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National Institute of Infectious Diseases and Tuberculosis and Infectious Diseases Control Division, Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Enterohemorrhagic *Escherichia coli* (EHEC) infection, as of April 2017, Japan

Enterohemorrhagic *Escherichia coli* (EHEC) infection is a systemic infection of pathogenic *E. coli* that produces Verotoxin/Shiga toxin (VT/Stx) and/or possesses the VT encoding genes. Main signs and symptoms are abdominal pain, watery diarrhea, and bloody diarrhea. Fever (~38°C) and/or vomiting are occasionally observed. EHEC that produces VT can cause hemolytic uremic syndrome (HUS) consisting of thrombocytopenia, hemolytic anemia and acute renal failure.

EHEC infection is a category III notifiable infectious disease under the Infectious Diseases Control Law. A physician who has made a diagnosis of EHEC infection shall notify the case immediately to a health center (HC). The information is reported from HCs to the National Epidemiological Surveillance of Infectious Diseases (NESID) system (http://www.nih.go.jp/niid/images/iasr/37/435/de4351.pdf). When an EHEC infection is notified as food poisoning by a physician or is classified as such by the director of the HC, the local government investigates the incident and submits the report to the Ministry of Health, Labour and Welfare (MHLW) in compliance with the Food Sanitation Law. Prefectural and municipal public health institutes (PHIs) conduct isolation/identification of EHEC and serotyping of isolates and typing of VT (VT or the VT gene), and report the laboratory results to NESID (see p. 89 of this issue). The Department of Bacteriology I of the National Institute of Infectious Diseases (NIID) conducts confirmatory tests upon request and conducts molecular epidemiology using multiple-locus variable-number tandem-repeat analysis (MLVA) and pulsed-field gel electrophoresis (PFGE) (see pp. 100 & 101 of this issue). NIID's analysis results are fed back to PHIs and, where necessary, to the local governments through the National Epidemiological Surveillance of Foodborne Disease (NESFD) system.

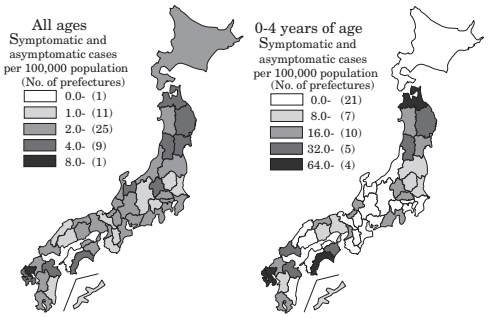
Cases notified under NESID system: In 2016, a total of 3,645 EHEC cases were reported. Among them 2,246 were symptomatic and 1,399 were asymptomatic (asymptomatic cases are detected during active surveillance of outbreaks or routine stool specimen screening of food handlers) (Table 1). The number of reports peaked in summer as usual (Fig. 1). Reports from Tokyo, Kanagawa, Osaka, Fukuoka, Chiba and Saitama Prefectures occupied 41% of all the notified cases (asymptomatic cases included). The annual number of reported patients per 100,000 population was highest in Saga (10.2) followed by Aomori (7.4) and Nagasaki (6.1) Prefectures (Fig. 2). The notification rates per 100,000 among 0-4 year old children was highest in Saga and Aomori Prefectures,

Table 1. Notified cases of EHEC infection

Year of diagnosis [Jan.1 - Dec.31]	No. Cases*	(Symptomatic cases)	(%)
2007	4,617	(3,083)	(67)
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	3,645	(2,246)	(62)
2017**	204	(126)	(62)

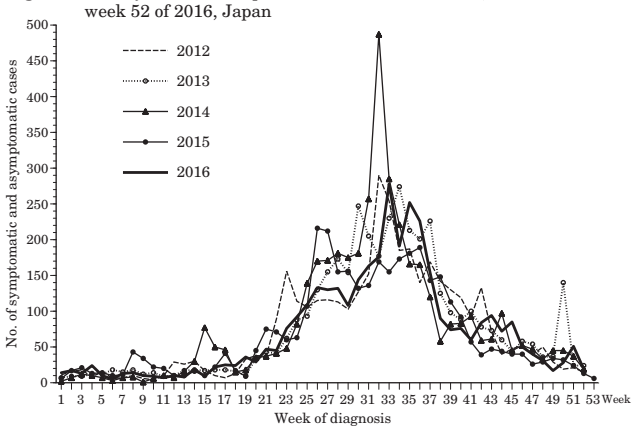
*Including asymptomatic cases **Jan.1-Apr.9
(National Epidemiological Surveillance of Infectious Diseases: as of April 12, 2017)

