kong.

Background

2. Listeriosis, being an uncommon but important infectious disease, is of significant public health concern as it can result in severe complications, such as sepsis and meningitis, which carry high fatality rates[1]. Transmission of listeriosis from pregnant women to the foetuses can result in abortion, stillbirth or neonatal listeriosis[1,2]. Common-source outbreaks of listeriosis have been reported from many countries worldwide[1].

The bacteria

3. Listeriosis is an infection caused by the Gram-positive, rod-shaped and facultatively anaerobic bacterium *Listeria monocytogenes*[3]. There are 13 recognised serotypes of *L. monocytogenes* but most human infections are caused by serotypes 1/2a, 1/2b and 4b[4].

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4. *L. monocytogenes* is able to tolerate adverse environmental conditions with low temperatures, high acidity and high salt concentrations[5,6]. Unlike many other bacteria that cause foodborne diseases, *L. monocytogenes* can survive at -7ºC and multiply over a wide range of temperatures from 0ºC to 45ºC[3,7]. Therefore, even when *L. monocytogenes* is initially present at a low level in a contaminated food, its ability to grow at low temperatures can lead to an increase in its level during refrigerated storage of the contaminated food[3,5,6].

Reservoirs

5. *L. monocytogenes* is widely distributed in nature and can be found in soil, water, sewage, vegetation and the faeces of some animals[1]. It can also be found at many different sites of food processing plants and can contaminate a variety of foods[3,8]. In particular, ready-to-eat (RTE) products that have a long refrigerated shelf-life and are consumed without further listericidal treatment, such as cheese, unpasteurised milk, processed meat, smoked seafood, raw vegetables and salad, are considered high-risk[3,8,9].

Mode of transmission and incubation period

6. Listeriosis is primarily foodborne. In pregnancy-related neonatal listeriosis, the disease is acquired from the mother transplacentally, during passage through the birth canal or by ascending infection from vaginal colonisation[6,10].

7. Listeriosis may manifest as febrile listerial gastroenteritis (a mild form of the disease) or invasive listeriosis (a severe form of the disease)[1]. The incubation period of febrile listerial gastroenteritis is a few days while that of invasive listeriosis is usually one to two weeks but can range from a few days to three months[1].

Susceptible groups and clinical presentation

8. Individuals who are considered to be at high risk of contracting listeriosis include pregnant women, neonates, older adults and those on immunosuppressive therapy or with immunocompromising conditions such as diabetes, cirrhosis, renal diseases, malignancies and acquired immune deficiency syndrome[8,10,11].

9. In otherwise healthy people, listeriosis usually manifests as febrile

listerial gastroenteritis. Symptoms include diarrhoea, fever, headache and myalgia and are typically acute and self-limiting[3,11]. In older adults and individuals who are immunocompromised, listeriosis may manifest as invasive listeriosis. Clinical presentations include fever, myalgia, sepsis and meningitis[1]. Other less common clinical manifestations include peritonitis, hepatitis, liver abscess, endocarditis, arterial infection, myocarditis, lung and pleural fluid infection, septic arthritis and osteomyelitis[3]. In invasive listeriosis, symptoms are severe and the case fatality rate is high (20-30%)[1].

10. Pregnant women are about 20 times more likely to contract listeriosis than other healthy adults[1,12]. Listeriosis in pregnant women is usually asymptomatic or only causes mild symptoms such as mild flu-like symptoms, fever, myalgia, diarrhoea and vomiting[2,6]. However, invasion of the placenta by *L. monocytogenes* may give rise to serious complications affecting the foetus, namely, spontaneous abortion, stillbirth, preterm birth and severe infections affecting the newborn[6,13].

11. Neonatal listeriosis is often severe and may be fatal. Neonates may present with an early-onset (less than seven days old) or late-onset (between eight to 28 days of life) form of listeriosis[3]. Neonates with early-onset listeriosis are commonly born preterm and present with sepsis, meningitis, respiratory distress, circulatory failure and occasionally granulomatosis infantisepticum (a condition characterised by disseminated inflammatory granulomata)[3,6,8]. Neonates with late-onset listeriosis are usually born at full term and remain healthy at birth, and commonly present with meningitis subsequently[3,6,8]. The case fatality rates in early-onset and late-onset listeriosis are 15-50% and 10-20%, respectively[3].

