# IASR

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

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# <THE TOPIC OF THIS MONTH>

### Enterohemorrhagic Escherichia coli infection, as of April 2016, Japan

Enterohemorrhagic *Escherichia coli* (EHEC) infection is a systemic infection of pathogenic *E. coli* that produces Verotoxin/ Shiga toxin (VT/Stx) or possesses the VT encoding genes. Main signs and symptoms consist of abdominal pain, watery diarrhea, and bloody diarrhea. High fever (38°C) and/or vomiting are occasionally observed. Hemolytic uremic syndrome (HUS), which can be fatal for the young and the elderly, can be caused by VT that causes thrombocytopenia, hemolytic anemia and/or acute renal failure.

EHEC infection is a category III notifiable infectious disease under the Infectious Diseases Control Law. A physician who has made the diagnosis of EHEC infection shall notify the case to a health center (HC) immediately, who then transmits the information 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 the reporting physician or judged 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, serotyping of the isolates and typing of VT (VT or the VT gene) and submit the laboratory results to NESID (see p. 87 of this issue). The Department of Bacteriology I of the National Institute of Infectious Diseases (NIID) conducts molecular epidemiological analysis using multiple-locus variable-number tandem-repeat analysis (MLVA) or pulsed-field gel electrophoresis (PFGE) and when necessary conducts confirmatory tests of the isolates sent from PHIs (see pp. 93 & 95 of this issue). The NIID's analysis results are fed back to PHIs and, where necessary, to local governments through the National Epidemiological Surveillance of Foodborne Disease (NESFD) system.

Cases notified under NESID: In 2015, a total of 3,565 EHEC cases were reported. Among them 2,336 were symptomatic and 1,229 were asymptomatic (asymptomatic cases are detected during active surveillance of outbreaks or routine stool specimen screening of food handlers) (Table 1). Weekly number of reported cases in 2015 peaked during summer as usual (Fig. 1). Reports from Osaka, Tokyo, Kanagawa, Fukuoka and Hokkaido prefectures occupied 37.6% of all notified cases (asymptomatic cases included). The annual notification rate per 100,000 population was highest in Shimane prefecture (11.91) followed by Tottori (10.45) and Miyazaki (9.96) prefectures (Fig. 2). The notification rates within the 0-4 year old population were highest in Tottori and Miyazaki prefectures (Fig. 2). A large proportion of symptomatic cases were among those <30 years and  $\ge$ 60 years of age as in previous years (Fig. 3).

A total of 79 HUS cases (3.4% of symptomatic cases) were reported in 2015. EHEC was isolated from 50 of those cases (see p. 97 of this issue), and the distribution by O-serogroup was: 41 O157 cases, three O26 cases, and one case each of O74, O76, O111 and O121; the remaining two isolates were untypable or unknown. Forty-seven isolates were positive for VT2 or VT2&VT1; three were unknown for the VT-type. Among symptomatic EHEC cases, the proportion of HUS was highest among those 5-9 years of age (6.3%). There were three fatal cases, including those diagnosed by methods other than isolation of the bacteria.

Table 1. Notified cases of EHEC infection

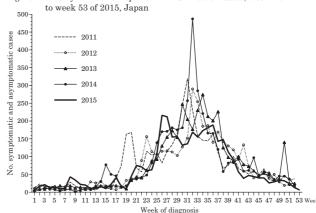
Year of diagnosis [Jan.1 - Dec.31]	No. Cases*	(Symptomatic cases only)	(%)
2006	3,922	(2,515)	(64)
2007	4,617	(3,083)	(67)
2008	4,329	(2,822)	(65)
2009	3,879	(2,602)	(67)
2010	4,135	(2,719)	(66)
2011	3,939	(2,659)	(68)
2012	3,770	(2,363)	(63)
2013	4,045	(2,623)	(65)
2014	4,156	(2,840)	(68)
2015	3,565	(2,336)	(66)
2016**	169	(87)	(51)

<sup>\*</sup>Including asymptomatic cases

\*\*Jan.1-Apr.10

(National Epidemiological Surveillance of Infectious Diseases: as of April 13, 2016)

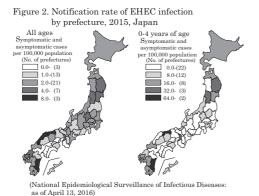
Figure 1. Weekly number of reported EHEC infection cases, week 1 of 2011

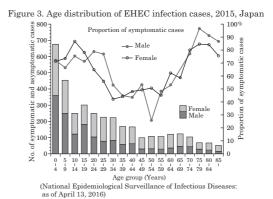


Week of diagnosis
(National Epidemiological Surveillance of Infectious Diseases: as of April 13, 2016)

(Continued on page 86')

#### (THE TOPIC OF THIS MONTH-Continued)





**EHEC isolated by PHIs**: In 2015, PHIs reported 1,709 EHEC isolations. While considerably less than the number of reported EHEC patients (n=3,565) (Table 1), this discrepancy was due to the current situation where many isolates from clinical or commercial settings are not sent to PHIs.

