

Epidemiological Studies of Coincidental Outbreaks of Enterohemorrhagic *Escherichia Coli* O157:H7 Infection and Infectious Gastroenteritis in Niimi City

Kenji TSUMAGARI^{a*}, Hideki YAMAMOTO^a, Narufumi SUGANUMA^b, Masahiko KATO^a, Satoru IKEDA^c, Kaori IMAI^d, Shohei KIRA^a and Kazuhisa TAKETA^a

^aDepartment of Public Health, Okayama University Medical School, Okayama 700-8558, Japan, ^bDepartment of Environmental Health, Fukui Medical School, Fukui 910-1193, Japan, ^cDepartment of Medical Technology, Faculty of Health Science, Okayama University Medical School, Okayama 700-8558, Japan and ^dDepartment of Nursing III, University of Occupational and Environmental Health, Kitakyushu 807-8555, Japan

A sharp rise in the number of patients with infectious gastroenteritis was observed in the 25th week of year 1996 in the Takahashi-Ashin district by researchers with the Infectious Disease Surveillance Program for tuberculosis and other infectious diseases in the Okayama Prefecture. This sharp rise occurred coincidentally with an outbreak of enterohemorrhagic *Escherichia coli* O157:H7 (EHEC O157) infection in Niimi City of the Takahashi-Ashin district. However, this phenomenon of coincidental outbreaks was not observed during the outbreak of EHEC O157 infection in Oku Cho. By reviewing outpatients' charts in a sentinel hospital in Niimi City for the Infectious Disease Surveillance Program, it was noted that patients with acute gastrointestinal infection visiting the hospital during the increased incidence of infectious gastroenteritis may have been included as misclassified cases of EHEC O157 infection. On the other hand, the exponential probability plotting of symptomatic patients with EHEC O157 infection in Niimi City revealed a breaking point which suggested a dual exposure to contaminated food or an overlap with other acute gastrointestinal infections. The latter possibility was discounted, because stool culture-positive patients with EHEC O157 infection also exhibited a similar breaking point, and furthermore, the coincidental increase in infectious gastroenteritis in the same area was attributable to the EHEC O157 infection. The present study demonstrates the association between the sharp rise in gastroenteritis and the out-

break of EHEC O157 in the Takahashi-Ashin district. A careful analysis of the cases of infectious gastroenteritis by the Infectious Disease Surveillance Program would have predicted the outbreak of EHEC O157.

Key words: enterohemorrhagic *Escherichia coli* O157 infection, infectious gastroenteritis, Niimi City, epidemiological studies, surveillance

Enterohemorrhagic *Escherichia coli* O157:H7 (EHEC O157) is a Shiga toxin-producing pathogen that causes a wide variety of clinical symptoms from asymptomatic disorders to hemorrhagic colitis, and nearly 10% of patients infected with this pathogen develop a life-threatening hemolytic uremic syndrome (HUS). Since the identification of EHEC O157 in 1982 as a human pathogen, several outbreaks of EHEC O157 infection have been reported, mostly in developed countries, including Japan (1-4).

In the Okayama prefecture, there were 2 outbreaks of EHEC O157 infection in 1996, one starting on May 24 in Oku Cho, a town located on the east side of Okayama City, and the other starting on June 11 in Niimi City, located 80.3 km northwest of Okayama City (5). Prior to the outbreak in Niimi City, there was another outbreak starting on June 7, 1996, in Toujo Cho, Hiroshima prefecture, a town located 20 km west of Niimi City (6). The Division of Environmental Health, Department of

* To whom correspondence should be addressed.

Health and Social Welfare, Okayama Prefecture (DEH-Okayama) organized a task force to control the infection and conducted epidemiological studies of the 2 outbreaks in the Okayama prefecture (5).

At the same time, the Division of Public Health Policy, Department of Health and Social Welfare, Okayama Prefecture (DPEP-Okayama), had undertaken a project of infectious disease surveillance by instituting surveillance of tuberculosis (Tb) and 24 other infectious diseases and had observed a sharp rise in the incidence of infectious gastroenteritis in the Takahashi-Ashin district, which included Niimi City, at nearly the same time as the outbreak of EHEC O157 infection in Niimi City. Such a rise in the incidence of infectious gastroenteritis was not observed in the Okayama-Toubi district, which included Oku Cho, at the time of the outbreak of EHEC O157 infection in Oku Cho (7).

DPHP-Okayama suggested that the temporal association between the 2 outbreaks of different infectious diseases was affected by a warning against the outbreak of EHEC O157 infection that had been broadcast through the mass media in Niimi City, resulting in the increased number of patients other than those with the EHEC O157 infection visiting the hospital. We reviewed outpatients' charts (medical records) at a hospital in the Niimi City, which was the sole sentinel hospital for Infection Surveillance in the Takahashi-Ashin district, in order to see if any patients suspected of and diagnosed with EHEC O157 infection had been reported as cases of infectious gastroenteritis. The incidence of infectious gastroenteritis obtained from the medical records was compared with that reported by the infectious disease surveillance or that of the EHEC O157 infection in Niimi City.

Incidentally, a difference in the frequency distribution of patients with EHEC O157 infection, as expressed in terms of days of onset after putative exposure, was observed between Oku Cho and Niimi City. This was also analyzed in relation to the increased incidence of infectious gastroenteritis in Niimi City.