Figure 2. Notification rate of EHEC infection by prefecture, 2016, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of April 12, 2017)

Figure 1. Weekly number of reported EHEC infection cases, week 1 of 2012 to week 52 of 2016, Japan



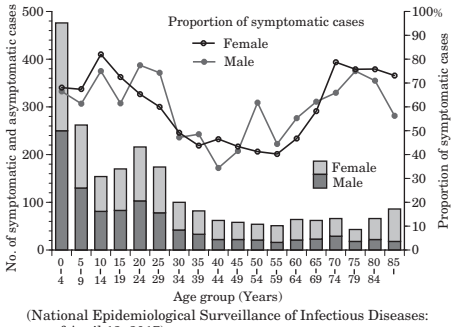
(National Epidemiological Surveillance of Infectious Diseases: as of April 12, 2017)

(Continued on page 88′)

which experienced EHEC outbreaks in nursery schools (Fig. 2). The proportion of symptomatic patients was high in age groups younger than 30 years and those 60 years or older, similar to previous years (Fig. 3).

EHEC was isolated from 61 cases among a total of 96 HUS cases (4.3% of symptomatic cases). The O-serogroup was O157 in 51 cases and the toxin type was VT2 (VT2 alone or VT1 & VT2) in 47 cases. Among symptomatic cases, HUS was most frequent in 5-9 year olds (8.4%). There were nine fatal cases at the time of notification, some of whom were diagnosed by methods other than the bacterial isolation (see p. 102 of this issue).

Figure 3. Age distribution of EHEC infection cases, 2016, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of April 12, 2017)

EHEC isolated by PHIs: In 2016, PHIs reported EHEC from 1,669 isolations. The figure was considerably less than the number of EHEC cases reported (n=3,645). The discrepancy was due to the current situation where many isolates from clinical settings and commercial laboratories are not sent to PHIs. The most frequently detected O-serogroup was O157 (53%), followed by O26 (32%), and O103 (3.6%) (see table in p. 89 of this issue). In 2016, 55% of O157 isolates were VT1&VT2-positive, while 98% of O26 and 97% of O103 were VT1-positive. Main clinical signs and symptoms of 877 cases, from whom O157 was isolated, were diarrhea (54%), abdominal pain (52%), bloody diarrhea (42%) and fever (22%).

Outbreaks: Among EHEC outbreaks reported by PHIs to NESID in 2016, 17 were outbreaks with ≥10 EHEC-positive cases. Among them, ten were due to person-to-person transmission in nursery schools (Table 2). Under the Food Sanitation Law, 14 EHEC food poisoning outbreaks with a total of 252 patients (including EHEC isolation negatives) were reported (13 outbreaks with 105 patients in 2013; 25 outbreaks with 766 patients in 2014, and 17 outbreaks with 156 patients in 2015: see p. 90 of this issue). The main events in 2016 were: (i) O157 outbreak at a barbecue beef restaurant in Shiga Prefecture in July (39 patients) (see p. 97 of this issue); (ii) O157 outbreak from July to August among visitors to Okinawa Prefecture (28 patients) attributed to contaminated sugarcane juice (see pp. 94 & 95 of this issue); (iii) O157 food poisoning in August in nursing homes for the elderly in Chiba and Tokyo Prefectures attributed to *yukari*-seasoned cucumber (84 patients including 10 deaths) (see p. 92 of this issue); and (iv) O157 food poisoning in October caused by frozen minced meat cutlet produced in Shizuoka Prefecture (67 patients) (see pp. 90 & 91 of this issue).

