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SHORT REPORT
Nationwide survey of human *Listeria monocytogenes* infection in Japan

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SUMMARY

Listeriosis, caused by *Listeria monocytogenes*, is a significant public-health concern as a result of its clinical severity and high mortality. Large foodborne outbreaks of listeriosis have occurred during the last two decades in Europe and the United States, but to date there have been no food-mediated epidemics of the disease and very little information is available on the number of cases of listeriosis in Japan. We performed a nationwide surveillance study of listeriosis. The data were collected between 1980 and 2002, and 95 case reports were identified from 1996 to 2002. We divided 13·6 (cases per year between 1996 and 2002) by the ratio of the number of beds in hospitals that replied to the questionnaire, to that of all the hospitals in Japan and estimated that there is an average of 83 cases of listeriosis per year and an incidence of 0·65 cases per million of the population in Japan.

Listeriosis, caused by *Listeria monocytogenes*, is an infection of great public-health concern due to its clinical severity, which may lead to meningitis or bacteraemia with high fatality. The infection is found mostly in neonates, pregnant women, the elderly and immunocompromised patients. Recent epidemiological investigations have shown that retail foods, especially ready-to-eat foods contaminated with *L. monocytogenes*, may cause large outbreaks of infection in populations [1]. As a consequence, listeriosis is categorized as a foodborne infectious disease and surveillance systems have been established to determine the incidence of the disease in affected countries [2].

Listeriosis has occurred only sporadically in Japan and no foodborne outbreak has been reported so far. The number of cases of bacterial meningitis is reported to the Infectious Disease Surveillance Centre (IDSC) by approximately 500 sentinel hospitals throughout Japan. This reporting system has operated since 1987 with its main purpose being the monitoring and analysis of disease trends. The identification of pathogens is not required, so information about each bacterial species associated with meningitis cases is patchy and inconsistently reported. Further, it is very difficult to obtain accurate numbers of the incidence of the disease owing to the lack of a mandatory notification system, reference centre or comprehensive national surveillance of *L. monocytogenes* isolates and listeriosis in Japan. A single case of listeriosis was reported in 1999, but none has been reported since then. We postulated that the current voluntary reporting system considerably underestimates the number of listeriosis cases. To this end we set out to determine the incidence of reported listeriosis cases and to estimate the annual number of cases occurring in Japan.

We chose to perform a questionnaire-based surveillance of hospitals because it was a more active system than that currently used in this country. It is mandatory for all Japanese people to join the national health insurance system so we assumed that patients with symptoms of listeriosis would require medical

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Fig. 1. Geographical distribution of 205 listeriosis cases reported by 89 hospitals in 36 prefectures is shown.

attention in hospital and their medical records would reflect this. Information about *L. monocytogenes* infection was collected by contacting clinical and laboratory specialists in each of 2258 hospitals out of 9266 hospitals in Japan which have more than 100 beds. This represented 686 902 beds out of a total of 1 647 253 beds in the year 2000. They included acute-care and general hospitals which provide mainly secondary care, and university teaching hospitals. All studies were in accord with the guidelines of the Ethics Committee of the National Institute of Infectious Diseases, Tokyo. They were asked to identify retrospectively the total number of patients in their hospitals with listeriosis and of *L. monocytogenes* isolates from the period before 1980, and during 1981–1990, 1991–1995 and 1996–2002. Listeriosis was defined as the growth of *L. monocytogenes* from any body site of a patient with clinical symptoms. Isolates were identified by standard methods in the microbiology laboratory in each medical centre. Perinatal cases were defined as the isolation of *L. monocytogenes* from a pregnant woman and/or from her offspring within the first 31 days of life. Questionnaires were completed from 773 hospitals, which represented 16% of the total number of hospital beds in Japan, and were distributed throughout all 47 prefectures of the country. Of these, a total of 194 hospitals, reported a case of diagnosed listeriosis and/or isolated *L. monocytogenes* from clinical samples.

Reports were received of 205 listeriosis cases from 89 clinical sites (Fig. 1), which included 12 (6%) perinatal cases and 193 (94%) non-perinatal cases: 4 cases before 1980, 63 cases in the period 1981–1990, 43 cases in 1991–1995 and 95 cases in 1996–2002. From a total of 177 laboratory sites, 575 samples were reported: 54 samples before 1980, 141 samples in 1981–1990, 151 samples in 1991–1995 and 229 samples in 1996–2002. Bacterial meningitis and bacteraemia were the most frequent clinical presentations. To estimate the annual number of cases and the incidence of listeriosis we examined the data of 95 cases from 56 hospitals in 1996–2002. These recent data were considered to better reflect the current situation, as few clinical records were kept before the 1980s. Data from hospitals founded after 1990 were also included. We divided 13·6 (cases per year for 1996–2002) by the ratio of the number of beds in hospitals that replied to the questionnaire, to the number of beds in all the hospitals in Japan (1:6·1) and arrived at an estimate of 83 listeriosis cases per year. The incidence of listeriosis was thus 0·65 per million inhabitants in Japan (Table).