Subjects and Methods

The numbers of symptomatic patients with EHEC O157 infection organized according to the date of onset of outbreaks in Oku Cho and Niimi City (5) were analyzed by the exponential probability plotting of Sartwell (8) in order to estimate the date of exposure, mode of exposure (single or multiple), and incubation period. Symptomatic

patients were defined as those who had been exposed to suspected contaminated meals and had either one or more of the following gastrointestinal symptoms: abdominal pain, diarrhea, bloody stool, nausea and vomiting (9). Results of stool culture for EHEC O157, carried out by the Oku Regional Health Center and the Ashin Health Center in collaboration with the Okayama Prefectural Institute for Environmental Science and Public Health, were also taken into account in order to identify asymptomatic carriers.

Surveillance curves of infectious gastroenteritis, expressed as the numbers of patients per sentinel hospital in relation to the week of onset, in the Takahashi-Ashin district, the Okayama-Toubi district and the whole Okayama prefecture, were used as references. These were reported by DPHP-Okayama via the infectious disease surveillance program, which was acting under the Ministry of Health and Welfare of Japan before April 1, 1999 (7). The criteria for infectious gastroenteritis defined by the infectious disease surveillance program were as follows: acute gastroenteritis caused by viral infection, excluding infantile vomiting and diarrhea, and by bacterial infection by the *Salmonella* group, including *Campylobacter jejuni*, *Yersinia enterocolitica*, pathogenic *Escherichia coli* (*E. coli*), *Vibrio parahaemolyticus*, etc.

In order to investigate the possibility that cases of EHEC O157 infection had been included in the group of infectious gastroenteritis cases reported by the sentinel hospital in Niimi City, we reviewed outpatients' medical records from the hospital. Since the names of the patients with infectious gastroenteritis had not been recorded, we checked the charts of all outpatients who had visited the outpatient clinic from week 18 (May 2) through week 35 (August 31) in 1996. Based on the medical records obtained from outpatients' charts, we found 213 patients who were diagnosed with either infectious gastroenteritis or acute gastrointestinal infection compatible with the criteria for infectious gastroenteritis. Since the diarrhea caused by *E. coli* (infection with pathogenic *E. coli*) had been believed to include that caused by EHEC O157 (10) until August 6, 1996, when legislation dictated that EHEC O157 was an infection to be legally reported through a regional health center, cases of stool culture positive for EHEC O157 with or without symptoms as well as those suspected of EHEC O157 infection were also selected. The following patients were classified into the infectious gastroenteritis group: 1) those with a

diagnosis of infectious gastroenteritis described on patients' charts, 2) those with diarrhea, abdominal pain, vomiting or other related symptoms after ruling out apparent EHEC O157 infection, 3) those with stools sent for culture for suspected bacterial gastroenteritis, 4) those treated with antibiotics for suspected gastroenteritis and 5) those, excluding healthy subjects, who visited the hospital for examination of EHEC O157 infection or for treatment with antibiotics for prophylaxis against EHEC O157 infection. The following patients were classified into the EHEC O157 infection group: 1) those with results of stool culture positive for EHEC O157 with or without symptoms and 2) severe cases of acute gastrointestinal infection with HUS or bloody stool and those treated before stools were tested for culture. The latter patients were dealt with separately as cases of infectious gastroenteritis (medical records) and EHEC O157 infection (medical records) from infectious gastroenteritis (reported), as reported by the Infectious Disease Surveillance Program.

The number of patients with infectious gastroenteritis reported by a sentinel hospital for the Okayama-Toubi district, where most of the patients in Oku Cho visited, was made available from April to September, 1996 by the DPHP-Okayama.

Statistical analysis was performed on a personal computer with EpiInfo Version 6 (CDC, Atlanta, GA, USA and WHO, Geneva, Switzerland).

Results

The total number of symptomatic patients reported during the outbreak of EHEC O157 in Oku Cho was 450, including 82 patients with positive stool cultures (18.2%). Graphic analysis of Sartwell (8) was performed on these patients by exponential probability plotting against logarithm days of onset after putative exposure to contaminated food in the outbreak that started on May 24, 1996 (Fig. 1). After some patients with secondary infections were included, straight line was drawn for all the symptomatic patients, with an apparent upward deviation on days 11 and 12 as reported by the Okayama Prefectural Government (9), and this suggested that a common single exposure to the pathogen had occurred. Stool culture-positive patients deviated upward slightly more from the line of total symptomatic patients. The day of exposure to the contaminated food was estimated to be May 23, 1996 from the chart in Fig. 1 with a mean incubation period of

5 days; this agreed with the exposure date of May 23, 1996 determined by epidemiological studies (5).

For the outbreak of EHEC O157 infection in Niimi City, exponential probability plotting of 360 symptomatic patients with EHEC O157 infection, including 137 patients with positive stool culture (38.1%), was more accurate when 2 lines were drawn with an apparent breaking point (Fig. 2). This was contrasted to the reported straight line (10), even though the patients with secondary infections of EHEC O157 were excluded from this population also. The exposure dates were calculated

