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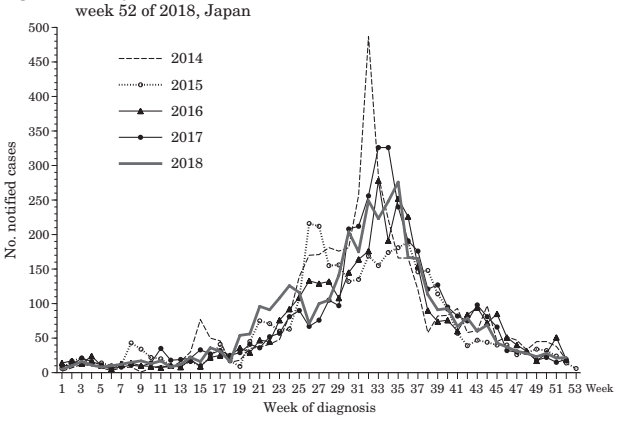
National Institute of Infectious Diseases and Tuberculosis and Infectious Diseases Control Division, Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Enterohemorrhagic *Escherichia coli* (EHEC) infection, as of March 2019, Japan

Enterohemorrhagic *Escherichia coli* (EHEC) 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 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 (PHIs) 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, when necessary, to local governments through the National Epidemiological Surveillance of Foodborne Disease (NESFD) system.

Figure 1. Weekly number of notified EHEC infection cases, week 1 of 2014 to week 52 of 2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 20 March 2019)

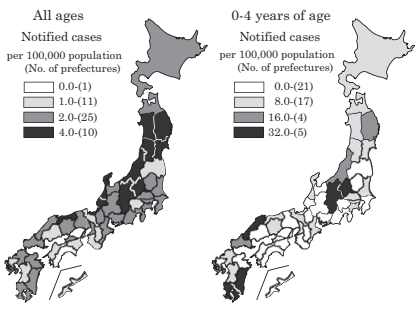
Cases notified under the NESID system: In 2018, a total of 3,852 cases of EHEC infection were reported. Among them, 2,581 were symptomatic, and 1,271 were asymptomatic (asymptomatic cases are detected during active epidemiologic investigations or routine stool specimen screening of food handlers) (Table 1). Consistent with yearly trends, the number of reports peaked in summer (Fig. 1). Reports from 8 prefectures, including Tokyo, Kanagawa, Saitama, Chiba, Osaka, Hokkaido, Fukuoka, and Aichi, accounted

Table 1. Notified cases of EHEC infection

Year of dianosis [Jan 1- Dec 31]	No. notified cases*	(No. of symptomatic cases) (%)
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	(2,624) (65)
2014	4,156	(2,839) (68)
2015	3,568	(2,338) (66)
2016	3,647	(2,246) (62)
2017	3,904	(2,606) (67)
2018	3,852	(2,581) (67)
2019**	213	(132) (62)

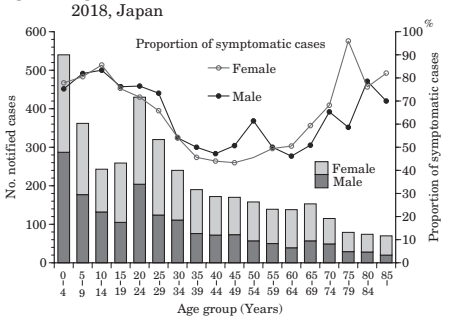
*Including asymptomatic cases **Jan 1- Mar 17
(National Eidemioloical Surveillance of Infectious Diseases: as of 20 March 2019)

Figure 2. Notification rate of EHEC infection by prefecture, 2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 20 March 2019)

Figure 3. Age distribution of notified EHEC infection cases, 2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 20 March 2019)

(Continued on page 72′)

(THE TOPIC OF THIS MONTH-Continued)

Table 2. Outbreaks of EHEC infection in 2018 (Data based on reports from public health institutes received before 20 March 2019)

No.	Prefecture or 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*
1	Osaka C.	May 18-Jun 4	Person to person	Nursery school	O26:H11	VT1	52	・・・	56/319	Yes(13)
2	Kanagawa P.	Jun 20-Sep 11	Person to person	Nursery school	O26:HNT	VT1	11	・・・	34/261	Yes(12)
3	Hyogo P.	Jul 23-Aug 16	Foodborne**	Restaurant	O157:H7/H-	VT1&VT2	7	146	13/36	N.D.
	Himeji C.	Jul 25-Aug 15					2	4	4/9	No
4	Miyazaki P.	Jul 23-Aug 24	Person to person	Nursery school	O26:H11	VT1	12	・・・	14/40	Yes(7)
5	Nagasaki P.	Aug 3-9	Person to person	Nursery school	O26:H11	VT1	35	・・・	11/162	Yes(10)
6	Nagano P.	Aug 4-Sep 18	Person to person	Nursery school	O26:H11	VT1	18	・・・	29/260	Yes(9)
7	Ibaraki P.	Aug 8-Sep 6	Person to person	Nursery school	O26:H11	VT1	35	・・・	11/98	Yes(4)
8	Koshigaya C.	Aug 16-Sep 14	Person to person	Nursery school	O26:H11	VT1	15	・・・	28/198	Yes(11)
9	Gunma P.	Aug 29-Sep 13	Unknown	Nursery school	O26:H11	VT1	13	・・・	21/195	Yes(6)
10	Fukui P.	Sep 27-Oct 13	Foodborne	Restaurant	O157:H7	VT1&VT2	12	107	13/28	N.D.
11	Himeji C.	Oct 15-Nov 1	Unknown	Nursery school	O157:H7	VT1&VT2	25	・・・	10/60	Yes(1)

