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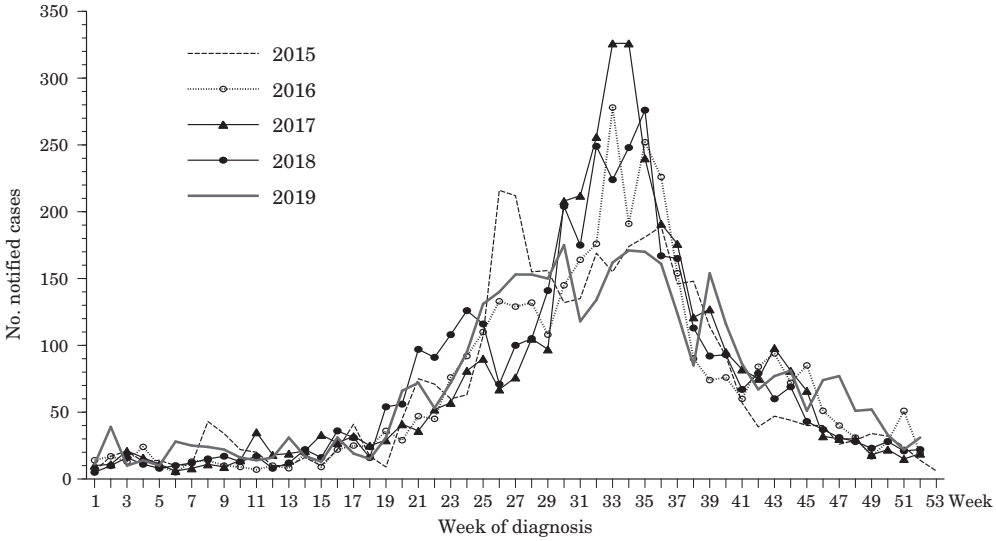
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Enterohemorrhagic *Escherichia coli* (EHEC) infection as of March 2020 in Japan

Figure 1. Weekly number of notified EHEC infection cases, week 1 of 2015 to week 52 of 2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 30 March 2020)

Enterohemorrhagic *Escherichia coli* (EHEC) is an important diarrheagenic *E. coli* that 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 develop, with potentially fatal outcomes.

In Japan, EHEC infection is 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 the 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.67 of this issue). The Department of Bacteriology I of the National Institute of Infectious Diseases (NIID) performs confirmatory tests upon request, and conducts molecular epidemiological analysis of EHEC using multiple-locus variable-number tandem-repeat analysis (MLVA) and pulsed-field gel electrophoresis (PFGE) (see p.70 and 71 of this issue). The results of the analyses are fed back to the PHIs and, as necessary, to local governments through the National Epidemiological Surveillance of Foodborne Disease (NESFD) system.

Cases notified under the NESID system: In 2019, a total of 3,744 cases of EHEC infection were reported. Among them, 2,511 were symptomatic and 1,233 were asymptomatic (asymptomatic cases are detected during active epidemiological investigations or routine stool specimen screening of food handlers) (Table on p.66). Consistent with yearly trends, the number of reports peaked in the

(Continued on page 66′)

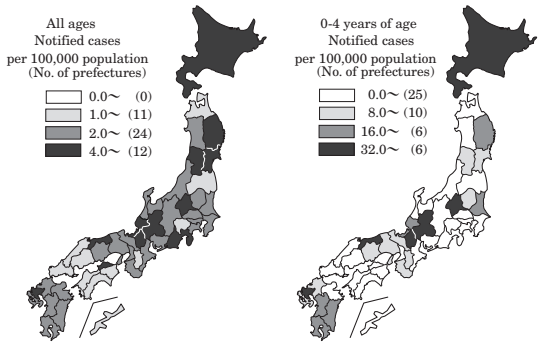
(THE TOPIC OF THIS MONTH-Continued)

Table. Notified cases of EHEC infection

Year of diagnosis [Jan 1- Dec 31]	No. notified cases*	(No. symptomatic cases) (%)
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	3,855	(2,584) (67)
2019	3,744	(2,511) (67)
2020**	250	(158) (63)