Department of Bacteriology I, NIID, identified EHEC strains with identical MLVA or PFGE patterns among isolates from geographically widely dispersed patients. Though their epidemiological relationship was not established among these sporadic cases, widespread diffuse EHEC transmission was suggested (see pp. 100 & 101 of this issue).

Prevention and measures to be implemented: In response to food poisoning events caused by raw beef, MHLW revised the standards of the beef marketed for raw consumption (MHLW notice No. 321, October 2011). Further, upon the detection of EHEC O157 in the inner part of marketed cattle liver, MHLW banned marketing of cattle liver for raw consumption (notice No. 404 in July 2012). In 2012, in response to the O157 food poisoning outbreaks attributed to contaminated pickles, MHLW revised the hygiene code for processing pickles (Food Safety Inspection notice 1012, No. 1, October 2012). Many food poisoning events attributed to restaurants occurred in 2016 (Table 2, also see p. 90 of this issue). For preventing EHEC, it is crucial to observe the principles of proper food hygiene and continue risk communication activities to refrain from eating raw or undercooked meat.

As EHEC establishes infection at a dose as low as ~100 bacteria, it can easily spread from an infected person to another directly through contact or indirectly through foods or food products. In 2016, EHEC outbreaks continued to occur in large numbers in nursery schools (Table 2, also see p. 99 of this issue). For preventing 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 November 2012). When a case of EHEC is detected in households or care facilities, HCs should ensure that appropriate measures are strictly implemented to prevent further transmission.

Table 2. Outbreaks of EHEC infection, 2016 (Data based on reports from public health institutes received before April 4, 2017 and references in IASR)

No.	Prefecture /City	Period	Suspected route of infection	Setting of outbreak	Serotype	VT type	No. of symptomatic cases	No. of consumers	No. of positives /examined	Familial infection*	Reference in IASR
1	Saga P.	Jun.5-12	Unknown	Nursery school	O26:H11	VT1	2	･･･	10 / 96	Yes	
2	Shiga P.	Jul.2-13	Foodborne	Restaurant	O157:H7	VT1&VT2	39	78	28 / 54	N.D.	p.97 of this issue
3	Hyogo P.	Jul.16-Sep.23	Person to person	Nursery school	O26:H11	VT1	16	･･･	35 / 198	Yes	
4	Okinawa P.	Jul.25-Aug.14	Foodborne*1)	Restaurant	O157:H7	VT2	28	55	31 / 42	N.D.	pp.94&95 of this issue
5	Osaka P.	Jul.29-Sep.15	Person to person	Nursery school	O26:H11	VT1	13	･･･	17 / 140	Yes	
6	Osaka P.	Jul.30-Sep.8	Person to person	Nursery school	O145:H-	VT2	19	･･･	31 / 241	Yes	
7	Saitama C.	Aug.5-Sep.22	Person to person	Nursery school	O26:H11	VT1	5	･･･	11 / 91	Yes	
8	Aomori P.	Aug.10-Sep.5	Person to person	Nursery school	O157:H7	VT2	65	･･･	78 / 291	Yes(11)	
9	Saga P.	Aug.10-Sep.14	Person to person	Nursery school	O157:H7	VT2	12	･･･	51 / 627	Yes	
10	Nagasaki P.	Aug.12-15	Person to person	Nursery school	O26:H11	VT1	7	･･･	15 / 121	Yes	
11	Nagasaki P.	Aug.16-22	Person to person	Nursery school	O26:H11	VT1	25	･･･	13 / 127	Yes	p.99 of this issue
12	Ibaraki P.	Aug.21-Sep.22	Person to person	Nursery school	O157:H7	VT2	13	･･･	12 / 177	Yes	
13	Fukuoka P.	Aug.22-Oct.3	Unknown	Nursery school	O26:H11	VT1	18	･･･	56 / 262	Yes	
14	Chiba P.a) Tokyo	Aug.28-Oct.14 Aug.27-Sep.4	Foodborne*2)	Nursing homes for the elderly	O157:H7	VT1&VT2	52 32	125 94	54 / 228 44 / 170	No N.D.	p.92 of this issue
15	Hamamatsu C.	Sep.3-12	Person to person	Nursery school	O26:H11	VT1	1	･･･	22 / 64	Yes(8)	
16	Kanagawa P.b)	Oct.12-Nov.7	Foodborne*3)	Homes, Restaurant	O157:H7	VT2	67	160	66 / 103	Yes	pp.90&91 of this issue
17	Toyama P.	Dec.8 -Jan.18	Unknown	Dormitory	O26:H11	VT1	8	･･･	33 / 168	No	