The most frequently detected O-serogroup was O157 (61%), followed by O26 (21%), and O103 (4.2%) (see p. 87 of this issue). While 56% of O157 isolates were VT1&VT2 positive, most of the O26 and O103 isolates were positive solely for VT1 (85% and 97%, respectively). Information on clinical signs and symptoms was reported for 1,018 of 1,040 O157 cases [abdominal pain (57%), diarrhea (56%), bloody diarrhea (43%) and fever (19%)].

Outbreaks: Among EHEC outbreaks reported by PHIs to NESID in 2015, 12 were outbreaks that included 10 or more EHEC-positive patients. Seven outbreaks were attributable to person-to-person transmission in nursery schools (Table 2). Under the Food Sanitation Law, 17 EHEC food poisoning events affecting a total of 156 persons (including cases negative for EHEC isolation) were reported in 2015 (see p. 88 of this issue). In previous years, there were 16 such events with 392 patients in 2012, 13 events with 105 patients in 2013, and 25 events with 766 patients in 2014. Notable events in 2015 were: O157 food poisoning in Fukuoka Prefecture in May (10 patients), which was possibly linked to the consumption of contaminated raw horse meat (see p. 88 of this issue); O26 person-to-person infection in a nursery school in Osaka Prefecture in June, including 157 patients with confirmed EHEC (see p. 92 of this issue); O157 food poisoning linked to a restaurant in Tokyo in June (17 patients) (see p. 90 of this issue); O157 food poisoning at a high school dormitory in Shimane Prefecture in August (approximately 70 patients with confirmed EHEC) (see p. 91 of this issue); and O157 food poisoning possibly linked to consumption of seared beef liver served at several branches of a chain restaurant in Nara Prefecture in September-October (12 patients) (see pp. 88 & 89 of this issue). In addition, the Department of Bacteriology I, NIID, identified identical MLVA or PFGE patterns among EHEC isolates derived from sporadic, widely dispersed patients, suggesting widespread diffuse EHEC transmission (see pp. 93 & 95 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). Though the number of EHEC cases reported in 2015 was the lowest since 2006, many food poisoning cases still occur, and it is important to continue to communicate the risks associated with consumption of raw or insufficiently cooked meat. Food poisoning events attributed to restaurants continue to be reported (Table 2, see p. 88 of this issue), and it will be important to continue to implement and practice strict food handling at restaurants.

As EHEC establishes infection at a dose as low as ~100 bacteria, it can easily spread from an infected person to another person directly or indirectly through foods or food products. In 2015, a notable number of EHEC outbreaks at nursery schools continued to be reported (Table 2; see p. 92 of this issue). Preventing such outbreaks requires appropriate hygienic practice, such as routine hand washing and sanitation and hygiene management at children's swimming pools (per "Infection Control Guidelines for Nurseries" revised November 2012). To prevent further secondary transmission within families and welfare facilities, HCs should provide complete instructions when a case occurs.

Table 2. Outbreaks of EHEC infection, 2015	(Data based on the reports from public health institutes received before April 4, 2016 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. positi /exan	ves	Familial infection*	Reference in IASR
1	Sakai C.	Jan.30-Mar.23	Person to person	Nursery school	O157:H7	VT2	37		37 /	201	Yes	
2	Sapporo C.	Feb.16-Mar.11	Person to person	Nursery school	O26:HNT	VT1&VT2	45	•••	25 /	99	Yes	
	Osaka P.	Jun.12-Jul.28	Person to person	Nursery school	O26:H11	VT1	79	• • •	157 /	470	Yes	p. 92 of this issue
4	Aomori P.	Jun.25-Jul.9	Animal contact	Nursery school	O157:H7	VT2	27		20 /	129	Yes (7)	
5	Tokyo	Jun.25-Jul.2	Foodborne	Restaurant	O157:H7	VT2	17	33	12 /	N.D.	No	p. 90 of this issue
6	Iwate P.	Jul.29-Oct.1	Person to person	Nursery school	O26:H11	VT1	8	• • •	18 /	167	Yes	
7	Okayama P.	Aug.4-Aug.18	Foodborne	Nursing home for the elderly	O157:H7	VT1&VT2	20	134	12 /	104	No	
8	Saitama P.	Aug.5-Aug.24	Unknown	After-school child day care	O26:H11	VT1&VT2	22	• • •	14 /	165	N.D.	
9	Yamagata P.	Aug.12-Sep.10	Person to person	Nursery school	O76:H7	VT2	7	• • •	22 /	206	Yes	
10	Shimane P.	Aug.22-Sep.14	Foodborne	Dormitory	O157:H7	VT2	62	117	70 /	152	No	p. 91 of this issue
11	Okinawa P.	Sep.10-Nov.25	Person to person	Nursery school	O121:H19	VT2	9	• • •	12 /	154	Yes (5)	
12	Higashiosaka C.	Dec.25-Feb.10	Person to person	Nursery school	O26:H11	VT1	3	• • •	15 /	215	Yes	

Including 10 or more EHEC-positives, P.: Prefecture, C.: City, NT: Not typed, 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.