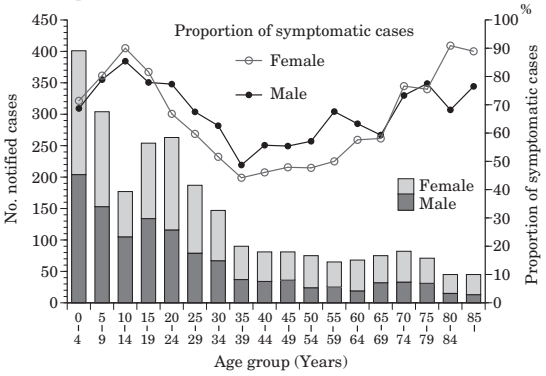
*Includes asymptomatic cases **Jan 1- Mar 27
(National Epidemiological Surveillance of Infectious Diseases: as of 30 March 2020)

Figure 2. Notification rate of EHEC infection by prefecture, 2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 30 March 2020)

Figure 3. Age distribution of notified EHEC infection cases, 2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 30 March 2020)

summer (Fig. 1). Reports from 9 prefectures (Tokyo, Hokkaido, Fukuoka, Osaka, Kanagawa, Aichi, Shizuoka, Hyogo, and Saitama) accounted for 50% of all notified cases (including asymptomatic cases). The annual number of notified cases per 100,000 population was highest in Saga Prefecture (13.4), followed by Iwate (5.6), Hokkaido (5.3), Gunma (5.2), and Gifu (5.1) prefectures (Fig. 2). The notification rate per 100,000 population among 0-4-year-olds was highest in Saga prefecture (126.5), followed by Gifu (58.7) and Shiga (44.3) prefectures (Fig. 2). The proportion of symptomatic cases among notified cases was high among those aged <30 years and ≥60 years, which is consistent with findings from previous years (Fig. 3). Among the 78 HUS cases (3.1% of symptomatic cases), EHEC was isolated from 45. The O-serogroup was O157 in 34 cases and the toxin type was VT2 (VT2 alone or VT1 & VT2) in 41 cases. Among the symptomatic cases, HUS was most frequent in 0-4-year-olds (6.0%) (see p.73 of this issue). At the time of notification, three cases were fatal. EHEC was not isolated from approximately 30% to 40% of the HUS cases, and these were confirmed as being due to EHEC infection by the toxin detected in the stool or the increase in antibody titers for the major O-serogroups.

EHEC isolated by PHIs: In 2019, PHIs reported 1,784 isolations of EHEC (see p.67 of this issue). This figure was considerably lower than the number of notified cases of EHEC infection (Table). This discrepancy is due to 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 (54%), followed by O26 (16%), O103 (5.8%), and O111 (5.7%) (see p.67 of this issue). Regarding toxin type, in 2019, VT1 & VT2-positive was the most frequent type in O157 as in recent years, accounting for 58% of O157, and VT2-positive accounted for 40%. Although VT1-positive was the most frequent type in O26 as in recent years, accounting for 91%, VT2-positive accounted for 8.5%, which was higher than that in previous years (less than 1% in previous years). The main clinical signs/symptoms among the 955 cases in which O157 was isolated were diarrhea (61%), abdominal pain (61%), bloody diarrhea (46%), and fever (22%).

Outbreaks: Many EHEC outbreaks at facilities, such as nursery schools, were also reported in 2019 and were presumed to be caused by person-to-person transmission. On the other hand, under the Food Sanitation Law, 20 EHEC-related food poisoning outbreaks involving a total of 165 cases (includes EHEC isolation-negative cases) were reported in 2019 (14 outbreaks involving 252 cases in 2016; 17 outbreaks involving 156 cases in 2017; and 32 outbreaks involving 456 cases in 2018). Based on the analysis by the Department of Bacteriology I, strains exhibiting the same MLVA type among sporadic cases of unknown epidemiological association were confirmed to be isolated from a wide geographic area (see p.71 and 74 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, following 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, it can easily spread from infected persons to uninfected persons or to food/food products. EHEC-associated food poisoning events attributed to restaurants also occurred in 2019 (see p.68 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. 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, 2019年

Clinical manifestation of EHEC cases in Japan, according to bacterial serotype, 2019