Diagnosis and management

12. Listeriosis is confirmed by isolation of *L. monocytogenes* from a normally sterile site such as blood, cerebrospinal fluid (CSF), amniotic fluid, placental or foetal tissue[10]. Stool culture is of limited use as an average of 2 – 10% of the general population are carriers of *L. monocytogenes* without any apparent adverse consequences[3]. Isolation of *L. monocytogenes* from stool specimen from a sporadic case is only suggestive but not diagnostic of listeriosis[11].

13. Isolates of *L. monocytogenes* can be characterised using serological and molecular subtyping, which is a useful tool for epidemiological investigation, including identification of the incriminated food source. In outbreaks of listeriosis, modern technologies using genetic fingerprint, such as Whole Genome Sequencing (WGS) and pulsed-field gel electrophoresis, enable more rapid identification of the food source by matching *L. monocytogenes* isolated from patients with those isolated from foods[1,14].

14. As febrile listerial gastroenteritis is usually self-limiting, treatment with antibiotics is generally not required[11]. However, patients with invasive listeriosis should be treated with intravenous penicillin or ampicillin, which are often combined with an aminoglycoside[10,15]. When infection occurs during pregnancy, prompt administration of antibiotics can prevent infection of the foetus or newborn[1,16].

Global situation

15. Sporadic cases and outbreaks of listeriosis occur worldwide. According to the World Health Organization, the incidence varies from 0.01 to one case per 100,000 population per year depending on the countries and regions[1]. The incidences of listeriosis in overseas countries and areas are shown in Table 1.

Country/area	Year	Incidence (per 100,000 population)
Australia	2010-2014	0.3-0.4[17]
Canada	2011-2014	0.36-0.41[18]
European Union/ European Economic Area	2011-2015	0.4-0.5[19]
United States	2011-2015	0.24-0.31[20]

Table 1. The incidences of listeriosis of overseas countries or areas

16. In the following section, we reviewed three listeriosis outbreaks involving multiple countries recently reported in overseas countries.

17. In Europe, an outbreak of listeriosis confirmed by WGS and linked

to frozen corn and possibly to other frozen vegetables has been ongoing in five countries (Austria, Denmark, Finland, Sweden and the United Kingdom) since 2015[21]. From 2015 to 15 June 2018, 47 cases have been reported and nine patients died due to or with the infection, giving a case fatality rate of 19%[21]. The outbreak was first reported by Finland in November 2017 regarding three WGS confirmed *L. monocytogenes* clusters from different parts of Finland in 2017. The concerned strain was *L. monocytogenes* serogroup IVb, multi-locus sequence type 6 (ST6). An investigation was launched and four more countries reported human cases with isolates closely matching the Finnish *L. monocytogenes* ST6 cluster. The WGS analysis linked the human and the non-human isolates from various food samples and environmental samples, which indicated a common source related to frozen corn and other frozen vegetable mixes including corn. The source of contamination was traced back to a Hungarian freezing plant[21]. On 29 June 2018, the Hungarian Food Chain Safety Office banned the marketing of all frozen vegetable and frozen mixed vegetable products produced by the Hungarian plant between August 2016 and June 2018, and ordered their immediate withdrawal and recall. New cases of listeriosis are expected in view of its long incubation period and the possible consumption of the contaminated products purchased before the recalls[21].

