What is Learned from Cryptosporidiosis Outbreak Cases in Japan

日本のクリプトスポリジウム集団感染事例から学んだこと

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Whilst previous models used to explain the causal event(s) to induce large-scale outbreak of cryptosporidiosis have studied the affects of turbidity increase either in drinking-water or in source water on the spread of the disease to consumers, a new model used in the current study tests the affects of other variables such as an increased temperature and thus inducing changes in quantities of unboiled water consumed by individuals.

All the data used in the present manuscript are those already reported elsewhere by other workers, some were in Japanese and others were in English.

1. Case report

There have been three outbreaks of large-scale cryptosporidiosis in Japan[1-2].

1.1. Hiratsuka Case:

The first recognized cryptosporidiosis outbreak was in August and September 1994. As of September 3, Kanagawa Prefectural Health Department received information that 22 customers who visited either of 10 public houses in a building at Hiratsuka City, which is located in Kanagawa prefecture complained of cholera-like or flu-like symptoms. Epidemiological surveys by questionnaires revealed that 461 out of 736 individuals who visited one of the public houses/restaurants became ill with the clinical manifestations including mucous and/or watery diarrhea (96.7%), abdominal cramps (61.6%), fever (54.2%: lower than 39℃ = 84.1%, higher than 39℃ = 15.9%), malaise (37.1%), nausea (32.8%) and headache (29.3%). Five were hospitalized. Interviews with the patients showed no evidence of food items served in the public houses that might significantly be associated with risk for developing illness. Oocysts of *C. parvum* were identified in12 (48.0%) out of 25 stool specimens. Cryptosporidial oocysts were also demonstrated in tap water and other water samples from a receiving tank, an elevated tank, a domestic sewage pit, a sanitary sewage pit and an artesian well water tank. Tanks and pits were constructed adjacent to each other on a basement floor of the building and there were cross connections between tanks and pits at the upper part of the tanks to reduce inner pressure in the receiving tank. Accidental malfunction of the drainage system, according to the owner of the building, caused contamination of drinking water with sanitary sewage through the cross connection.

1.2. Ogose case:

The second case of the waterborne outbreak of cryptosporidiosis was detected when there was a sudden increase in absentees among school children due to severe diarrhea and abdominal cramps during early June to the middle of July, 1996, in Ogose, which is located in Saitama prefecture, approximately 50 km northwest from Tokyo. Routine stool, food or beverage cultures failed to yield a pathogen. Stools subsequently were sent to laboratories at Saitama Provincial Institute of Health, where *C. parvum* was isolated one week after the onset of a large-scale outbreak. It took another one week to identify the oocysts from the city's tap water.

Of the total population of 13,809, 12,345 (89%) were interviewed. Of those, 8,812 (71.4%) had illnesses with watery diarrhea and abdominal cramps; 24 were admitted to hospital. None of the patients developed bloody stool. Average length of illness was 4.1 days. Illnesses had subsided by the beginning of July.

Around 75% of the city's total water supply came from a mixture of surface waters (including river-bed water) from the Oppe River, its tributary and from a ground water (deep well), and was treated with prechlorination, coagulation and sedimentation, followed by rapid filtration. Approximately 0.4 km upstream from water intake, there is an effluent opening for the treated domestic and sanitary sewage (Fig. 1). According to the business log there, there was little rainfall during the middle of May to June, 1996 resulting in severe drought. Approximately one week before the onset of outbreak (on May 25), unusually high turbidity 92 Unit (1U≒0.65NTU) was recorded in sedimentation tank water.

1.3. Awaji case

The third case was reported in February, 2002. As of March 3, Hyougo Prefectural Health Department received information that 31 high school students and the teaching staff who went to Hokkaido on a school excursion complained of severe diarrhea. Epidemiological surveys by questionnaires revealed that 129 out of 212 individuals became ill with the clinical manifestations including watery diarrhea (96.7%) and other symptoms.

2. Persons with brief exposure

Study participants met the following criteria: (1) They were nonresidents of the cities (or buildings) where outbreaks occurred; (2) they had visited only once there during outbreaks; and (3) they had either laboratory-confirmed cryptosporidiosis or watery diarrhea (clinical cryptosporidiosis). For each of the following cases, three reconstructed the incubation distribution curves in lines are presented in Fig. 2.

2.1. Hiratsuka case

As the outbreak of diarrhea has occurred among customers who visited either of 10 public houses in a building at Hiratsuka City, 299 the patients met the above criteria. The mean incubation period was 6.0 days (95% C.I. 5.9-6.2 days). The solid line in Fig. 2 corresponds to a log-logistic distribution with median 5.5 days and 95% quantile: 7.6 days.