（病原微生物検出情報：2020年３月23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	3	632	317	933	188	584	860	−	2	27	19	1,784	100.0
O157:H7:VT1	−	−	−	2	−	−	2	−	−	−	−	3	0.2
O157:H7:VT2	−	104	71	204	42	146	191	−	1	9	7	350	19.6
O157:H7:VT1&VT2	1	74	103	273	68	228	288	−	1	7	7	411	23.0
O157:H-:VT1	−	2	−	2	−	2	3	−	−	−	−	5	0.3
O157:H-:VT2	−	3	4	12	1	8	14	−	−	1	−	18	1.0
O157:H-:VT1&VT2	−	38	18	52	10	31	49	−	−	−	−	101	5.7
O157:HUT:VT2	−	3	1	2	1	1	2	−	−	−	−	5	0.3
O157:HUT:VT1&VT2	−	1	−	1	−	−	1	−	−	−	−	2	0.1
O157:HNT:VT1	−	1	1	2	1	−	2	−	−	−	−	3	0.2
O157:HNT:VT2	−	2	5	7	3	6	5	−	−	1	1	13	0.7
O157:HNT:VT1&VT2	−	10	7	27	4	20	27	−	−	1	−	41	2.3
O157**	−	−	−	2	−	2	2	−	−	3	2	3	0.2
O157小計 subtotal	1	238	210	586	130	444	586	−	2	22	17	955	53.5
O26:H11:VT1	−	89	39	103	20	34	87	−	−	−	−	215	12.1
O26:H11:VT2	−	5	6	15	8	9	17	−	−	1	−	23	1.3
O26:H11:VT1&VT2	−	−	−	1	−	1	1	−	−	−	−	1	0.1
O26:H-:VT1	−	13	8	12	−	10	8	−	−	−	−	28	1.6
O26:HUT:VT1	−	−	−	2	−	1	2	−	−	−	−	2	0.1
O26:HNT:VT1	−	5	4	8	−	4	7	−	−	−	−	13	0.7
O26:HNT:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O26小計 subtotal	−	113	57	141	28	59	122	−	−	1	−	283	15.9
O103:H2:VT1	−	30	9	32	5	10	16	−	−	−	−	64	3.6
O103:H2:VT1&VT2	−	3	−	−	−	−	−	−	−	−	−	3	0.2
O103:H11:VT1	−	1	1	2	−	−	1	−	−	−	−	3	0.2
O103:H25:VT1	−	−	−	2	−	1	1	−	−	−	−	2	0.1
O103:H-:VT1	−	2	1	2	1	−	1	−	−	−	−	4	0.2
O103:HUT:VT1	−	2	1	1	1	−	1	−	−	−	−	3	0.2
O103:HNT:VT1	−	9	−	11	1	4	9	−	−	−	−	24	1.3
O103小計 subtotal	−	47	12	50	8	15	29	−	−	−	−	103	5.8
O111:H-:VT1	−	7	3	11	1	−	13	−	−	−	−	20	1.1
O111:H-:VT2	−	−	1	1	−	−	1	−	−	−	−	1	0.1
O111:H-:VT1&VT2	−	16	8	25	3	9	16	−	−	−	1	50	2.8
O111:HUT:VT1	−	16	−	6	−	1	3	−	−	−	−	22	1.2
O111:HUT:VT1&VT2	−	2	1	1	−	1	1	−	−	−	−	4	0.2
O111:HNT:VT1	−	2	1	1	−	−	1	−	−	−	−	3	0.2
O111:HNT:VT2	−	−	1	1	−	1	1	−	−	−	−	1	0.1
O111:HNT:VT1&VT2	−	−	−	1	−	1	1	−	−	−	−	1	0.1
O111小計 subtotal	−	43	15	47	4	13	37	−	−	−	1	102	5.7
O121:H10:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O121:H19:VT1	−	−	1	1	1	1	1	−	−	−	−	1	0.1
O121:H19:VT2	1	14	6	32	7	17	30	−	−	2	1	58	3.3
O121:H-:VT2	1	−	−	1	−	−	1	−	−	−	−	2	0.1
O121:HNT:VT2	−	1	−	1	−	1	1	−	−	−	−	2	0.1
O121:HNT:VT1&VT2	−	−	1	1	−	−	−	−	−	−	−	1	0.1
O121小計 subtotal	2	16	8	36	8	19	33	−	−	2	1	65	3.6
O145:H28:VT2	−	−	−	2	−	1	1	−	−	−	−	2	0.1
O145:H-:VT1	−	1	1	1	1	1	1	−	−	−	−	2	0.1
O145:H-:VT2	−	6	3	16	2	17	21	−	−	1	−	30	1.7
O145:HNT:VT2	−	2	−	1	1	−	1	−	−	−	−	3	0.2
O145小計 subtotal	−	9	4	20	4	19	24	−	−	1	−	37	2.1
O91:H14:VT1	−	4	1	−	−	−	−	−	−	−	−	6	0.3
O91:H14:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O91:H21:VT2	−	3	−	2	−	1	2	−	−	−	−	5	0.3
O91:H-:VT1	−	4	−	−	−	−	−	−	−	−	−	4	0.2
O91:H-:VT1&VT2	−	1	−	1	−	−	1	−	−	−	−	2	0.1
O91:HUT:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O91:HNT:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O91:HNT:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O91小計 subtotal	−	18	1	3	−	1	3	−	−	−	−	23	1.3
O8:H9:VT2	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O8:H19:VT2	−	6	−	1	−	−	1	−	−	−	−	7	0.4
O8:H49:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O8:HNT:VT2	−	6	−	−	−	−	−	−	−	−	−	6	0.3
O8小計 subtotal	−	15	−	1	−	−	1	−	−	−	−	16	0.9
O115:H5:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O115:H10:VT1	−	5	1	1	−	−	1	−	−	−	−	7	0.4
O115:HNT:VT1	−	2	−	−	−	−	1	−	−	−	−	3	0.2
O115小計 subtotal	−	8	1	1	−	−	2	−	−	−	−	11	0.6
O4:H2:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O5:H-:VT1	−	−	−	1	−	−	1	−	−	−	−	1	0.1
O15:H18:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O15:H-:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O18:H7:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O18:H7:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O18:HUT:VT2	−	−	1	1	−	1	1	−	−	−	−	1	0.1
O23:H14:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O24:H18:VT1	−	−	1	1	−	−	−	−	−	−	−	1	0.1
O34:H32:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1