18. In South Africa, an outbreak of listeriosis has been ongoing since the start of 2017[22]. Before 2017, an average of 60 to 80 laboratory-confirmed listeriosis cases were reported per year in South Africa[23]. From 1 January 2017 to 20 June 2018, 1,053 laboratory-confirmed cases of listeriosis have been reported to the National Institute for Communicable Diseases from all provinces with the majority of cases from Gauteng (58%), Western Cape (13%) and KwaZulu-Natal Provinces (8%)[23]. WGS was performed on isolates from a large subset of patients and 91% of the strains belonged to *L. monocytogenes* ST6[22]. The same ST6 sequence type was also identified from a widely consumed RTE processed meat product[22]. On 4 March 2018, the Ministry of Health of South Africa announced that this product was believed to be the source of the outbreak and initiated product recall[22,23]. The product had been exported to 15 countries in the African region and all of these countries issued recalls for the implicated products[22]. Since then, the number of cases reported per week has been decreasing[23]. In this outbreak, 42% of the cases were neonates who acquired the infection from their mothers during gestation or delivery, making neonates the

most commonly affected age group[22,23].

19. In Australia, from 17 January to 6 April 2018, 20 outbreak cases of listeriosis were reported[24]. All of the cases were hospitalised and there had been seven deaths and one miscarriage associated with the outbreak[24]. More than 30 samples of rockmelons (cantaloupe melons) from a single grower in Australia through the supply chain were tested positive to *L. monocytogenes* and all positive samples had the same genetic sequence as the human cases[24]. As the epidemiological and environmental investigations suggested that the source of the outbreak wasrockmelons produced by this grower, a recall of the incriminated rockmelons was initiated on 27 February 2018[24]. The concerned batch of rockmelons was exported to ten countries and areas including Hong Kong[24]. In Hong Kong, the Centre for Food Safety (CFS) of the Food and Environmental Hygiene Department issued food alerts and press releases to raise public awareness on the incident and a recall of the rockmelons was initiated according to CFS' advice[25,26]. No human listeriosis case related to rockmelons was recorded in Hong Kong in 2018.

Local situation

20. In Hong Kong, listeriosis is a notifiable disease under the Prevention and Control of Disease Ordinance (Cap 599). From 2009 to 2018 (as of 30 June), the Centre for Health Protection (CHP) of the Department of Health (DH) recorded a total of 169 cases of listeriosis. From 2009 to 2017, the annual number of cases ranged from six to 26 and the annual incidence ranged from 0.09 to 0.36 cases per 100,000 population (Figure 1), which was comparable to the incidences of the countries and areas listed in Table 1. In the first six months of 2018, nine cases have been recorded. Cases were recorded all year round and there was no seasonal trend observed (Figure 2).