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.

<特集関連資料> 腸管出血性大腸菌検出例の血清型別臨床症状,2015年

(病原微生物検出情報:2016年4月4日現在報告数)

Clinical manifestation of EHEC cases, according to bacterial serotype in Japan, 2015

	Clinical m	anifestatio	on of E	HEC case					apan, 2015				
血清型 Serotype							manifestatio					例数	%
	不詳 <sup>1)</sup> 42	無症状2) 615	発熱 <sup>3</sup> 302		<sup>)</sup> 嘔気嘔吐 14				B) 脳症 <sup>9)</sup>	HUS <sup>10)</sup> 20	腎機能障害 <sup>11)</sup> 14	Cases 1,709	100.0
検出報告総数 Total O157:H7:VT1	- 42	6	302	1			1 4		<u> </u>	- 20	- 14	1,709	0.6
O157:H7:VT2	12	137	62		3:	2 9	6 157	7 .		4	1	355	20.8
O157:H7:VT1&VT2	-	91	86		5				-	11	8	419	24.5
O157:H-:VT1 O157:H-:VT2		9 5	2 8			$\frac{1}{3}$ 2	9 10 0 26			-		24 35	1.4 2.0
O157:H-:VT1&VT2	_	21	14			5 3			_	_	_	68	4.0
O157:HUT:VT1&VT2	-	3	1			-	-		_	-	-	5	0.3
O157:HNT:VT1	-	-	1				1		-	-	-	2	0.1
O157:HNT:VT2 O157:HNT:VT1&VT2	1 9	17 27	3 16			1 7 3	3 7 7 52		-	1	1	27 95	1.6 5.6
O157小計 Subtotal	22	316	193		10:				-	16	10	1,040	60.9
O26:H11:VT1	2	96	44			8 5				-	-	239	14.0
O26:H11:VT1&VT2	-	16	3			7 1				1	1	41	2.4
O26:H-:VT1 O26:H-:VT1&VT2	-	11 6	5 1				1 8		-	1	1	27 9	1.6 0.5
O26:HUT:VT1	-	1	-	_		_	-			-	1	1	0.3
O26:HNT:VT1	7	14	5	17		3	8 15	5 .		_	-	42	2.5
O26:HNT:VT1&VT2	1	2	1				1 :			-	-	4	0.2
O26 小計 Subtotal O103:H2:VT1	10	146 29	59 10		2	$\frac{1}{3}$ $\frac{8}{1}$				2	2	363 56	21.2 3.3
O103:H2:VT1&VT2	-	29	10				1 1			-	-	1	0.1
O103:H11:VT1	-	3	1				1 2			_	-	7	0.4
O103:H11:VT1&VT2	-	-	-	-		-	-			-	-	1	0.1
O103:H25:VT1	-	-	1	-		1	- 1	1 .		-	-	1	0.1
O103:H-:VT1	-	1	1	-		1	- 1	 I	-	-	-	1 1	0.1 0.1
O103:HUT:VT1 O103:HNT:VT1	1	2	1	_		-	-			-	-	3	0.1
O103 小計 Subtotal	1	35	14	25		6 1	5 24	1			-	71	4.2
O111:H8:VT1	-	-	-	1		-	- :	1 .	-	-	-	1	0.1
O111:H-:VT1	-	11	10				5 1			-	-	32	1.9
O111:H-:VT1&VT2 O111:HNT:VT1	-	$\frac{4}{2}$	1	10		1	5 9		-	1	1	15 2	0.9
O111:HNT:VT1&VT2	1	_	-	. 1		-	1 :			-	-	2	0.1
O111 小計 Subtotal	1	17	11			2 1				1	1	52	3.0
O121:H19:VT2	-	3	4			4 1				-	-	25	1.5
O121:H-:VT2	-	-	1				1 2		-	-	-	2	0.1
O121:HNT:VT2 O121 小計 Subtotal	1 1	5	7			1 5 1	1 5 6 19		-	-		33	1.9
O91:H14:VT1	-	5		- 24		-	- 1		-			5	0.3
O91:H14:VT1&VT2	-	1	-	-		-	-		_	-	-	1	0.1
O91:H21:VT2	-	1	-	-		-	-			-	-	1	0.1
O91:H-:VT1	-	2	-	1		-	1 2	2 .	-	-	-	4	0.2
O91:H-:VT1&VT2 O91:HUT:VT1	-	3 1	1	1		-	-		-	-	-	4 2	0.2