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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]		
O36:HUT:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O38:H21:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O40:H8:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O55:HUT:VT2	−	−	−	1	−	−	−	−	−	−	−	1	0.1
O59:H19:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O65:H19:VT1&VT2	−	−	−	1	−	1	−	−	−	−	−	1	0.1
O66:H25:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O69:H11:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O74:H20:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O76:H19:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O76:H19:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O77:H45:VT2	−	−	−	1	−	−	1	−	−	−	−	1	0.1
O81:HUT:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O84:H-:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O87:H16:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O88:H25:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O102:H8:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O113:H21:VT2	−	−	−	1	1	−	1	−	−	−	−	1	0.1
O116:H9:VT1	−	−	−	1	−	−	−	−	−	−	−	1	0.1
O118:H2:VT1	−	−	−	1	−	1	2	−	−	−	−	2	0.1
O119:HNT:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O128:H2:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O128:H2:VT1&VT2	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O128:H21:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O128:HNT:VT1	−	−	−	−	1	−	−	−	−	−	−	1	0.1
O128:HNT:VT2	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O130:H11:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O136:H16:VT1	−	−	−	1	1	−	−	−	−	−	−	1	0.1
O146:H10:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O146:H21:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O146:H-:VT2	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O150:H10:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O152:H8:VT1	−	−	−	1	−	−	−	−	−	−	−	1	0.1
O152:H8:VT1&VT2	−	−	−	1	1	−	1	−	−	−	−	1	0.1
O156:H25:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O165:H25:VT2	−	−	1	1	−	1	1	−	−	−	−	1	0.1
O165:H-:VT2	−	−	−	−	−	1	−	−	−	−	−	1	0.1
O165:H-:VT1&VT2	−	−	2	2	−	1	2	−	−	−	−	2	0.1
O166:H15:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O166:HNT:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O168:HNT:VT1	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O171:H-:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O174:H2:VT1	−	−	−	−	1	−	1	−	−	−	−	1	0.1
O174:H2:VT1&VT2	−	4	−	−	−	−	−	−	−	−	−	4	0.2
O174:H-:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O177:H25:VT2	−	−	1	1	−	1	1	−	−	−	−	1	0.1
O179:H8:VT1&VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O182:H25:VT1	−	2	−	−	−	−	−	−	−	−	−	2	0.1
O185:H7:VT2	−	1	−	−	−	−	−	−	−	−	−	1	0.1
O186:H2:VT2	−	2	−	5	−	3	3	−	−	−	−	8	0.4
Others	−	2	1	1	1	−	−	−	−	−	−	3	0.2
O untypable	−	70	2	26	−	4	8	−	−	1	−	107	6.0

UT: Untypable, NT: Not typed, *2つ以上の臨床症状が報告された例を含む **O抗原凝集抗体検出 **detection of antibodies against *Escherichia coli* O groups
*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 March 23, 2020)