Supplemental questionnaires were sent to the 56 clinical specialists who reported listeriosis cases during 1996–2002 to verify the cases and request patient data such as sex, age, underlying illness and season of infection. Detailed information was received on 42 (44%) individual listeriosis cases, 8 were neonates

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Table. *The number of annual cases and the incidence of listeriosis in Japan, France, the United States and United Kingdom*

Country	Cases per year	Incidence/ per million	Year	Ref.
Japan	83 (estimated)	0·65	1996–2002	This study
France	242	5·4	1997	[10]
United States	2518 (estimated)	4·8	1997	[9, 14]
United Kingdom	85–129	1·6–2·5	1990s	[2]

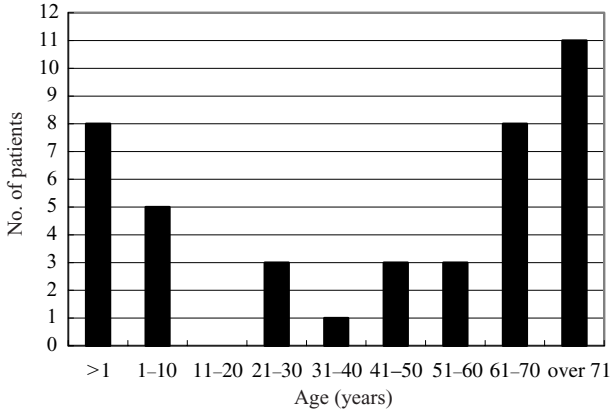

Fig. 2. Age distribution of 42 listeriosis patients in Japan, from 1996 to 2002.

less than 1 year old and 19 were over 60 years (Fig. 2). Approximately 70% of the elderly patients had underlying illnesses such as diabetes or hepatitis. Two patients aged 20–40 years with ulcerative colitis were identified. Meningism was the most frequent clinical sign (59%) and 7 perinatal cases of meningitis (17%) were reported. Fatalities were confined to patients more than 60 years old (9/19). Cases were distributed equally between the sexes and occurred throughout the year with no seasonal bias (results not shown). The infection was found mostly in pregnancy-associated, immunocompromised and elderly patients as reported by other investigators [3–5].

Since 1987, most industrialized countries have developed surveillance systems for listeriosis following outbreaks that demonstrated the importance of foodborne transmission of the disease [2]. However, in Japan we have only a surveillance system for bacterial meningitis and not specifically for listeriosis. Terao [6] reviewed the annual number of listeriosis patients in Japan from 1958 to 1988, 2 cases were reported in 1958 and the number reported annually gradually increased to 62 cases in 1982 but thereafter decreased to 19 cases in 1988. However, these data were collected by an individual and not based on national surveillance reports.

In this study, we found a questionnaire-based surveillance system could provide us with the data required for the estimation of the occurrence of listeriosis in Japan. The estimated total annual cases and incidence in Japan were lower than those reported in France, the United States and United Kingdom (Table), although the rates should be interpreted in the context of the methods used for case ascertainment and reporting in each country. Nevertheless, compared with listeriosis incidence estimates from other countries [7], the incidence in Japan was still low. However, in a recent study in The Netherlands, the mean annual incidence per 100 000 individuals was 0·07 in 1991–1995 [8], only sporadic cases were reported and no outbreaks were identified. This was also true in Japan and this appears to accord with our low estimated incidence.

The questionnaire-based surveillance system had several limitations, such as under-reporting of cases and reliance on voluntary responses. Replies were obtained from only one-third of all hospitals, and detailed information was available on 44% of individual cases for 1996–2002. Regarding the under-reporting of cases, Mead et al. [9] applied the multiplier of 2 to account for this and estimated the number of listeriosis cases in the United States, on the assumption that most cases would come to medical attention because of the severity of their symptoms. We considered that we did not need to apply a multiplier since the Japanese national health insurance system generally leads to hospitalization of patients with severe symptoms like those of listeriosis. Therefore, we simply divided the number of cases per year by the proportion of the number of beds in the reporting hospitals and extrapolated this to the total number of hospitals in the country. There was a precedent for this approach since Goulet et al. [10] had estimated the total number of cases in France by a similar method.

A population-based or reporting surveillance system would be helpful and more effective for gathering detailed information about cases with little under-reporting [11]. We consider that such a system in combination with the questionnaire would give us more detailed and confident data for analysis. In a separate study we have shown that the level of *L. monocytogenes* contaminating retail food in Japan is almost the same as that in Europe and the United States, where large outbreaks have occurred [12]. Japan has, therefore, a similar potential as other countries for experiencing foodborne listeriosis outbreaks. There is good evidence that surveillance measures functioned effectively, and that industry, regulatory, and educational efforts together with a multi-state, laboratory-based active surveillance system were associated with the reduction of the incidence of listeriosis from 1989 to the end of 1993 in the United States [13]. It is our hope that the present study will provide a good scientific basis for the design of effective measures for the prevention of listeriosis in Japan.

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