2.2. Ogose case

During the outbreak period, 16 individuals, 7 primary school boys and 9 adult visitors, had stayed less than 24 hours and reported having consumed tap water or beverages containing unboiled tap water while in the Ogose Water Work service area. The mean incubation period was 6.4 days (95% C.I. 6.0-6.8 days). The dotted line in Fig. 2 corresponds to a log-logistic distribution with median 5.8 days and 95% quantile: 7.0 days.

2.3. Awaji case

Altogether 126 individuals with severe diarrhea who went to Hokkaido on a school excursion met the study participant criteria. The mean incubation period was 6.4 days (95% C.I. 6.2-6.6 days). The broken line in Fig. 2 corresponds to a log-logistic distribution with median 5.9 days and 95% quantile: 7.6 days.

3. Water consumption

Recent questionnaire survey (n=859) on daily intake of unboiled tap water showed that approximately 50% of the people did not use unboiled tap water or bottled water at all for drinking, and the average quantity of water consumed by individuals was 209 ml (Fig. 3) (3). From our preliminary estimation, the daily intake of unboiled tap water consumed automatically through dietary process, tooth brushing and others is something around 20 ml or less.

According to a marketing survey done by one of the biggest beer companies, people change their drinking items properly as temperature increases; at 23-25°C and below they enjoy drinking coffee, tea or other liquid items just for their tastes; over 25°C they stop drinking hot drinks; at 28-30°C and beyond they consume plain water to quench their thirst (personal communication). In summary, there is a threshold temperature, at 25 C, beyond which people start to have plain water and other cold liquid items to relieve their thirst.

4. Causal event(s) leading up to the large-scale outbreak of cryptosporidiosis in Ogose

4.1. Trends by date of onset over time

In the current study, reported date of onset of illness identified by a questionnaire from May 1 through July 15, 1996 (Fig. 4) was reexamined. The figure shows that the counted number of diarrhea events among survey participants peaked periodically every 5 days, starting from May 10 through June 20 (Fig 4, dotted line). This might represent available approximation of the date of onset of those who had vague recollection of the date of onset of the disease. To smooth a data series and to identify changes in trends, the predicted number of cases with a 5-day moving average is depicted in the same figure (solid line).

4.2. Correlation between turbidity and illness

Like other cryptosporidiosis outbreak cases, the Ogose outbreak was preceded by a sharp increase in the turbidity of source water to 92 KTU (1 KTU = 1.7NTU) for a short period (Fig. 5). This was believed to have affected the treatment plant and resulted in the high load of cryptosporidial oocysts in the tap water to a level high enough to cause a large-scale outbreak of cryptosporidiosis. However, there was no evidence that supports this presumption of cause and effect. With a single exposure, even if it were high doses of the oocysts in drinking water due to elevated turbidity, onset of illness would have ceased within a few days after initial onset of the event (Fig. 2), while the outbreak continued for a month from June 1 to July 4, 1996. Time series of both daily maximum and average turbidities of the source water before and during the outbreak and daily counts of illness are shown in Figs. 6a-f. No correlation was observed between daily counts of onset of cryptosporidiosis and turbidity at given lag periods from 7 to 9days; based on a distribution of incubation periods in the population of 6 days (median incubation period) + days required for water treatment and distribution.

4.3. Correlation between temperature and illness

Alternatively, the current analysis suggests that there may also have been a small increase in transmission of gastroenteritis cases in 2-3 weeks before the large outbreak, regardless of elevation of turbidity (Fig. 5).

Since it was a time of seasonal transition from spring to summer when the Ogose outbreak occurred, we drew attention to the correlation between temperature and illness. It is assumable that people drinks more water as temperature increased, which may, in turn, result in the increase in the risk of infection if water were polluted to a certain extent by cryptosporidial oocysts. The daily maximum temperature before May 21 was below 22 °C, then gradually increased to 25 °C in successive 3 days. From May 24, it exceeded 25°C, and reached to 28 °C on May 26, the 6 day before the first peak of date of onset (93 diarrhea cases) (Fig. 7).

Figure 8 shows the relation between the gastroenteritis events and the daily maximum temperature with a lag of 6 days during pre-outbreak period. The daily counts of illness increase markedly when daily maximum temperature exceeded at 25 C, the threshold temperature as was reported trend of water drinking habit. Provided that people there started to drink a cup of unboiled tap water (200 ml) to relieve their thirst as the daily maximum temperature exceeded the threshold temperature, and that there was low level of contamination of *Cryptosporidium* oocysts in drinking water as seen in Fig. 5, the risk of infection due to *Cryptosporidium* increased 10 times, resulting in approximately 100 gastroenteritis cases in a day.