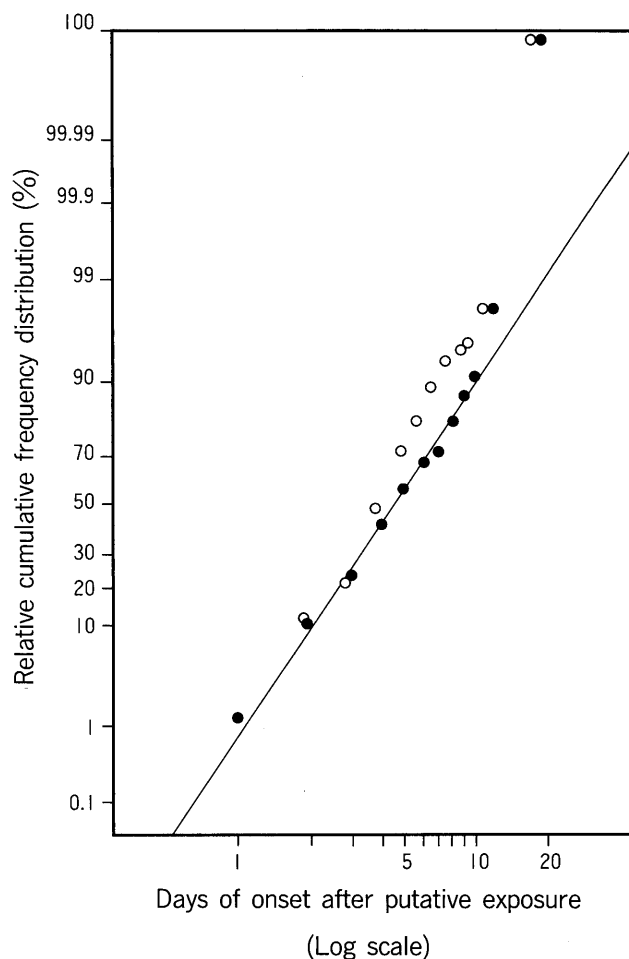


Fig. 1 Exponential probability plotting of symptomatic patients with EHEC O157 infections against log days of onset after putative exposure in the outbreak of EHEC O157 infection in Oku Cho. ●, total symptomatic patients; ○, symptomatic patients with stool cultures positive for EHEC O157. The best line was drawn visually for the total number of symptomatic patients.

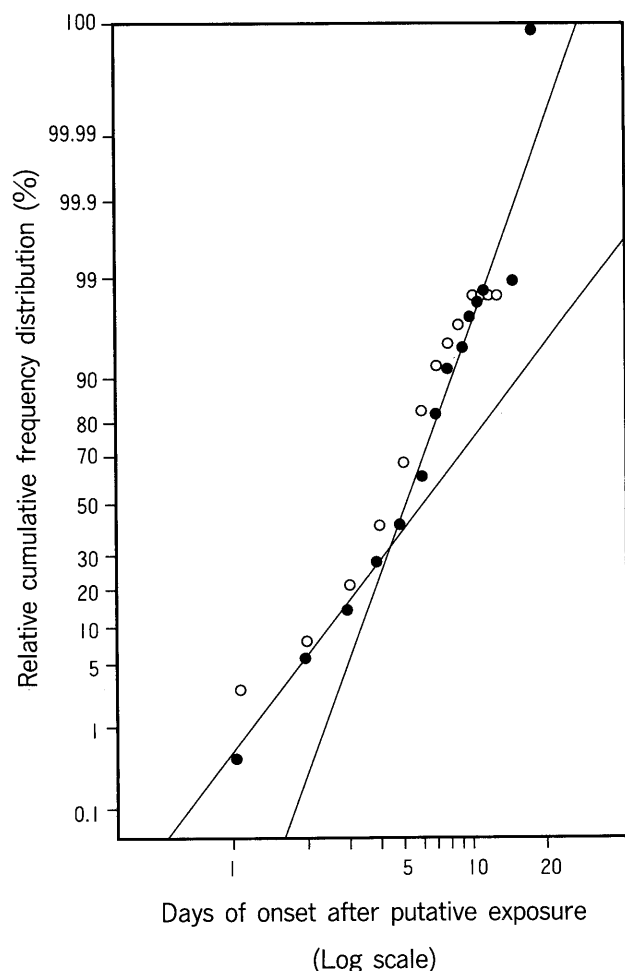


Fig. 2 Exponential probability plotting of symptomatic patients with EHEC O157 infections against log days of onset after putative exposure in the outbreak of EHEC O157 infection in Niimi City. ●, total symptomatic patients; ○, symptomatic patients with stool cultures positive for EHEC O157. Two best lines could be drawn visually for the total number of symptomatic patients.

from the 2 lines to be June 11 and 12 with a mean incubation period of 5 days. The earlier exposure date of June 11 agreed with the reported date. Plotting of the 137 stool culture-positive patients, with a stool culture-positive rate of 38.1%, showed a similar distribution and breaking point.

Surveillance curves for the incidence of infectious gastroenteritis per sentinel hospital in 1996 and 1995 drawn against the week of onset of the disease in the Takahashi-Ashin district, which includes Niimi City, the