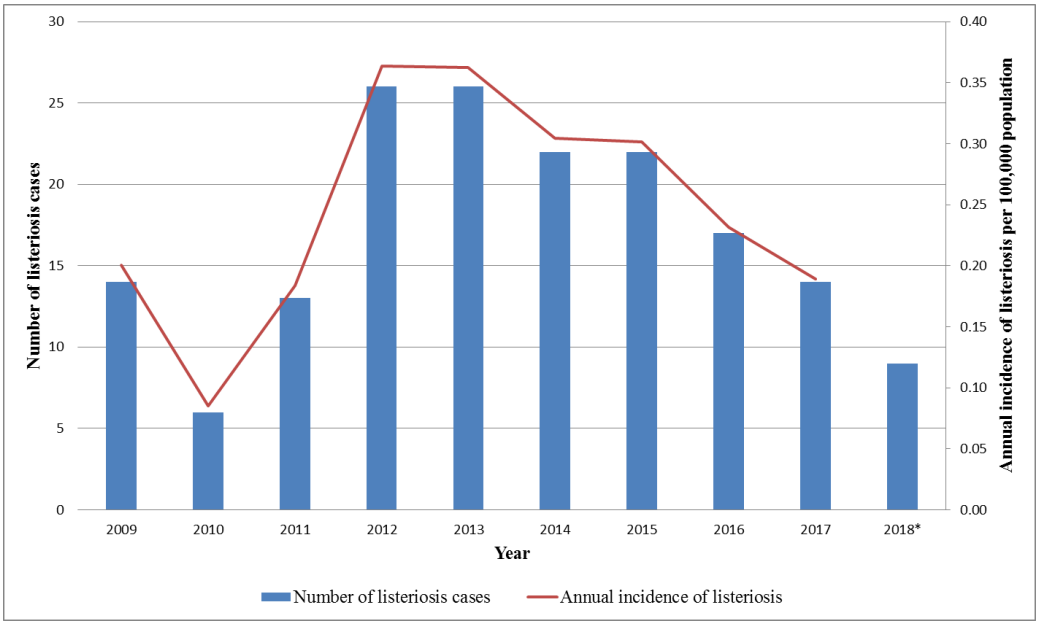

Figure 1. Number of cases and incidence of listeriosis by year in Hong Kong, 2009-2018 (*as of 30 June 2018)

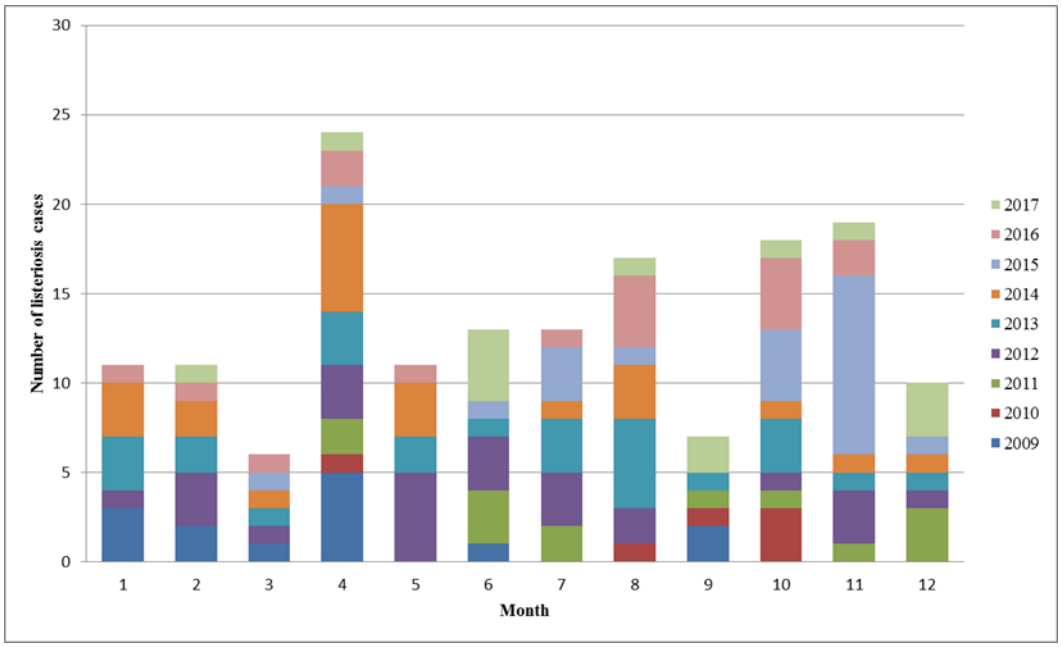

Figure 2. Cumulative monthly number of listeriosis cases in Hong Kong, 2009-2017

21. Among the 169 cases, 59 (34.9%) were male and 110 (65.1%) were female. Their ages ranged from less than one day old to 95 years with a median of 60 years. Higher incidence was observed in infants less than one year old and elderly aged 65 years or above (Figure 3).