O91:HUT:VT1&VT2	_	1	-	_		_	_				-	1	0.1
O91:HNT:VT1	1	9	-	-		-	-			-	-	10	0.6
O91:HNT:VT2	-	1	-	-		-	-			-	-	1	0.1
O91:HNT:VT1&VT2	1	- 04	-	-		-			-	-	-	1	0.1
091 小計 Subtotal 0145:H-:VT1	2	24 1	1	2			1 2 1 i	<u>.</u> L .	-		-	30	1.8 0.2
O145:H-:VT2	-	6	2				5 8			-	-	14	0.2
O145:H-:VT1&VT2	-	-	1				1 :		_	-	-	1	0.1
O145:HNT:VT1&VT2	-	3	1				1			-	-	4	0.2
O145 小計 Subtotal O1:H20:VT1	-	10	4				8 10		-		-	23	1.3 0.1
O1:HNT:VT2	1	-	-	_		-	_			_	-	1	0.1
O5:H-:VT1	-	2	3	2	;	3	2 4	1 .		-	-	6	0.4
O5:H-:VT1&VT2	-	1	-	-		-	-		-	-	-	1	0.1
O8:H16:VT1&VT2 O8:H19:VT2	-	1 1	-	-		-	-		-	-	-	1 1	0.1 0.1
O8:HUT:VT1&VT2		2	_	_		_	_			-		2	0.1
O8:HNT:VT2	1	-	-	-		-	-			-	-	1	0.1
O18:H21:VT2	-	1	-	-		-	-		-	-	-	1	0.1
O55:H12:VT1	-	1	- 1			1	1 :	 I .	-	-	-	1	0.1
O57:H-:VT1&VT2 O63:HNT:VT2	1	-	1	1		1	1 :			-	-	1 1	0.1 0.1
O69:H11:VT1	-	-	1				1			-	-	2	0.1
O71:H8:VT1&VT2	-	-	1				1 :		-	-	-	1	0.1
O74:H20:VT2	-	- 1	-	1		-	1		-	1	1	1	0.1
O74:H-:VT1 O74:HUT:VT2	-	1 1	-	-		-	-			-	-	1 1	0.1 0.1
O78:H-:VT1&VT2	-	1	-			-	_			-	-	1	0.1
O79:H14:VT1&VT2	-	1	-	-		-	-			-	-	1	0.1
O84:HUT:VT1	-	2	-	-		-	-			-	-	2	0.1
O100:H-:VT2 O101:H-:VT2	-	1	-	-		-	-		-	-	-	1	0.1
O101:H-:V12 O110:H45:VT1	-	1	1			-	- 1	 I :		-	-	1	0.1 0.1
O113:H21:VT2	-	1	-	-		-	-			-	-	1	0.1
O115:H10:VT1	-	5	-	-		-	-			-	-	5	0.3
O115:HNT:VT1	-	-	-	1		-	-			-	-	1	0.1
O128:H2:VT1 O128:HNT:VT2	1	4	-	-		-	-			-	-	4	0.2
O136:H16:VT1	1	-	-	1		-	- 1			-	-	1	0.1
O142:H38:VT1	-	1	-	-		-	-			-	-	1	0.1
O146:H21:VT1	-	2	1					1 .		-	-	4	0.2
O146:H21:VT1&VT2	-	- 1	-	1		-	-		-	-	-	1	0.1
O146:H-:VT2 O146:H-:VT1&VT2	-	1 2	-	-		-	-		-	-	-	1 2	0.1 0.1
O146:H-:VT1&VT2 O146:HNT:VT1	-	2 1	-	-		-	-			-	-	1	0.1
O146:HNT:VT1 O152:H-:VT1	-	1	-	-		-	-			-	-	1	0.1
O156:H25:VT1	-	1				_	_			-	-	1	0.1
O150:H125:VT1	-	1	-			-	_			-	-	1	0.1
O165:H25:VT2	-	1	-	_		-	_			-	-	1	0.1
O165:H-:VT2	-	-	1	1		-	2 2	2 .		-	-	2	0.1
O165:H-:VT1&VT2	-	1	-	_			2 :	3 .		-	-	4	0.2
O168:HUT:VT2	-	-	1	1		1	-		-	-	-	1	0.1
O168:HNT:VT2	-	1	-	-		-	-		-	-	-	1	0.1
O183:H18:VT1	-	1 20	-	-		-	-			-	-	1	0.1
O untypable UT: Untypable, NT: Not	1	20	3					3 原体個票」の		-	-	30	1.8

O untypable
 1
 20
 3
 7
 3
 2
 6

 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「病原体側票」の報告による。

 \*Including cases for which 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 4, 2016)