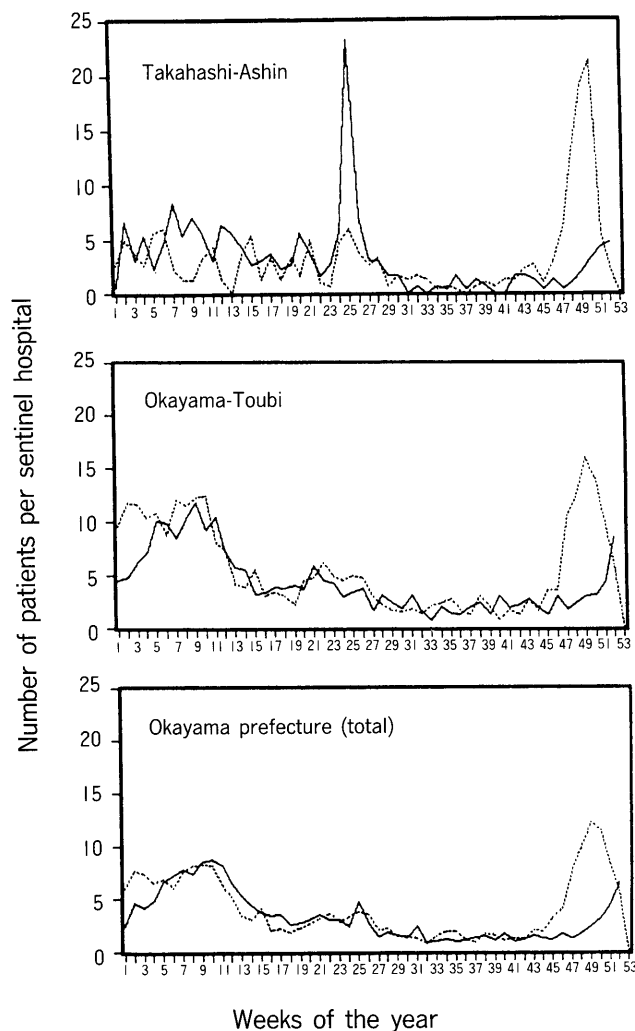


Fig. 3 Number of patients with infectious gastroenteritis per sentinel hospital for the infection surveillance system plotted against the week of onset of the disease in the Takahashi-Ashin district, the Okayama-Toubi district and the total in the Okayama prefecture. Modified from reference 9. ---, 1995; —, 1996.

Okayama-Toubi district, which includes Oku Cho, and the Okayama prefecture as a whole are shown in Fig. 3. These were partially reproduced from the results reported by the Infectious Disease Surveillance Program of Okayama Prefecture (7). There was a sharp rise in the incidence of infectious gastroenteritis in Niimi City during week 25 (June 16–25) corresponding to the week of outbreak of EHEC O157 infection. No such peak in incidence was observed in the surveillance curves for Okayama-Toubi or Okayama prefecture as a whole during

the outbreak of EHEC O157 in Oku Cho from week 21 (May 10–25) to week 22 (May 26–June 1). No such peak was observed in 1995 either in Niimi City or in other districts.

The numbers of patients with acute gastrointestinal infection according to the date of first visit to the sentinel hospital in Niimi City from week 19 through week 35 are shown in Fig. 4. The largest number of patients with infectious gastroenteritis (medical records) visited the hospital during week 25 (32 patients), which coincided with the reported peak in the same week 25. There was a tendency for infectious gastroenteritis (medical records) to increase from week 24 to week 27 as observed in the reported cases of infectious gastroenteritis in the Takahashi-Ashin district. It may be noted further that 32 patients with EHEC O157 infections (medical records) visited the hospital during week 25. They consisted of 15 symptomatic patients with positive stool culture, 14 suspected cases and 3 asymptomatic carriers. On the other hand, 43 patients, consisting of 12 symptomatic patients with positive stool culture, 1 suspected case and

30 asymptomatic carriers, also visited the hospital during week 26. A similar large number of patients with infectious gastroenteritis were observed for week 26 (14 patients). Thus, for weeks 25 and 26, there were 42 symptomatic patients with EHEC O157 infections, including 27 stool culture-positive cases, and there were 46 patients who were diagnosed with infectious gastroenteritis. Thus, the total number of patients with symptoms of acute gastrointestinal disease was 88 (42 plus 46). Most of the 33 asymptomatic carriers of EHEC O157 infection (medical records) for weeks 25 and 26 visited the hospital for eradication of EHEC O157 after being informed of the results of stool cultures performed by the Ashin Health Center.

The above results of EHEC O157 infection (medical records) were expressed on a daily basis and compared with the number of patients with EHEC O157 infections (reported) in Niimi City as reported by the Okayama prefecture (5) (Fig. 5). The first peak in the number of patients with EHEC O157 infections (medical records) was observed on June 17, 1996, one day after the first