Including 10 or more EHEC-positives, P.: Prefecture, C.: City, N.D.: No data, ･･･: Not applicable because person to person infection was suspected.
*Secondary taransmission within family. Number in ( ) refer to infections from secondary transmission.
a) Includes 10 fatal cases, b) Includes cases in six prefectures (Kanagawa, Tokyo, Chiba, Hiroshima, Akita, and Hyogo)
*1) sugarcane juice, *2) *yukari*-seasoned cucumber, *3) frozen minced meat cutlet

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 Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

Infectious Disease Surveillance Center, National Institute of Infectious Diseases
Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, JAPAN Tel (+81-3)5285-1111

＜特集関連資料1＞　腸管出血性大腸菌検出例の血清型別臨床症状, 2016年

Clinical manifestation of EHEC cases, by bacterial serotype in Japan, 2016

（病原微生物検出情報：2017年4月12日現在報告数）

血清型 Serotype	臨床症状* Clinical manifestation*											例数 Cases	%
	不詳[1]	無症状[2]	発熱[3]	下痢[4]	嘔気嘔吐[5]	血便[6]	腹痛[7]	意識障害[8]	脳症[9]	HUS[10]	腎機能障害[11]		
検出報告総数　Total	6	724	291	746	119	479	655	1	2	17	14	1,669	100.0
O157:H7:VT1	-	1	-	4	-	2	2	-	-	-	-	5	0.3
O157:H7:VT2	2	114	52	128	26	88	122	1	1	6	7	290	17.4
O157:H7:VT1&VT2	1	74	95	235	38	198	239	-	-	2	3	359	21.5
O157:H-:VT1	-	3	-	3	-	-	3	-	-	-	-	6	0.4
O157:H-:VT2	-	10	9	20	3	11	17	-	-	2	1	33	2.0
O157:H-:VT1&VT2	1	20	17	31	7	19	26	-	-	-	-	55	3.3
O157:HNT:VT1	-	10	2	6	1	4	5	-	-	-	-	18	1.1
O157:HNT:VT2	1	23	8	16	5	16	16	-	-	1	-	45	2.7
O157:HNT:VT1&VT2	-	30	11	29	2	30	30	-	-	1	1	71	4.3
O157 小計　Subtotal	5	285	194	472	82	368	460	1	1	12	12	882	52.8
O26:H11:VT1	1	218	52	148	20	48	90	-	-	-	-	405	24.3
O26:H11:VT1&VT2	-	3	1	2	-	1	2	-	-	-	-	6	0.4
O26:H-:VT1	-	7	4	10	-	6	8	-	-	-	-	20	1.2
O26:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O26:HNT:VT1	-	61	4	23	3	9	19	-	-	-	-	95	5.7
O26:HNT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O26 小計　Subtotal	1	291	61	183	23	64	119	-	-	-	-	528	31.6
O103:H2:VT1	-	15	6	14	1	3	10	-	1	1	-	34	2.0
O103:H2:VT1&VT2	-	-	-	-	-	1	-	-	-	-	-	1	0.1
O103:H11:VT1	-	-	1	2	-	2	2	-	-	-	-	3	0.2
O103:H25:VT1	-	1	1	3	1	1	2	-	-	-	-	4	0.2
O103:H-:VT2	-	-	-	1	-	-	1	-	-	-	-	1	0.1
O103:HUT:VT1	-	3	1	2	1	2	1	-	-	-	-	5	0.3
O103:HNT:VT1	-	7	-	5	-	1	3	-	-	-	-	12	0.7
O103 小計　Subtotal	-	26	9	27	3	10	19	-	1	1	-	60	3.6
O121:H19:VT2	-	11	7	18	7	9	15	-	-	2	1	31	1.9
O121:H19:VT1&VT2	-	-	1	2	-	1	2	-	-	-	-	2	0.1
O121:H-:VT2	-	-	-	1	-	1	1	-	-	-	-	1	0.1
O121:HUT:VT2	-	-	1	1	-	-	1	-	-	-	-	1	0.1
O121:HNT:VT2	-	2	3	3	-	2	3	-	-	1	1	5	0.3
O121 小計　Subtotal	-	13	12	25	7	13	22	-	-	3	2	40	2.4
O111:H8:VT1	-	-	-	1	-	1	1	-	-	-	-	1	0.1
O111:H-:VT1	-	8	3	9	1	6	6	-	-	-	-	18	1.1
O111:H-:VT1&VT2	-	2	1	9	-	4	8	-	-	-	-	11	0.7
O111:HUT:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O111:HNT:VT1	-	1	1	3	-	-	3	-	-	-	-	4	0.2
O111 小計　Subtotal	-	13	5	22	1	11	18	-	-	-	-	36	2.2
O145:H-:VT1	-	3	-	2	-	1	3	-	-	-	-	6	0.4
O145:H-:VT2	-	3	2	5	1	4	4	-	-	1	-	9	0.5
O145:H-:VT1&VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O145:HNT:VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O145 小計　Subtotal	-	10	2	7	1	5	7	-	-	1	-	19	1.1
O91:H14:VT1	-	4	-	-	-	-	-	-	-	-	-	4	0.2
O91:H14:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O91:H-:VT1	-	3	-	-	-	-	-	-	-	-	-	3	0.2