The daily estimated number of oocysts in tap water was calculated base on the umber of reported cases in each day using 20 ml (below 25°C) and 200ml (25°C and beyond) for the amount of water consumed in accordance with the water drinking habit, and were plotted with a lag of 6 days on the Fig. 9. The number of oocysts remained to be around 0.5 oocysts/L in tap water during pre-outbreak and the initial stage of large outbreak from early May to May 29. Then the number of oocysts increased to the order of 10^0 oocysts/L on May 31, in consequence of sewage recharge system to put water back into the river (Fig. 1), leading up to the large-scale waterborne outbreak of cryptosporidiosis in Ogose. In other words, 0.5 oocysts/L is enough to induce 100 diarrhea cases (cryptosporidiosis) when 14,000 residents in Ogose drink a cap of unboiled tap water.

Although there are a number of data estimates being used in the present study as substitutes for data that do not currently exist, it is sensible to note that there was clear association between amount of drinking water consumed and cryptosporidiosis in

Ogose case.

5. References

1 Yamamoto N, Urabe K, Takaoka M, Nakazawa K, Gotoh A, Haga M, Fuchigami H, Kimata I, Iseki M. Outbreak of cryptosporidiosis after contamination of the public water supply in Saitama Prefecture, Japan, in 1996. Kansenshogaku Zasshi. 2000 Jun;74(6):518-26.

2 Kuroki T, Watanabe Y, Asai Y, Yamai S, Endo T, Uni S, Kimata I, Iseki M. [An outbreak of waterborne Cryptosporidiosis in Kanagawa, Japan] Kansenshogaku Zasshi. 1996 Feb;70(2):132-40. (In Japanese)

3 Yano K, Hosaka M, Otaki M, Tanaka A, Iyo T, Tosa K, Ichikawa H. Daily usage of tap water and bottled water for drinking in Japan. (2000) Japan Society on Water Environment. (In Japanese)

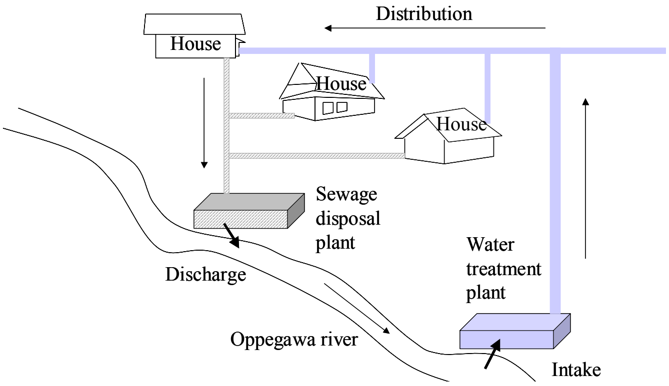

Fig. 1. Diagrammatic representation of sites of water and sewage treatment processes in Ogose.

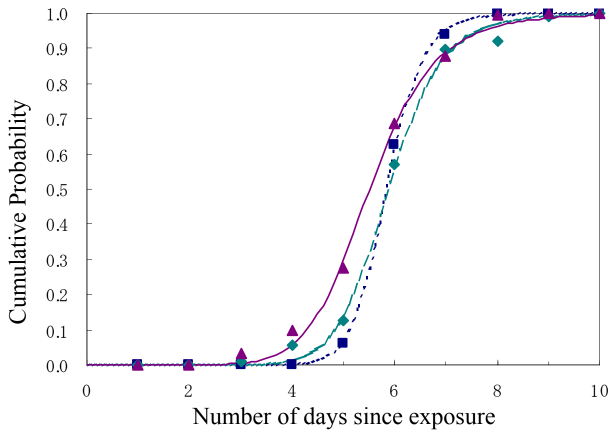

Fig. 2. Maximum likelihood fit of incubation distributions of persons with brief exposure among 3 outbreak cases.

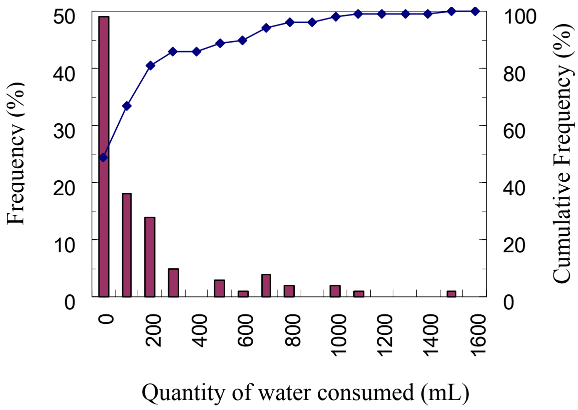

Fig. 3. Frequency of average daily intake of unboiled water and its cumulative frequency. (Redrawn from Yano et al. 2000)