Outbreaks with 10 or more EHEC-positive cases, P.: Prefecture, C.:City, N.D.: No data, ・・・: Not applicable because person to person infection was suspected.
*Secondary transmission within a family. The numbers in parentheses refer to infections from secondary transmission.
**undercooked hamburger steak

for 51% of all notified cases, including asymptomatic cases. The annual number of notified cases per 100,000 population was highest in Gunma Prefecture (6.1), followed by Akita (5.6), Iwate (5.3), Yamagata (5.3), Ishikawa (5.2), Fukui (5.0), and Nagano (5.0) Prefectures (Fig. 2 in p. 71). The notification rate per 100,000 population among 0-4-year-olds was highest in Miyazaki Prefecture (41.3), followed by Kagoshima (33.8), Nagano (33.8), Shimane (33.3), Gunma (32.4) Prefectures (Fig. 2 in p. 71). The proportion of symptomatic cases was high among the <30-year-old and ≥70 -year-old age groups, which is consistent with findings from previous years (Fig. 3 in p. 71).

EHEC was isolated from 47 of 69 HUS cases (2.7% of symptomatic cases). The O-serogroup was O157 in 33 cases, and the toxin type was VT2 (VT2 alone or VT1 & VT2) in 40 cases. Among the symptomatic cases, HUS was most frequent in 0-4-year-olds (6.5%) (see p.82 of this issue). At the time of notification, only one case was fatal.

EHEC isolated by PHIs: In 2018, PHIs reported 2,140 isolations of EHEC (Table in p. 73 of this issue). This figure was considerably lower than the number of notified cases of EHEC infection (Table 1 in p. 71). The discrepancy was due to the isolates from the clinical setting or commercial laboratories being sent to PHIs upon request on an as-needed basis. The most frequently detected O-serogroup was O157 (56%), followed by O26 (24%) and O121 (4%) (Table in p.73 of this issue). In 2018, 63% and 35% of O157 isolates were VT1 & VT2-positive and VT2-positive, respectively, whereas 97% of O26 isolates were VT1-positive and 100% of O121 isolates were VT2-positive. The main clinical signs/symptoms among the 1,198 cases in which O157 was isolated were diarrhea (62%), abdominal pain (61%), bloody diarrhea (47%), and fever (21%).

Outbreaks: Among the EHEC outbreaks reported by PHIs to NESID in 2018, 11 involved ≥10 EHEC-positive cases. Nine were due to person-to-person transmission at nursery schools (Table 2). Under the Food Sanitation Law, 32 EHEC-related food poisoning outbreaks involving a total of 456 cases, including EHEC isolation-negative cases, were reported (see p.74 of this issue) (17 outbreaks involving 156 cases in 2015, 14 outbreaks involving 252 cases in 2016, and 17 outbreaks involving 156 cases in 2017 (see p.74 of this issue)). The main EHEC outbreaks in 2018 were as follows: (i) an O157 outbreak at a nursing home in Saitama Prefecture in May (10 cases; see p.74 of this issue); (ii) an O157 outbreak due to the consumption of undercooked hamburger steak in Hyogo Prefecture in July (9 cases; Table 2); (iii) an outbreak at a restaurant in Tokyo in August (194 cases; see p.74 of this issue); (iv) an outbreak at a restaurant in Shizuoka Prefecture in August (60 cases; see p.74 of this issue); (v) an O121 outbreak at hamburger chain restaurants, in Nagano Prefecture in August (see p. 78 of this issue). In addition to these, it has become clear that strains exhibiting the same MLVA type among sporadic cases of unknown epidemiologic association were isolated from a wide area (see p.81 of this issue). The MHLW is engaged in unifying the genotyping method (MLVA method), and promoting coordination and cooperation among relevant organizations in order to strengthen responses to outbreaks (see p.83 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). In addition, the Ministry of Agriculture, Forestry and Fisheries is working on risk management to take necessary measures in advance from production to consumption in order to improve food safety, and is promoting sanitation management at the production stage to improve the production and supply of safe vegetables (see p.85 of this issue).