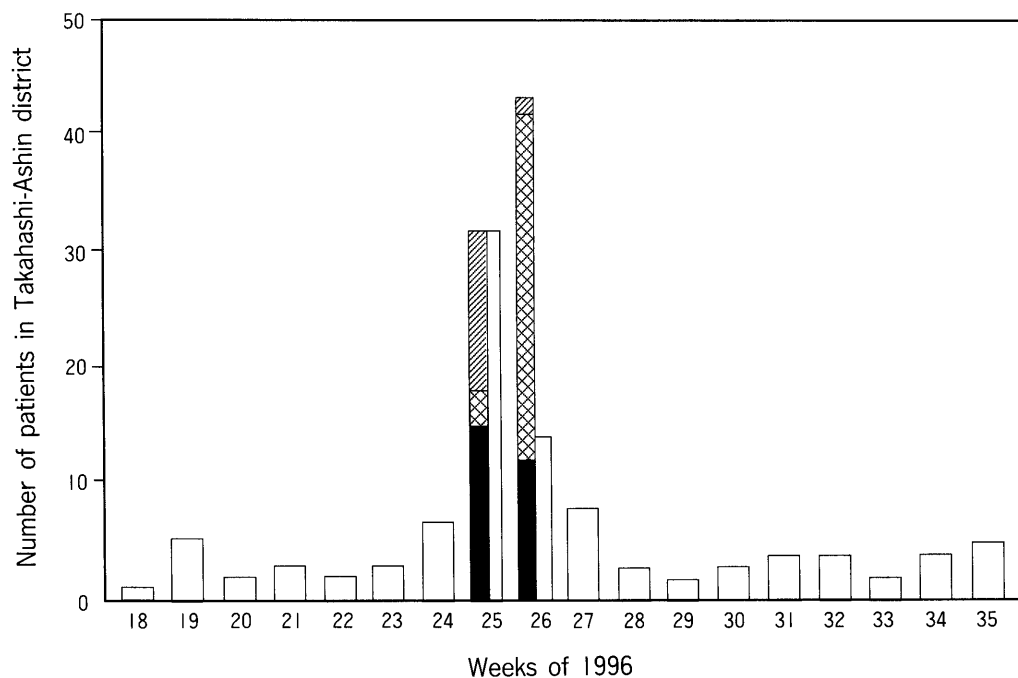


Fig. 4 Number of patients with infectious gastroenteritis and with EHEC O157 infections, including asymptomatic and suspected cases, who visited a hospital in Niimi City registered for the Surveillance System in the Takahashi-Ashin district during the period of week 18 (May 2) through week 35 (August 31), 1996. , infectious gastroenteritis; , EHEC O157 infection most likely; , asymptomatic patients with stool cultures positive for EHEC O157; and , symptomatic patients with stool cultures positive for EHEC O157.

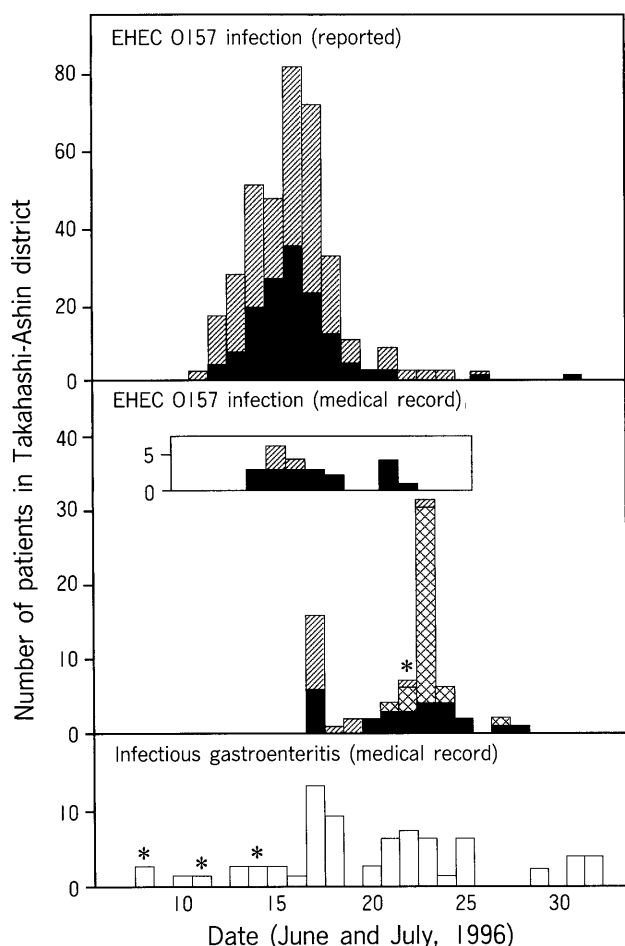


Fig. 5 Number of symptomatic patients with EHEC O157 infections (reported) with or without positive stool cultures in Niimi City (4) and number of patients with EHEC O157 infections (medical records) and of those with infectious gastroenteritis (medical records) in the sentinel hospital of the Takahashi-Ashin district given for the date of onset (top panel and inset) or the reported date (middle and bottom panels). For symbols, see the legend to Fig. 4. "*", residents of Toujo Cho.

announcement of the outbreak of EHEC O157 in Niimi City. Among the 29 patients with symptoms of acute gastrointestinal infection who visited the sentinel hospital on June 17, 1996, 16 patients (middle panel) were diagnosed as symptomatic EHEC O157 cases, including 10 cases with negative stool cultures and 6 with positive stool cultures, and the remaining 13 (bottom panel) were diagnosed as cases of infectious gastroenteritis. The second peak of patients with EHEC O157 infections occurred on June 23, 1996. Among the 38 patients with

acute gastrointestinal manifestations, 5 patients were diagnosed with EHEC O157 infections, including 4 stool culture-positive cases and 1 culture-negative cases, and the remaining 6 patients were diagnosed with infectious gastroenteritis. Thus, for the peak on June 23, 1996, 27 of the 32 patients with EHEC O157 infections were asymptomatic carriers, and they visited the hospital for eradication of the pathogen after being informed that the results of their stool cultures were positive for EHEC O157.

Among the symptomatic patients with EHEC O157 infections (medical records), the number of patients whose date of onset was known was plotted in the inset (middle panel) in Fig. 5. The distribution of the date of onset was similar to that of the reported EHEC O157 infection, although the number of patients was too small to enable comparisons to be made. Of the total number of 75 patients with EHEC O157 infections (medical records) shown in the middle panel of Fig. 5, 72 were primary and middle schoolchildren and only 3 were under the age of 6 years. Similarly, most of the 73 patients with infectious gastroenteritis (medical records) shown in the bottom panel of Fig. 5 were schoolchildren: 27 were below the age of 6 years and 2 above 19 years. As for the number of patients with infectious gastroenteritis (medical records), a peak of 13 patients was observed on June 17, 1996, when the first peak in the number of patients with EHEC O157 infections (medical records) was also observed. Of the 13 patients with infectious gastroenteritis, 12 of them were schoolchildren and 1 was under the age of 6 years. Incidentally, 1 patient with EHEC O157 infection (medical records) and 3 patients with infectious gastroenteritis (medical records) were residents of Toujo Cho, where an outbreak of O157 infection was observed from June 7 through June 30, 1996 (6).