O91:H-:VT1&VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O91:HUT:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O91:HNT:VT1	-	4	-	-	-	-	-	-	-	-	-	4	0.2
O91 小計　Subtotal	-	15	-	-	-	-	-	-	-	-	-	15	0.9
O1:H-:VT2	-	-	1	1	-	1	1	-	-	-	-	1	0.1
O2:H27:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O5:H-:VT1	-	-	1	1	-	3	3	-	-	-	-	3	0.2
O6:HNT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O8:H9:VT2	-	-	1	-	-	-	-	-	-	-	-	1	0.1
O8:H12:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O8:H19:VT2	-	3	1	1	-	-	-	-	-	-	-	4	0.2
O21:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O22:HNT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O28ac:H25:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O55:H12:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O76:H19:VT1	-	3	-	-	-	-	-	-	-	-	-	3	0.2
O80:H18:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O84:H-:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O89:H-:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O98:H-:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O113:H21:VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O115:H2:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O115:H10:VT1	-	2	1	3	1	-	3	-	-	-	-	6	0.4
O115:HNT:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O125:HNT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O126:H20:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O128:H2:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O128:H2:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O128:H2:VT1&VT2	-	4	-	1	1	-	-	-	-	-	-	5	0.3
O130:H11:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O136:H12:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O137:H41:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O146:H-:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O146:HNT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O148:H18:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O156:H25:VT1	-	2	1	-	-	1	-	-	-	-	-	3	0.2
O156:H25:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O165:HUT:VT1&VT2	-	-	1	1	-	1	1	-	-	-	-	1	0.1
O166:H15:VT2	-	-	-	-	-	-	1	-	-	-	-	1	0.1
O171:H2:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O174:H2:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O177:H-:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O178:H19:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O179:H8:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O182:H25:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O183:H18:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O186:H36:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.1
O untypable	-	21	1	2	-	2	1	-	-	-	-	25	1.5

UT: Untypable, NT: Not typed, *2つ以上の臨床症状が報告された例を含む。　地方衛生研究所からの「病原体個票」の報告による。

*Includes cases for whom two or more symptoms were reported, 1) no data, 2) no symptoms, 3) fever, 4) diarrhea,
5) nausea/vomiting, 6) bloody diarrhea, 7) abdominal pain, 8) disturbance of consciousness, 9) encephalopathy, 10) hemolytic uremic syndrome, 11) renal failure
(Infectious Agents Surveillance Report: Data based on the reports from public health institutes received before April 12, 2017)