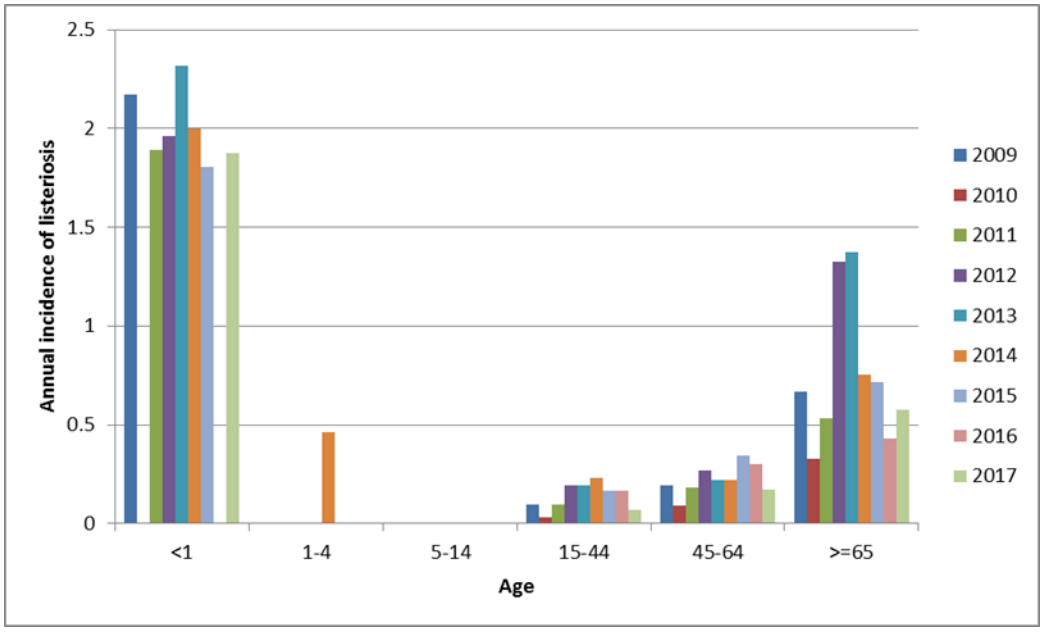

Figure 3. Age-specific annual incidence of listeriosis in Hong Kong, 2009-2017

22. The commonest presentation was fever (148, 87.6%), followed by chills/rigors (29, 17.2%), abdominal pain (28, 16.6%), headache (27, 16.0%) and diarrhoea (26, 15.4%). The majority of the patients (136, 80.4%) had *L. monocytogenes* isolated from blood. Other clinical specimens from which *L. monocytogenes* were isolated included CSF (14, 8.3%), placental swabs (12, 7.1%), peritoneal fluid (6, 3.55%) and other sites such as eye swabs, vitreous, bile and peripheral blood stem cells (5, 3.0%). Almost all patients (168, 99.4%) required hospitalisation. Sixteen patients died due to listeriosis, giving a case fatality rate of 9.5%.

23. Among the 169 cases, 36 (21.3%) were pregnancy-related (i.e. affecting pregnant women or neonates) while the remaining 133 cases (78.7%) were non-pregnancy-related (Figure 4). The majority of the cases (159, 94.1 %) were sporadic. There were four pairs of pregnancy-related cases in which both the mother and the neonate were affected. Another non-pregnancy-related cluster involved two members of the same family who consumed an RTE duck purchased in Mainland China.