As EHEC can cause infection at bacterial counts as low as ~100, 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 2018 (see p.74 of this issue). To prevent EHEC infections, it is essential to observe the principles of proper food hygiene and continue risk communication activities aimed at reducing the consumption of raw or undercooked meat. Furthermore, EHEC outbreaks continue to occur in large numbers in nursery schools (Table 2). 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 within a household or care facility, the relevant PHC should ensure that appropriate measures are strictly implemented to prevent further 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 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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<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, 2018年

Clinical manifestation of EHEC cases in Japan, according to bacterial serotype, 2018

(病原微生物検出情報 : 2019年3月20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]		
検出報告数 Total	36	688	408	1,159	233	728	1,068	-	1	31	25	2,140	100.0
O157:H7:VT1	-	1	-	2	-	2	1	-	-	-	-	3	0.1
O157:H7:VT2	5	97	73	207	49	161	197	-	-	8	3	360	16.8
O157:H7:VT1&VT2	2	118	138	417	89	315	418	-	-	10	10	614	28.7
O157:H17:VT1&VT2	-	-	1	1	1	1	1	-	-	-	-	1	0.0
O157:H-:VT1	-	3	1	5	-	3	5	-	-	-	-	8	0.4
O157:H-:VT2	1	7	7	14	4	13	12	-	-	1	2	26	1.2
O157:H-:VT1&VT2	2	21	12	54	11	30	51	-	-	-	-	87	4.1
O157:H-	-	-	-	-	-	1	1	-	-	-	-	1	0.0
O157:HUT:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O157:HUT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O157:HUT:VT1&VT2	2	-	1	5	1	3	4	-	-	-	-	7	0.3
O157:HNT:VT2	-	18	4	10	4	11	13	-	-	-	-	33	1.5
O157:HNT:VT1&VT2	-	26	7	20	8	16	20	-	-	-	-	48	2.2
O157:HNT:VT Other	-	3	4	4	2	4	5	-	1	4	3	8	0.4
O157小計 Subtotal	12	296	248	739	169	560	728	-	1	23	18	1198	56.0
O26:H11:VT1	1	148	76	215	20	64	149	-	-	-	-	416	19.4
O26:H11:VT2	-	6	2	2	1	2	2	-	-	1	1	8	0.4
O26:H11:VT1&VT2	-	2	1	3	2	2	3	-	-	-	-	5	0.2
O26:H11	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O26:H-:VT1	-	11	4	18	2	2	13	-	-	-	-	34	1.6
O26:HNT:VT1	13	24	4	9	1	3	9	-	-	-	-	47	2.2
O26小計 Subtotal	14	192	87	247	26	73	176	-	-	1	1	511	23.9
O121:H19:VT2	2	14	26	56	12	41	51	-	-	1	1	79	3.7
O121:H-:VT2	-	-	1	1	-	-	2	-	-	-	-	2	0.1
O121:HUT:VT2	-	-	-	2	1	1	2	-	-	-	-	2	0.1
O121:HNT:VT2	-	1	-	2	-	-	1	-	-	1	-	4	0.2
O121小計 Subtotal	2	15	27	61	13	42	56	-	-	2	1	87	4.1
O103:H2:VT1	-	18	11	23	7	10	20	-	-	1	-	46	2.1
O103:H2:VT1&VT2	-	-	1	1	-	2	2	-	-	1	1	2	0.1
O103:H2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O103:H8:VT1	-	1	1	3	-	1	3	-	-	-	-	6	0.3
O103:H11:VT1	-	1	-	4	1	3	4	-	-	-	-	6	0.3
O103:H25:VT1	-	-	-	1	-	-	1	-	-	-	-	1	0.0
O103:H51:VT1	-	-	1	1	1	1	1	-	-	1	1	1	0.0
O103:H-:VT1	-	2	-	2	-	-	1	-	-	-	-	4	0.2
O103:HUT:VT1	-	1	1	3	-	1	3	-	-	-	1	4	0.2
O103:HNT:VT1	-	1	-	1	-	-	-	-	-	-	-	3	0.1
O103小計 Subtotal	-	25	15	39	9	18	35	-	-	3	3	74	3.5
O111:H8:VT1	-	-	2	1	-	2	2	-	-	-	-	2	0.1
O111:H8:VT1&VT2	-	-	1	-	-	1	1	-	-	-	-	1	0.0
O111:H-:VT1	1	15	14	26	6	10	20	-	-	-	-	48	2.2
O111:H-:VT1&VT2	1	3	2	9	-	6	7	-	-	-	-	13	0.6
O111:HNT:VT1	-	-	1	1	-	1	1	-	-	-	-	2	0.1
O111:HNT:VT1&VT2	-	2	-	1	-	-	1	-	-	-	-	3	0.1
O111小計 Subtotal	2	20	20	38	6	20	32	-	-	-	-	69	3.2
O145:H7:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O145:H-:VT1	1	2	-	4	1	2	5	-	-	-	-	9	0.4
O145:H-:VT2	-	7	4	12	2	7	13	-	-	1	1	22	1.0
O145:HNT:VT2	-	-	1	2	1	2	4	-	-	-	-	4	0.2
O145小計 Subtotal	1	10	5	18	4	11	22	-	-	1	1	36	1.7
O91:H7:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O91:H8:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O91:H14:VT1	-	5	1	-	-	-	2	-	-	-	-	8	0.4
O91:H14:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O91:H-:VT1	-	8	-	-	-	-	-	-	-	-	-	9	0.4
O91:H-:VT1&VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O91:HUT:VT1	-	3	-	-	-	-	-	-	-	-	-	3	0.1