The number of patients with infectious gastroenteritis reported by a sentinel hospital of Infection Surveillance in the Okayama-Toubi district, where most of the patients in Oku Cho visit, was 89 from April (week 14) through September (week 39), 1996, and had no peak during the period (week 21 and thereafter) of the outbreak of EHEC O157 infection in Oku Cho (Fig. 3). The physician in this hospital did not report the patients suspected of EHEC O157 as cases of infectious gastroenteritis and referred all of them to affiliated hospitals for further evaluation and treatment of the diseases (personal communication).

Discussion

The present study attempted to elucidate the apparent temporal association between the outbreak of EHEC O157 infection in Niimi City with an increased incidence of infectious gastroenteritis (reported) in the Takahashi-Ashin district, in which Niimi City is located. Among the patients with acute gastrointestinal infections who visited a sentinel hospital in the Takahashi-Ashin district, a significant number of patients were discovered to have an EHEC O157 infection on the basis of stool culture positive for EHEC O157. Moreover, some patients were more likely to have an EHEC O157 infection as judged by the presence of bloody stool and/or HUS. The latter cases (without stool culture) may not have been suspected of having an EHEC O157 infection unless there had been a simultaneous outbreak of EHEC O157 infection in the same area.

During week 25 of 1996, when the peak incidence of infectious gastroenteritis (medical records) was observed, there was also the largest number of patients with EHEC O157 infections (medical records) including suspected cases. Since we cannot discount the presence of symptomatic patients with EHEC O157 infections and negative stool cultures or without stool cultures in the group of patients with infectious gastroenteritis (medical records), we have to assume that the increased incidence of infectious gastroenteritis was associated with the outbreak of EHEC O157 infection. In fact, out of 88 patients with acute gastrointestinal infections (medical records) for weeks 25 and 26 (42 cases of EHEC O157 infection, excluding asymptomatic carriers, and 46 cases of infectious gastroenteritis), 27 (31%) were positive for EHEC O157. The high rate of stool cultures positive for EHEC O157 (31%) is comparable to that (38.1%) in the reported outbreak of EHEC O157 in Niimi City. The putative number of EHEC O157-infected patients among the population of 88 patients with acute gastrointestinal infection, which includes 46 patients who would otherwise be considered cases of infectious gastroenteritis as reported, was calculated based on the 27 of culture-positive patients and the reported culture-positive rate of 38.1% in the outbreak in Niimi City. This calculation yielded 71 possible EHEC O157-infected patients (82%) out of 88 patients with acute gastrointestinal infections. Theoretically, 29 cases (71 minus 42) of EHEC O157 infection turned out to be mis-diagnosed as infectious gastroenteritis. This calculation is reasonable because 12 of 13

patients with infectious gastroenteritis, for example on June 17, were schoolchildren and most of them would have been exposed to the contaminated food.

The number of patients with infectious gastroenteritis reported per sentinel hospital in the Takahashi-Ashin district was 23 (Fig. 3) for week 25 (7). This number was slightly less than but sufficiently close to the actual number of 32 patients with infectious gastroenteritis found during the same week to warrant the results of the present study, which was based on reviewing medical records.

A question arises, then, as to why no such coincidental increase in the incidence of infectious gastroenteritis in the Okayama-Toubi district occurred at the time of the outbreak of EHEC O157 infection in Oku Cho. The answer is clearly stated in the Results section of the paper. It depended on the clinical management of the responsible doctor in the sentinel hospital for the infectious disease surveillance program. The doctor of the sentinel hospital in the area covering Oku Cho referred all suspected cases of EHEC O157 infection to other facilitated hospitals without reporting them as cases of infectious gastroenteritis. On the other hand, the doctor of the sentinel hospital in Niimi City reported the cases of infectious gastroenteritis according to the criteria of the infectious disease surveillance system unless patients showed positive results of stool culture for EHEC O157 or HUS.

One of the factors causing this ambiguity was the existence of 2 different reporting systems for gastroenteritis including food poisoning. In the year 1996, DPHP-Okayama was responsible for an infectious disease surveillance program that did not include food poisonings, while DEH-Okayama dealt solely with food poisonings. These 2 divisions of the Bureau of Health and Welfare of the Okayama Prefecture Government were working independently. This bureaucratic problem resulted in the incompatible observations of the 2 outbreaks in Niimi City which were considered unrelated infections. The infectious disease surveillance program failed to detect the outbreaks. Our study has pointed out the problems in the existing surveillance system for infectious diseases.

Although the matter was not solely dependent on the interpretation of EHEC O157, the definition of the disease to be surveyed was important. EHEC O157 had been classified under *E. coli* diarrhea (10) before August 6, 1996, whether or not doctors considered EHEC O157 infection separately or as a part of *E. coli* diarrhea or a pathogenic *E. coli* infection in a broad sense. After August 6, 1996, however, EHEC O157 was categorized

separately as a verotoxin-producing *E. coli* to be legally reported. Under the new Infectious Diseases Control Law, which was enacted in April 1999, the EHEC O157 infection was classified as a category III infection, requiring its surveillance and restrictions on patients working in certain occupations to prevent the spreading of the infection (12), thus avoiding ambiguities involved in reports on the patients.