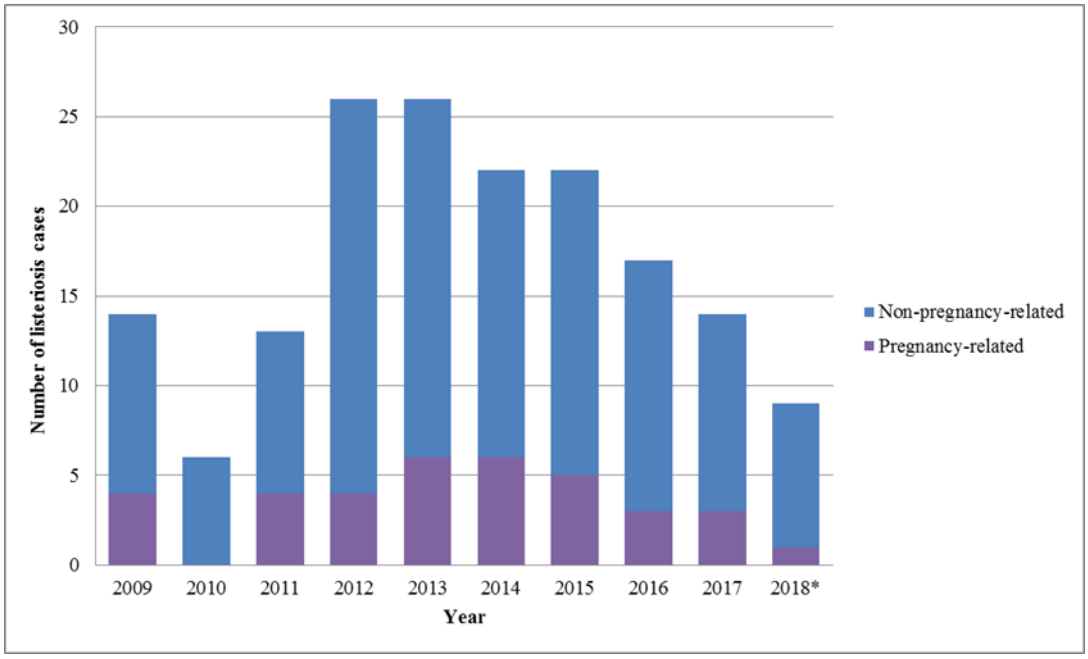

Figure 4. Number of pregnancy-related and non-pregnancy-related listeriosis cases, 2009-2018 (*as of 30 June 2018)

Non-pregnancy-related cases

24. Among the 133 non-pregnancy-related cases, the majority (124, 93.2%) had at least one chronic medical condition. The commonest medical condition was malignancies (61, 45.9%), followed by hypertension (43, 32.3%), cardiac diseases (29, 21.8%), autoimmune diseases (26, 19.6%), renal diseases (25, 18.8%), diabetes mellitus (23, 17.3%), neurological diseases such as stroke and Parkinson's disease (17, 12.8%) and post-organ transplantation status (6, 4.5%). A total of 38 (28.6%) patients were documented to be on immunosuppressive therapy for their underlying medical conditions.

25. There were 13 deaths due to listeriosis, giving a case fatality rate of 9.8%. Among the 13 deceased patients, all had at least one chronic medical condition, including immunocompromising conditions such as malignancies (4, 20.8%) and renal diseases (4, 30.8%). Three (23.1%) patients had a documented history of taking immunosuppressive therapy.

26. Patients aged 65 or above constituted a majority (74, 55.6%) of the non-pregnancy-related cases. Among these elderly patients, 71 (95.9%) had at least one chronic medical condition. Nine elderly patients died due to listeriosis, giving a case fatality rate of 12.2% among this age group.

Pregnancy-related cases

27. Among the 36 pregnancy-related cases, 29 (80.6%) were pregnant women and seven (19.4%) were neonates, with four pairs involving both the neonate and the mother. Among the 29 pregnant women, 25 (86.2%) had good past health while the other four had thyroid conditions (two cases), asthma (one case) and systemic lupus erythematous (one case), respectively. The commonest presentations among pregnant women included fever (27, 93.1%), pregnancy-related complications (15, 51.7%) and chills/rigors (8, 27.6%). Six of the 29 pregnant women had foetal loss, including three stillbirths and three spontaneous abortions. Among the remaining 23 pregnant women, five delivered their new-borns preterm.

28. Among the seven neonatal infections, the mothers of four cases were also diagnosed with listeriosis. Six neonates presented with early-onset listeriosis and the remaining one with late-onset listeriosis. Four (57.1%) of them stayed in intensive care unit and two (28.6%) in special care baby unit. A total of three neonatal cases died due to listeriosis, giving a case fatality rate of 42.9% for neonatal infections.