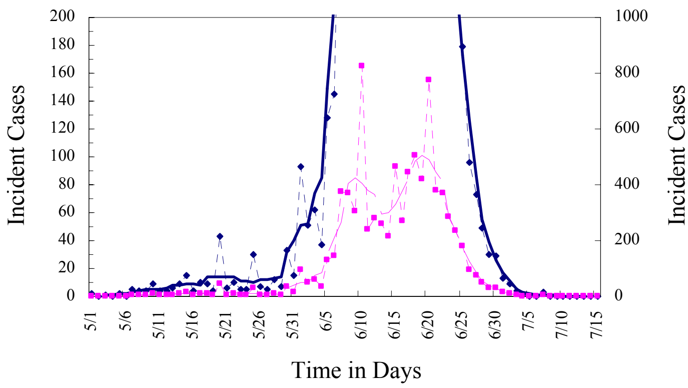

Fig. 4. A five days moving average view of onset of illness and observed number of cases in Ogose.

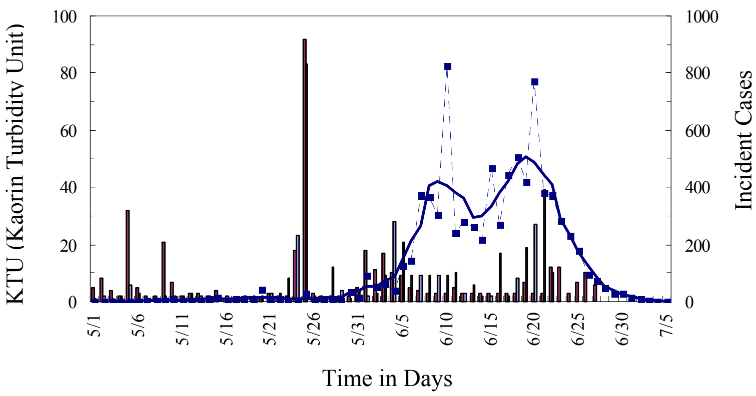

Fig. 5. Time series of daily counts of illness and daily maximum turbidity in source water of the Ogose water treatment plant.

