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<THE TOPIC OF THIS MONTH>

Enterohemorrhagic *Escherichia coli* (EHEC) infections in Japan, as of March 2018

Enterohemorrhagic *Escherichia coli* (EHEC) is an important diarrheagenic *E. coli*, which produces verotoxin/Shiga toxin (VT/Stx) and/or possesses VT-encoding genes. The main signs/symptoms of EHEC infections are abdominal pain, watery diarrhea, and bloody diarrhea. Fever (~38°C) and/or vomiting are occasionally observed. VT-producing EHEC can cause hemolytic uremic syndrome (HUS), which involves thrombocytopenia, hemolytic anemia, and acute renal failure; complications such as encephalopathy may occur, with potentially fatal outcomes.

In Japan, EHEC infections are classified as a category III notifiable infectious disease under the Infectious Diseases Control Law. When a physician diagnoses an EHEC infection, he/she must immediately notify a local public health center (PHC) regarding the case (<http://www.nih.go.jp/niid/images/iasr/37/435/de4351.pdf>). The information collected by the PHC is then reported to the National Epidemiological Surveillance of Infectious Diseases (NESID) system. When an EHEC infection is classified as food poisoning by a physician or the director of the PHC, the local government investigates the incident and submits a report to the Ministry of Health, Labour and Welfare (MHLW) in compliance with the Food Sanitation Law. Prefectural and municipal public health institutes (PHI) perform isolation/identification of EHEC, serotyping of the isolate, and typing of the VT (the VT or the VT gene), and report the laboratory results to NESID (see p.73 of this issue). The Department of Bacteriology I of the National Institute of Infectious Diseases (NIID) conducts confirmatory tests upon request and conducts molecular epidemiologic analysis of EHEC using multiple-locus variable-number tandem-repeat analysis (MLVA) and pulsed-field gel electrophoresis (PFGE) (see p.81 of this issue). The results of the analyses are fed back to the PHI and, where necessary, to local governments through the National Epidemiological Surveillance of Foodborne Disease (NESFD) system.

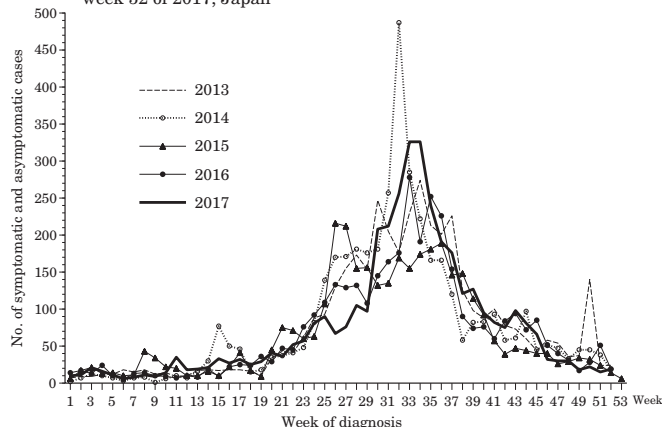
Cases notified under the NESID system: In 2017, a total of 3,904 cases of EHEC infection were reported. Among them, 2,606 were symptomatic, and 1,298 were asymptomatic (asymptomatic cases are detected during active epidemiologic investigations or routine stool specimen screening of food handlers) (Table 1). Consistent with yearly trends, the number of reports peaked in summer (Fig. 1). Reports from 10 prefectures, including Tokyo, Kanagawa, Saitama, Hokkaido, Chiba, Aichi, Fukuoka, Osaka, Iwate, and Nagano, accounted for 57% of all notified cases (including asymptomatic cases). The annual number of reported cases per 100,000 population was highest in Iwate Prefecture (12.3) followed by Nagano (6.6), Yamagata (5.6), Saga (5.4), and Gifu (5.0) Prefectures (Fig. 2). The notification rate per 100,000 population among 0-4-year-olds was highest in Iwate and Saga Prefectures, which experienced EHEC outbreaks in nursery schools (Fig. 2). The proportion of symptomatic cases was high among the <30