Another interesting observation of this study was the presence of breaking points in the lines of the analysis of cumulative frequency distribution of symptomatic patients plotted against log days of onset by the method of Sartwell (7). The existence of this breaking point had been reported by Kakuwa *et al.* as well as that suggested multiple exposure to the pathogens (13). There may be several possible explanations for this: 1) inappropriate estimation of the date of onset, resulting in cases missed in early stages of the outbreak, 2) intervention to prevent infected cases from developing, such as the use of antibiotics for a prophylactic purpose, 3) overlapping with other similar infections, *e.g.* infectious gastroenteritis, and 4) dual exposure to contaminated food.

Although the original questionnaires of schoolchildren filled out by staff members of the health center in the Takahashi-Ashin district were not available to estimate the date of onset were not available, the patient with the earliest reported EHEC O157 infection with a possible exposure date of June 11, 1996 was not likely to be a case of EHEC O157 infection as the symptoms of this patient could be attributed to other infections. The positive result of a stool culture which was carried out later may be better explained as the result of a secondary infection, as mentioned in the published report (5). Elimination of the doubtful first case would somewhat straighten the line in the exponential probability plotting. Antibiotics were given to asymptomatic carriers on June 18 or later after EHEC O157 was detected by stool culture among schoolchildren (9) and may not have contributed to changing the distribution. The overlap with other gastrointestinal infections may be ruled out, because the outbreak of infectious gastroenteritis (reported) observed simultaneously in the same city could be regarded as having included undiagnosed cases of EHEC O157 infection. Furthermore, the exponential probability plotting of stool culture-positive cases yielded a similar result with a breaking point.

The remaining possibility lies in dual exposure to or secondary infection with EHEC O157. An outbreak of

EHEC O157 via secondary infection among the staff members of the nursing home had been reported when they were not isolated from the patients. However, a large outbreak of EHEC O157 infection is not likely to be due to secondary infection, as for example, that observed among citizens of Sakai City which was apparently unrelated to school lunch (15). The patients with delayed onset in Niimi City were also mostly schoolchildren exposed to a contaminated school lunch, including the patients that visited the sentinel hospital. In the outbreak of EHEC O157 infection in Niimi City (11), students in 7 primary schools and 2 junior high schools were supplied with lunch solely by the Niimi City School Lunch-Supplying Center. No EHEC O157 was detected either in meals prepared from June 10 through June 14 or in the preserved original materials. However, 4 of the cooks who had eaten school lunches were positive for EHEC O157 according to stool cultures taken on June 16, 1996 or later (11). As they were asymptomatic carriers, they could have worked at the lunch supply center until it was semi-closed on June 17, 1996. The exposure date was estimated to be June 11 as a result of analysis of the master table (5). Thus, it is feasible that dual or multiple exposures occurred via the cooks positive for EHEC O157 before the center was closed, even though the exact dates when their stools became positive are not known. This explanation is supported by the fact that EHEC O157 is sometimes detected in cooked foods but not in uncooked materials as well as by the long-term resistance of this organism to dryness (16). Cooks could have been temporary carriers of EHEC O157, even though their monthly check for EHEC O157 was negative at the time of examination. Therefore, they may have transmitted EHEC O157 while they were working without using gloves.

There was a chronological overlap of outbreaks of EHEC O157 infection in Toujo Cho and Niimi City. Four patients of Toujo Cho visited the sentinel clinic in Niimi City, and one of them was found to be positive for EHEC O157. Therefore, it is reasonable to consider that direct transmission of EHEC O157 occurred from Toujo Cho to Niimi City. However, plasmid profile L4 and pulsed-field gel electrophoretic pattern Ia of EHEC O157 isolates in Toujo Cho were different from those in Niimi City, which were L3 and Ib, respectively (5, 17-19).

In conclusion, patients with EHEC O157 infections visited the registered hospital for a sentinel surveillance program in Niimi City, and this suggests that the in-

creased incidence of infectious gastroenteritis reported by the sentinel hospital during the same period as the outbreak of EHEC O157 in Niimi City was due to the fact that patients with undiagnosed EHEC O157 infection may have been diagnosed with infectious gastroenteritis. The pathogens of gastroenteritis are not routinely investigated because it is not cost-effective unless the patients are strongly suspected of having dysentery, salmonellosis, *E. Coli* O157 infection or other serious forms of infectious gastroenteritis. A large number of the asymptomatic or mild cases of diarrhea due to an *E. Coli* O157 infection would be diagnosed as cases of infectious gastritis by clinical diagnosis. Sporadic cases of EHEC O157 have been reported all over Japan since 1996. This study suggests that the infectious disease surveillance program for gastroenteritis is important and that it may be possible to predict an outbreak of EHEC O157 through the proper utilization of epidemiological information gathered by the infectious disease surveillance program.