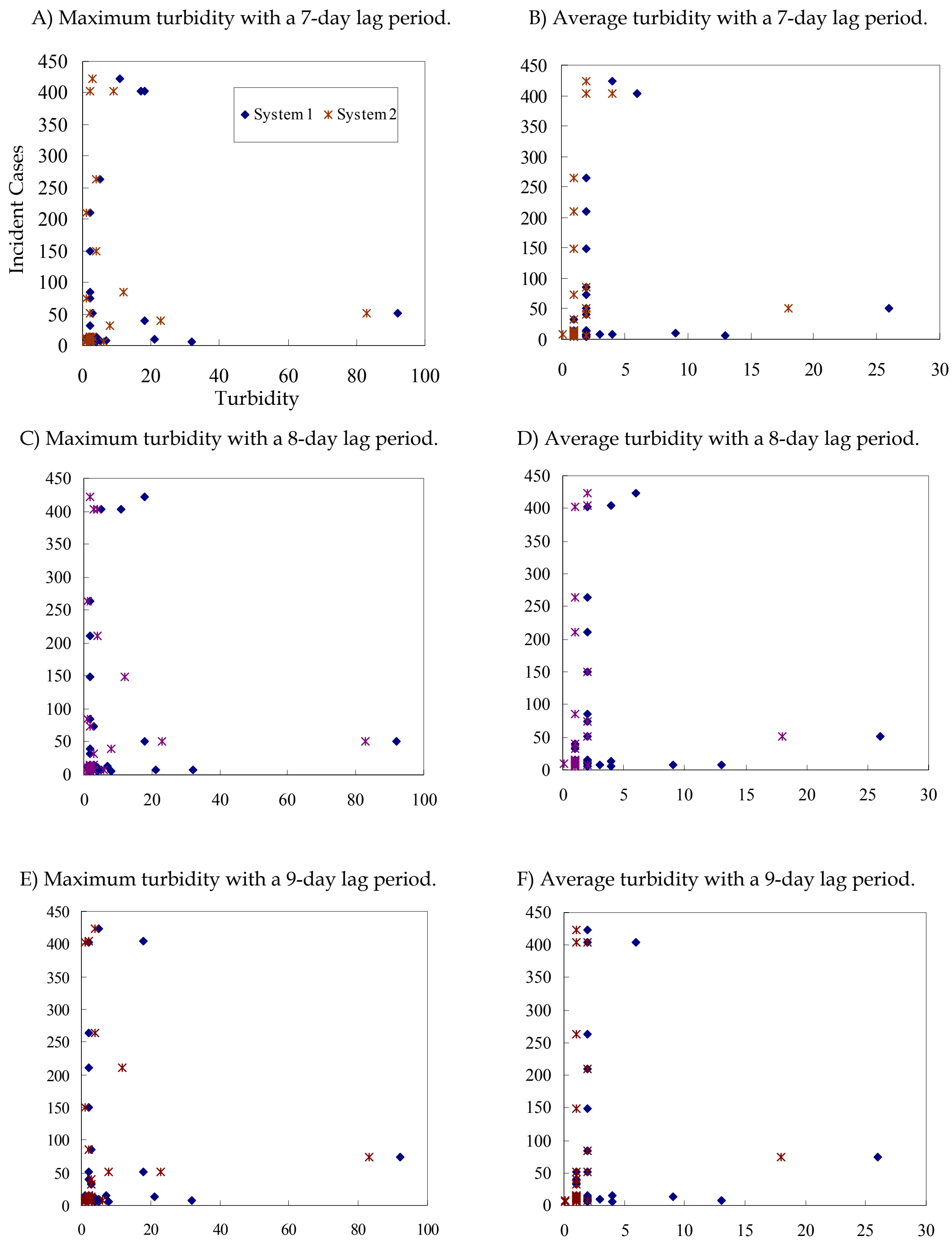

Fig. 6. Correlations between both daily maximum and average turbidities of source water and illness at lag periods of 7 - 9 days during pre-outbreak period.

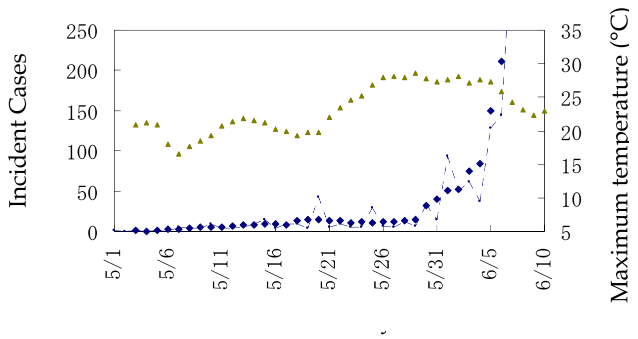

Fig. 7. Time series of daily counts of illness and daily maximum temperature.

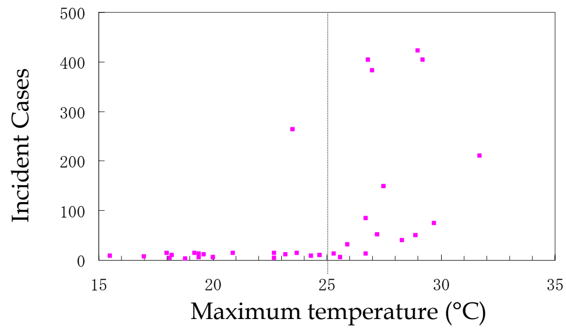

Fig. 8. Relation between daily counts of illness and maximum temperature at a lag period of 6 days during pre-outbreak period.

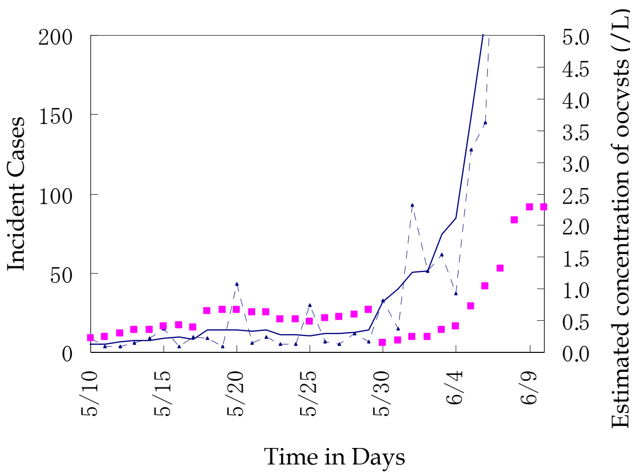

Fig. 9. Daily counts of illness and estimated number of oocysts in tap water at a lag period of 6 days during pre-outbreak period.

What is Learned from Cryptosporidiosis Outbreak Cases in Japan ?

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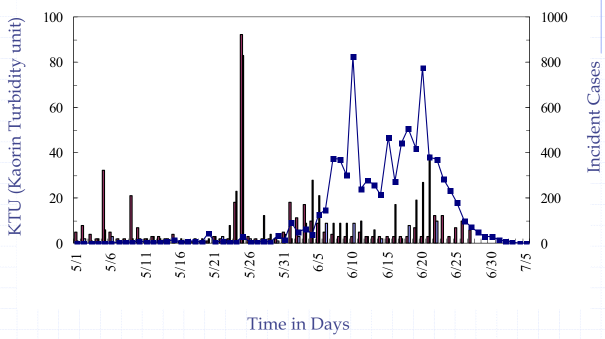
We had three large-scale outbreak of cryptosporidiosis cases in Japan