Table 1. Notified cases of EHEC infection

Year of diagnosis [Jan 1-Dec 31]	No. of cases*	(No. of symptomatic cases)	(%)
2008	4,329	(2,822)	(65)
2009	3,879	(2,602)	(67)
2010	4,135	(2,719)	(66)
2011	3,939	(2,659)	(68)
2012	3,770	(2,363)	(63)
2013	4,045	(2,623)	(65)
2014	4,156	(2,840)	(68)
2015	3,568	(2,339)	(66)
2016	3,647	(2,246)	(62)
2017	3,904	(2,606)	(67)
2018**	139	(85)	(61)

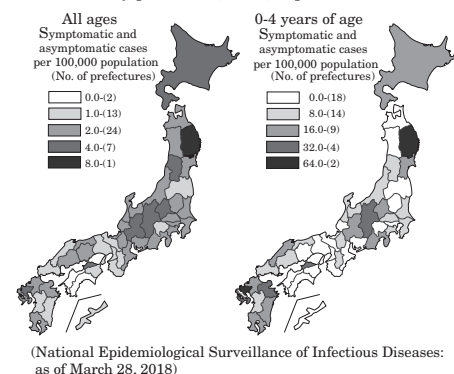
*Including asymptomatic cases **Jan 1-Mar 25
(National Epidemiological Surveillance of Infectious Diseases: as of March 28, 2018)

Figure 1. Weekly number of reported EHEC infection cases, week 1 of 2013 to week 52 of 2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of March 28, 2018)

Figure 2. Notification rate of EHEC infection by prefecture, 2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of March 28, 2018)

(THE TOPIC OF THIS MONTH-Continued)

years and ≥65 years age groups, which is consistent with findings from previous years (Fig. 3).

EHEC was isolated from 73 of 111 HUS cases (4.3% of symptomatic cases). The O-serogroup was O157 in 58 cases, and the toxin type was VT2 (VT2 alone or VT1 & VT2) in 59 cases. Among the symptomatic cases, HUS was most frequent in 5-9-year-olds (8.0%) (see p.82 of this issue). At the time of notification, 10 of the cases were fatal.

EHEC isolated by PHIs: In 2017, PHIs reported 1,689 isolations of EHEC. This figure was considerably lower than the number of reported cases of EHEC infection (n=3,904) (Table 1 in p.71). The discrepancy was due to the fact that isolates from the clinical setting or commercial laboratories were sent to PHIs upon request on an as needed basis. The most frequently detected O-serogroup was O157 (54%), followed by O26 (25%) and O103 (6.6%) (see table on p.73 of this issue). In 2017, 53% and 47% of O157 isolates were VT1 & VT2-positive and VT2-positive, respectively, while 99% of O26 isolates and 100% of O103 isolates were VT1-positive. The main clinical signs/symptoms among the 908 cases in whom O157 was isolated were diarrhea (60%), abdominal pain (59%), bloody diarrhea (48%), and fever (19%).

Outbreaks: Among the EHEC outbreaks reported by PHIs to NESID in 2017, 10 involved ≥10 EHEC-positive cases. Six were due to person-to-person transmission in nursery schools (Table 2). Under the Food Sanitation Law, 17 EHEC-related food poisoning outbreaks involving a total of 168 cases (including EHEC isolation-negative cases) were reported (see p.74 of this issue) (25 outbreaks involving 766 cases in 2014; 17 outbreaks involving 156 cases in 2015, and 14 outbreaks involving 252 cases in 2016). The main EHEC outbreaks in 2017 were as follows: (i) an O157 outbreak at a restaurant in Shiga Prefecture in May (11 cases); (ii) an O157 outbreak in Aichi Prefecture in August (36 cases), which was attributed to a lunch box; (iii) O157-based food poisoning in Saitama and Gunma Prefectures in August (involving 24 cases including one death) caused by foods sold at a delicatessen chain (see p. 74 of this issue); (iv) an O157 outbreak at a barbecue restaurant in Okayama Prefecture in August (16 cases); (v) an O157 outbreak at a restaurant in Aichi Prefecture in August (12 cases); and (vi) an O157 outbreak attributed to skewered meats in Niigata Prefecture in October (15 cases) (see p.77 of this issue).

In addition to these, the Department of Bacteriology I, NIID, identified EHEC strains with identical MLVA or PFGE patterns among the isolates collected from geographically widely dispersed cases (see p.81 of this issue).