Food items consumed

29. The high-risk food items most commonly consumed by patients during the incubation period* were dairy products (103, 60.9%), followed by salad or sandwiches (39, 23.0%), cheese (28, 16.6%) and raw or smoked seafood (18, 10.7%). Among those who consumed dairy products, 69 (67.0%) had consumed milk, milk powder or soymilk, and the other dairy products included ice-cream or yogurt. Nine patients had consumed salad that contained cold cuts or processed meat, eight had consumed salad that contained cheese and three had consumed salad that contained smoked seafood. Due to the long incubation period of listeriosis, a single source of infection could not be ascertained in most of the sporadic cases. The source of infection was identified in only one case, in which the *L. monocytogenes* isolates from the patient and the food sample, smoked salmon, were indistinguishable by laboratory test.

*More than one item in some cases

Prevention and control

30. Both DH and CFS have a number of measures in place for the prevention and control of listeriosis in Hong Kong, including disease surveillance, timely investigation of reported cases and implementation of control measures, health education and risk communication, food safety control and food surveillance.

Disease surveillance

31. Listeriosis is a notifiable disease under the Prevention and Control of Disease Ordinance (Cap 599) in Hong Kong. All registered medical practitioners are required to report cases of listeriosis to CHP for investigation.

Case investigation and control measures

32. Upon receiving a notification, CHP will initiate epidemiological investigation and implement control measures accordingly. Epidemiological investigation includes obtaining exposure history with regard to food consumption to identify possible source of infection. Food collaterals and household contacts, particularly those belonging to susceptible groups, will be traced and put under medical surveillance. When suspected food item(s) involving food business in Hong Kong are identified, CHP will collaborate with CFS to conduct investigation and implement control actions to prevent further spread of the disease.

33. The Public Health Laboratory Services Branch of CHP provides support for microbiological analysis of clinical specimens, food and environmental samples, and will perform typing of isolates as necessary to support epidemiological investigation of clusters.

Health education and risk communication

34. DH and CFS have produced a wide variety of health education materials for the general public, high-risk groups and the food industry to raise their awareness of listeriosis. CHP has published news and feature articles on listeriosis in its bi-weekly on-line publication "Communicable Diseases Watch" from time to time, aiming to provide healthcare professionals and members of the public with up-to-date news and knowledge on listeriosis.

35. DH and CFS have published pamphlets on the prevention of listeriosis in high-risk groups including pregnant women. The Family Health Service of DH has published a booklet on healthy eating during pregnancy and breastfeeding, which advises pregnant women and women preparing for pregnancy to avoid high-risk foods that may contain *L. monocytogenes*[27]. In addition, CFS would hold exhibitions on Food Safety Advice for Pregnant Women with advice to reduce risk of listeriosis. CFS has published advice related to some *Listeria*-related food incidents to both food trade and consumers on minimising the risk of listeriosis [28-30].

Food safety control and food surveillance

36. Since over 90% of foods in Hong Kong are imported, CFS has an effective food incident surveillance system in place to monitor, assess and manage daily food incidents reported from food authorities and media agencies worldwide. In addition, the Food Surveillance Programme of the CFS aims to monitor the safety of the food in Hong Kong. It is a three-tier approach to food surveillance consisting of routine, targeted and seasonal food surveillance[31]. Food samples are taken at import, wholesale and retail levels for microbiological, chemical and radiation testing [31].

37. Testing of *L. monocytogenes* in RTE food is under the targeted food surveillance project. In July 2017, CFS announced the results of a targeted surveillance on *L. monocytogenes* in RTE food[32]. The surveillance included high-risk food items such as cheese, frozen confections, cold cuts, sashimi, smoked seafood, etc. Out of the 500 food samples from different retail outlets, including online retailers and food factories, two samples were unsatisfactory[32].

Conclusion and recommendations

38. Listeriosis is a serious and potentially fatal foodborne disease. Pregnant women, neonates, elderly and those with immune deficiency are particularly at risk. In Hong Kong, there have been public health and food safety measures in place to prevent and control listeriosis. The current prevention and control measures should be maintained. CHP will keep abreast of the latest evidence and international practices on effective strategies in the surveillance, prevention and control measures of listeriosis.

Advice sought

39. Members are invited to note the information in this paper and advise on the enhancement of surveillance, prevention and control of listeriosis in Hong Kong.

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