- ◆1994 Hiratsuka 461 cases
- ◆1996 Ogose 8,812 cases
- ◆2002 Awaji 129 cases

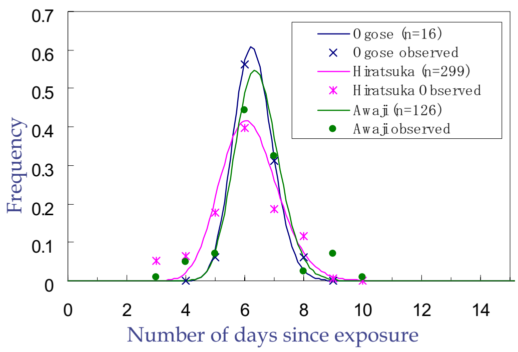
Time series of daily counts of gastroenteritis events and daily maximum turbidity in source water



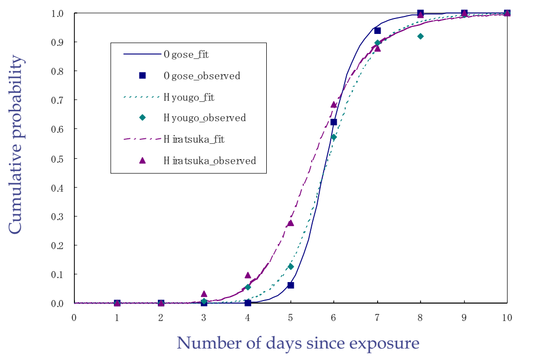
We had three large-scale outbreak of cryptosporidiosis cases in Japan

- ◆1994 Hiratsuka 461 cases
  299 brief exposure cases
- ◆1996 Ogose 8,812 cases
  16 brief exposure cases
- ◆2002 Awaji 129 cases
  126 brief exposure cases

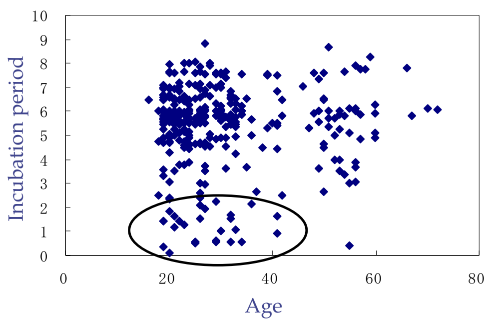
Incubation distribution of persons with a brief exposure



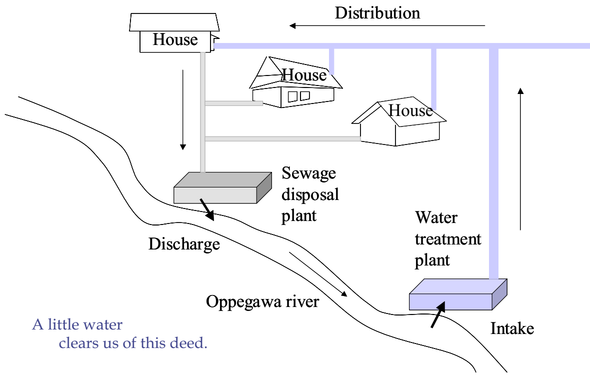
Maximum likelihood fit of incubation distributions of persons with brief exposure



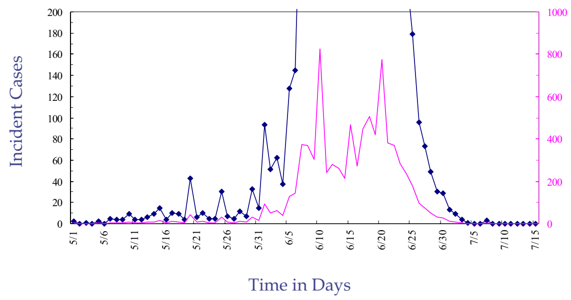
A scatterplot of incubation period against age



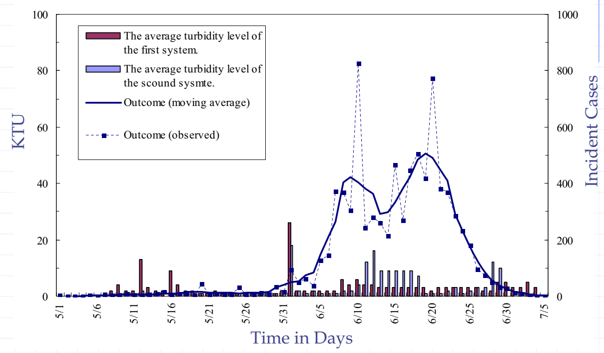
Diagrammatic representation of sites of water and sewage treatment processes in Ogose.