Prevention and measures to be implemented: In response to food poisoning events caused by raw beef, the MHLW revised the standards for beef sold for raw consumption (MHLW notice No. 321, October 2011). Furthermore, upon the detection of EHEC O157 from the inner section of cattle liver, the MHLW banned the sale of beef liver for raw consumption (notice No. 404 in July 2012). In 2012, in response to O157-based food poisoning outbreaks attributed to contaminated pickles, the MHLW revised the hygiene code for processing pickles (food safety inspection notice 1012, No. 1, October 2012).

As EHEC can cause infection at bacterial counts as low as ~100 bacteria, it can easily spread from infected persons to uninfected persons, either through direct contact or indirectly through food or food products. EHEC-associated food poisoning events attributed to restaurants also occurred in 2017 (see p.74 of this issue). To prevent EHEC infections, it is crucial to observe the principles of proper food hygiene and continue risk communication activities aimed at getting the public to refrain from eating raw or undercooked meat.

EHEC outbreaks continue to occur in large numbers in nursery schools (Table 2; see pp.78 & 79 of this issue). To prevent such outbreaks, appropriate hygienic practices, such as routine hand washing and hygiene management at children's swimming pools, should be implemented ("Infection Control Guidelines for Nurseries" revised in 2018). When a case of EHEC infection is detected in a household or care facility, the relevant PHC should ensure that appropriate measures are strictly implemented to prevent further transmission.

Table 2. Outbreaks of EHEC infection in 2017

(Data based on reports from public health institutes received before March 28, 2018 and references in IASR)

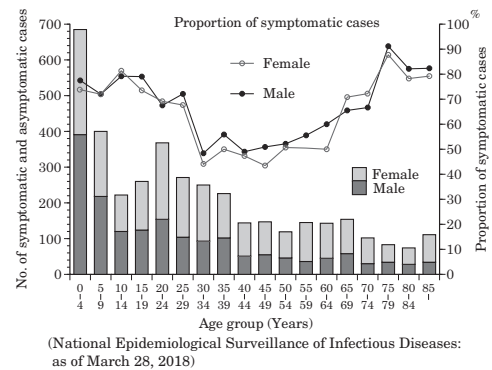
No.	Prefecture or City	Period	Suspected route of infection	Setting of outbreak	Serotype	VT type	No. of symptomatic cases	No. of positives /examined	Familial infection*	Reference in IASR
1	Iwate P.	Mar 11-31	Person to person	Nursing home for the elderly	O26:H11	VT1	8	21 / 194	No	
2	Kanagawa P.	Jun 22-Jul 10	Person to person	Nursery school	O26:H11	VT1	7	23 / 97	Yes(13)	p. 79 of this issue
3	Gifu P.	Jul 18-Aug 17	Person to person	Nursery school	O103:H11	VT1	58	37 / 291	Yes(5)	
4	Iwate P.	Jul 27-Aug 4	Person to person	Nursery school	O26:H11	VT1	15	26 / 74	Yes(12)	
5	Ibaraki P.	Jul 27-Aug 30	Unknown	Long-term healthcare facility for the elderly	O157:H7	VT1&VT2	43	26 / 195	No	
6	Nagano P.	Jul 29-Dec 1	Person to person	Nursery school	O26:H11 O157:H7	VT1 VT1&VT2	28	54 / 348 10 / 348	Yes(13) Yes(2)	p. 78 of this issue
7	Fukuoka C.	Aug 5-Aug 28	Person to person	Nursery school	O103:H2	VT1	10	18 / 267	Yes(5)	
8	Fukuoka C.	Aug 28-Sep 20	Person to person	Nursery school	O26:H11	VT1	11	17 / 237	Yes(1)	
9	Iwate P.	Sep 27-Oct 14	Person to person	Kindergarten	O111:H-	VT1	17	34 / 330	Yes	
10	Saga P.	Sep 29-Oct 30	Unknown	Childcare facility	O157:H7	VT2	4	19 / 81	Yes(2)	

Outbreaks with 10 or more EHEC-positive cases, P.: Prefecture, C.: City

*Secondary transmission within a family. The numbers in parentheses refer to infections from secondary transmission.

IASR: Infectious Agents Surveillance Report

Figure 3. Age distribution of EHEC infection cases, 2017, Japan



The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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