O91小計 Subtotal	-	21	1	-	-	-	2	-	-	-	-	25	1.2
O115:H10:VT1	-	11	-	1	1	-	1	-	-	-	-	12	0.6
O115:H10:VT1&VT2	-	-	-	-	-	1	-	-	-	-	-	1	0.0
O115小計 Subtotal	-	11	-	1	1	1	1	-	-	-	-	13	0.6
O128:H2:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O128:H2:VT2	-	-	-	1	-	-	1	-	-	-	-	1	0.0
O128:H2:VT1&VT2	-	3	-	-	-	-	-	-	-	-	-	3	0.1
O128:H45:VT2	-	-	-	1	-	-	-	-	-	-	-	1	0.0
O128:H-:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O128:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O128小計 subtotal	-	8	-	2	-	-	1	-	-	-	-	10	0.5
O1:H20:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O5:H9:VT1	-	-	-	1	1	1	1	-	-	-	-	1	0.0
O5:H-:VT1	-	1	-	1	1	1	1	-	-	-	-	2	0.1
O6:H34:VT2	-	-	-	-	-	-	-	-	-	-	-	1	0.0
O8:H19:VT2	-	8	-	-	-	-	-	-	-	-	-	8	0.4
O8:H19:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O8:H49:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O8:HUT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O9:H4:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O9:H-:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O15:H18:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O15:H27:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O18:H45:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O28ac:HUT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O43:H2:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O55:H12:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O55:HNT:VT1	-	-	1	-	-	1	1	-	-	-	-	1	0.0
O63:H6:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O66:H25:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O71:H2:VT1	-	-	-	1	-	-	1	-	-	-	-	1	0.0
O74:H42:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O74:HUT:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O74:HUT:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O76:H19:VT1	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O76:H19:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O77:H45:VT1	-	-	-	-	1	-	-	-	-	-	-	1	0.0
O78:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O80:HNT:VT2	-	-	-	1	-	-	-	-	-	1	1	1	0.0
O86a:H27:VT1	-	-	-	-	-	-	1	-	-	-	-	1	0.0
O88:H8:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O104:H10:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O112:H2:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O113:H4:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O113:H21:VT2	-	4	-	-	-	-	-	-	-	-	-	4	0.2
O113:H-:VT2	-	-	1	1	-	-	1	-	-	-	-	1	0.0
O116:H9:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O118:H2:VT1	-	-	-	-	-	-	1	-	-	-	-	1	0.0
O118:H16:VT1	-	-	1	2	-	-	1	-	-	-	-	2	0.1
O126:H20:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O136:H16:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O146:H21:VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O146:H-:VT2	-	3	-	-	-	-	-	-	-	-	-	3	0.1
O146:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O146:HNT:VT1&VT2	-	-	-	1	-	-	1	-	-	-	-	1	0.0
O150:H-:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O151:H16:VT1	-	-	-	1	-	-	-	-	-	-	-	1	0.0
O152:H8:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O156:H25:VT1	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O165:H25:VT2	-	-	1	1	-	-	1	-	-	-	-	1	0.0
O165:H-:VT1&VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O166:H28:VT1	-	4	-	-	-	-	-	-	-	-	-	4	0.2
O166:HUT:VT2	-	-	-	1	-	-	1	-	-	-	-	1	0.0
O168:H7:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O168:H8:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O179:H8:VT1&VT2	-	1	-	1	-	-	-	-	-	-	-	2	0.1
O181:H16:VT2	-	1	-	-	-	-	-	-	-	-	-	1	0.0
O183:H18:VT2	-	-	-	-	-	-	-	-	-	-	-	1	0.0
O185:H7:VT2	-	2	-	-	-	-	-	-	-	-	-	2	0.1
O untypable	5	28	1	2	2	-	4	-	-	-	-	37	1.7

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 System: Data based on reports from public health institues received before 20 March 2019)