Reported date of the onset of gastroenteritis in 8,812 cases of infection identified by a questionnaire survey of the Ogose area



Time series of daily counts of illness and daily average turbidity in source water of the Ogose water treatment plant at a lag of 7 days



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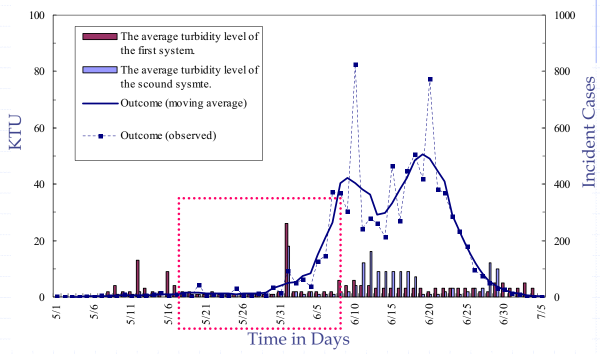
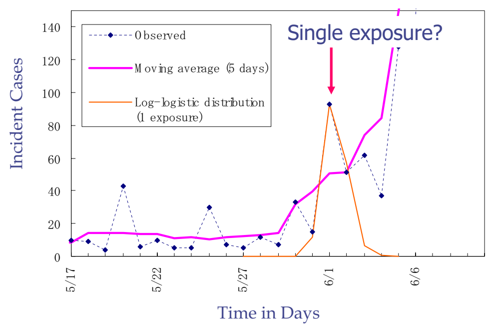
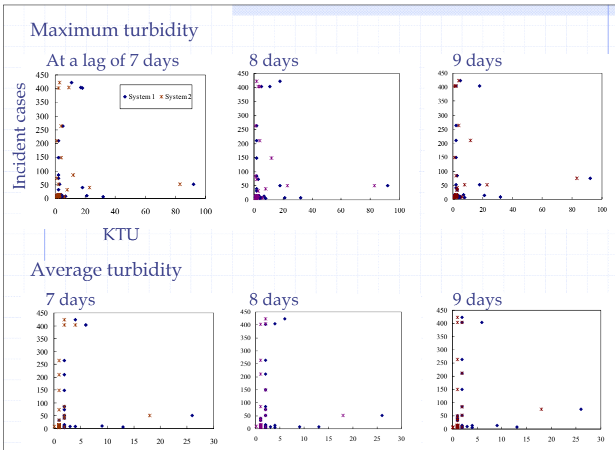


Time series of daily counts of illness



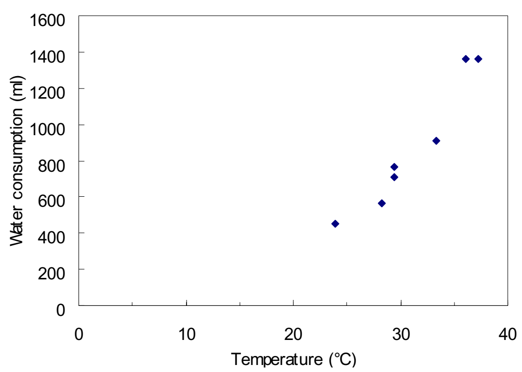


According to a marketing survey done by a beer company, people change their drinking items as temperature increases (personal communication)

- at 23-25 °C and below: they enjoy drinking coffee, tea or other liquid items just for their tastes
- over 25 °C: they stop drinking hot drinks
- at 28-30 °C and beyond: they consume plain water to quench their thirst.

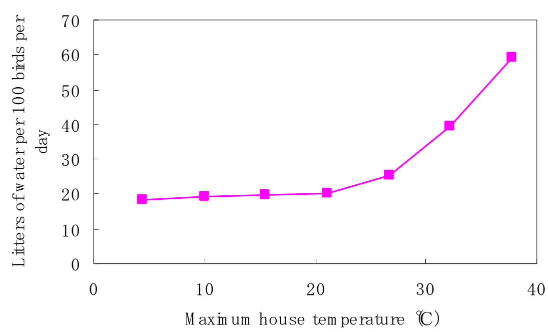
Effect of temperature on water intake in human beings

(From Applied Linear Statistical Model, 2nd Ed. Neter, et. Al. 1985.)