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References

1. Reilly A: Prevention and control of enterohaemorrhagic *Escherichia coli* (EHEC) infections: Memorandum from a WHO meeting. WHO Consultation on Prevention and Control of Enterohaemorrhagic *Escherichia coli* (EHEC) Infections. Bull World Health Organ (1998) **76**, 245-255.
2. Takeda Y: Enterohaemorrhagic *Escherichia coli* and its infection: From 1977 to 1995. Nippon Rinsho (1997) **55**, 635-640 (in Japanese).
3. Mead PS and Griffin PM: *Escherichia coli* O157: H7. Lancet (1998) **352**, 1207-1212.
4. Michino H, Araki K, Minami S, Takaya S, Sakai N, Miyazaki M, Ono A and Yanagawa H: Massive Outbreak of *Escherichia coli* O157: H7 Infection in Schoolchildren in Sakai City, Japan, Associated with Consumption of White Radish Sprouts, Am J Epidemiol (1999) **150**, 787-796.
5. Okayama Prefectural Government: I. Outline of outbreaks in Oku Cho and Niimi City and overall control measure; in Report (March 1997), Outbreaks of Food Intoxication Caused by Enterohemorrhagic *Escherichia coli* (O157: H7) in Oku Cho, Oku Gun and Niimi City, Okayama Prefectural Government, Okayama (1997) pp2-36 (in Japanese).
6. Committee for Control of the Outbreak of Pathogenic (Enterohemorrhagic) *Escherichia coli* Infection in Hiroshima Prefecture: I. Outbreak of Pathogenic (Enterohemorrhagic) *Escherichia coli* O-157 infection in Tojo Primary School; in Measure to Control Pathogenic (Enterohemorrhagic) *Escherichia coli* O-157 Infection (Hiroshima Prefectural Government). Department of Social Welfare and Health, Hiroshima Prefectural Government, Hiroshima (1996) pp1-154 (in Japanese).
7. Division of Public Health Policy, Department of Health and Social Welfare, Okayama Prefectural Government: Infectious gastroenteritis; in Surveillance System of Tuberculosis and Other Infectious Diseases. Vol. 15, Okayama Prefectural Government, Okayama (1996) pp16-17 (in Japanese).
8. Sartwell PE: The distribution of incubation periods of infectious disease. Am J Hygiene (1950) **51**, 310-318.
9. Okayama Prefectural Government: II. Oku Cho; in Report (March 1997), Outbreaks of Food Intoxication Caused by Enterohemorrhagic *Escherichia coli* (O157: H7) in Oku Cho, Oku Gun and Niimi City, Okayama Prefectural Government, Okayama (1997) pp75-157 (in Japanese).
10. Abe M and 43 authors: *Escherichia coli* diarrhea (Food poisoning); in Densenbyou-yobou-hikkei, Shigematsu I and 6 eds, 4th Ed, 1st Suppl, Japan Public Health Association, Tokyo (1995) pp188-191 (in Japanese).
11. Okayama Prefectural Government: II. Niimi City; in Report (March 1997), Outbreaks of Food Intoxication Caused by Enterohemorrhagic *Escherichia coli* (O157: H7) in Oku Cho, Oku Gun and Niimi City, Okayama Prefectural Government, Okayama (1997) pp173-243 (in Japanese).
12. National Institute of Infectious Diseases and Infectious Diseases Control Division, Ministry of Health and Welfare: Target diseases of the New Infectious Diseases Control Law. Infectious Agents Surveillance Report (1999) **20**, 90 (in Japanese).
13. Kakuwa K, Ogata M, Kondo Y, Koike D and Mandai M: Incubation Periods of Infectious Disease II -The Outbreak of Food Poisoning by Enterohemorrhagic *Escherichia coli* O157- in Niimi City, Kawasaki Iryo Fukushi Gakkai-shi (1997) **7**, 199-203 (in Japanese).
14. Carter AO, Borczyk AA, Carlson JA, Harvey B, Hockin JC, Karmali MA, Krishnan C, Korn DA and Lior H: A Severe outbreak of *Escherichia coli* O157: H7-associated hemorrhagic colitis in a nursing home. N Engl J Med (1987) **317**, 1496-1500.
15. Epidemiology Research Group and Clinical Medicine Research Group: IV Report of Clinical Medicine Research group and Epidemiology Research Group; in Report on the Outbreak of *E. coli* O157 Infection in Sakai City (Outline of Mass Outbreak of Food-Borne Infection with Enterohemorrhagic *Escherichia coli* O157), Task Force on the Mass Outbreak of Diarrhea in School Children of Sakai City. Sakai City office (1997) pp14-101 (in Japanese).
16. Iijima Y, Matsumoto M, Higuchi K, Furuta T and Honda T: Resistance to dryness of *Escherichia coli* O157: H7 strains from outbreak in Sakai City, Japan, 1996. Emerg Infect Dis (1998) **4**, 340-341.
17. Izumiya H, Terajima J, Wada A, Inagaki Y, Itoh KI, Tamura K and Watanabe H: Molecular typing of Enterohemorrhagic *Escherichia coli* O157: H7 isolates in Japan by using pulsed-field gel electrophoresis. J Clin Microbiol (1997) **35**, 1675-1680.
18. Izumiya H, Masuda T, Ahmed R, Khakhria R, Wada A, Terajima J, Itoh K, Johnson WM, Konuma H, Shinagawa K, Tamura K and Watanabe H: Combined use of bacteriophage typing and pulsed-field gel electrophoresis in the epidemiological analysis of Japanese isolates of enterohemorrhagic *Escherichia coli* O157: H7. Microbiol Immunol (1998) **42**, 515-519.
19. Funamori Y, Fujinaga Y, Yokota K, Inoue K, Hirai Y, Oguma K, Kira S and Taketa K: Molecular typing of enterohemorrhagic *Escherichia coli* O157: H7 isolated in Okayama prefecture using pulsed field gel electrophoresis and random amplification of polymorphic DNA. Acta Med Okayama (1999) **53**, 193-200.

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