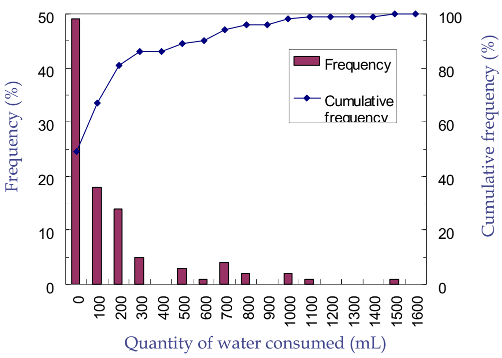


Effect of temperature on water intake in white leghorns

(Redrawn from North MO, 1976 Poultry Digest 35:499-502)

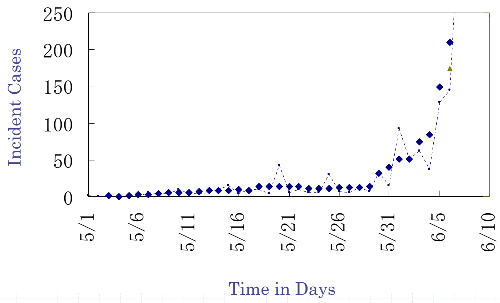


Frequency of average daily intake of unboiled water and its cumulative frequency.
(Redrawn from Yano et al. 2000)



- There is a threshold temperature: at 25 C = 77 F
- Beyond which temperature people start to have plain water.
- Average quantity of tap water used for drinking is about 200 ml a day
- Minimum daily intake of unboiled tap water is ~20 ml through dietary processes

Time series of daily counts of illness and daily maximum temperature



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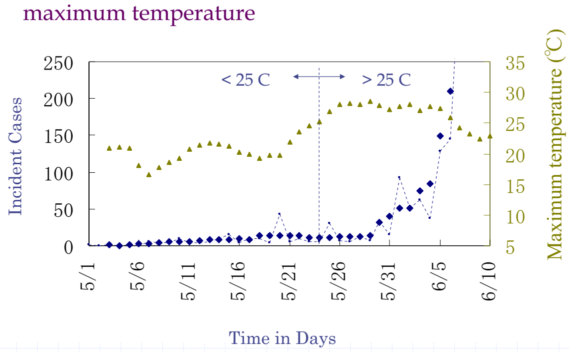
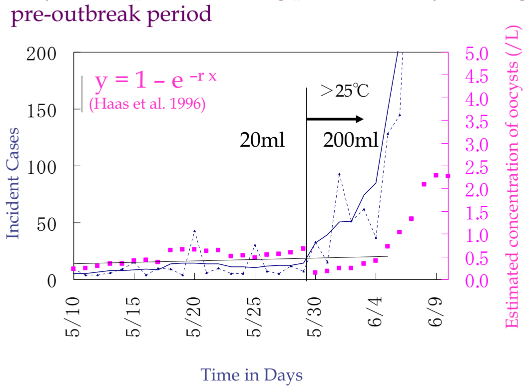
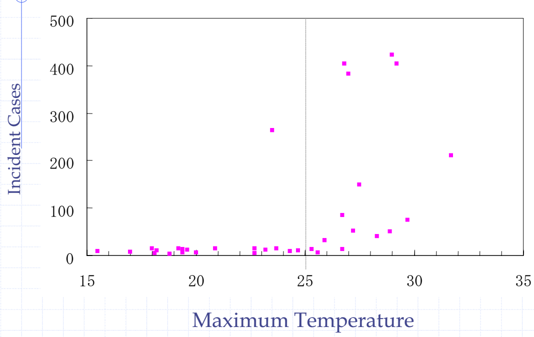
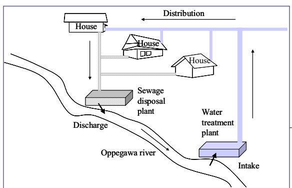


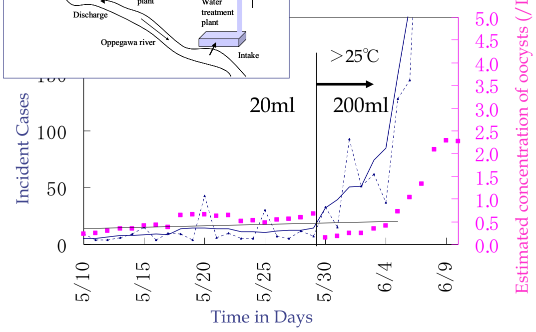
Daily counts of illness and estimated number of oocysts in tap water at a lag period of 6 days during pre-outbreak period



Relation between daily counts of gastroenteritis events and maximum temperature at a lag period of 6 days during pre-outbreak period.







Summary

- Whilst previous models used to explain the causal event(s) to induce large-scale outbreak of cryptosporidiosis have studied the affects of turbidity increase either in drinking-water or in source water on the spread of the disease to consumers, the new model used in the current study tests the affects of other variables such as temperature and thus inducing changes in quantities of water consumed by individuals.

Summary

- Although there are a number of data estimates used in the present study as substitutes for data that do not currently exist, it is sensible to note that there was clear association between temperature shift (amount of drinking water consumed) and cryptosporidiosis in Ogose in 1996.
  - 0.5 oocysts/L is enough to initiate a large-scale outbreak when 14,000 residents in Ogose drank a cup of unboiled tap water at 25 C and beyond.