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AN OUTBREAK OF APPENDICITIS IN ONEIDA COUNTY

Objectives:

Following this exercise, the student should be able to:

1. List data sources other than the notifiable disease reporting system.
2. Use descriptive epidemiology to describe an outbreak.
3. Discuss advantages and disadvantages of different study designs.
4. Select and calculate appropriate measures of association and tests of significance.

Part I

On September 27, 1976, a 14-year-old male student at Holland Patent Middle School in Oneida County, New York became ill with mid-abdominal pain and fever. One day later he was admitted to a local hospital with right lower quadrant abdominal pain and fever of 104° F. Because other symptoms, signs, and tests also were consistent with acute appendicitis, he underwent an emergency appendectomy. The pathology report noted thickening and inflammation of a 4 cm strip of the distal ileum, but the appendix was normal. The boy was treated with a 3-day postoperative course of vibramycin, and was discharged on the 7th post-op day. About two weeks later, on October 18, he was readmitted for a wound infection. Cultures taken from the infected site grew Yersinia enterocolitica.

The hospital reported this case to the New York State Health Department. Shortly thereafter, the Holland Patent School District nurse reported an increase in absenteeism due to "appendicitis."

Further investigation identified 12 children in Oneida County who, in late September, had undergone appendectomies for suspected appendicitis not confirmed by pathological examination. Yersinia enterocolitica was isolated from the stools of 3 of the children and from a postoperative wound infection site of a 4th child.

The situation was discussed with officials at the New York State Health Department and the Centers for Disease Control (CDC). Subsequently, 2 CDC epidemiologists departed for Oneida County.

BACKGROUND

Oneida County, located in the center of New York State, had a population of 273,037 in 1970. Most of the people live in rural areas, and dairy farming is a major industry.

The Holland Patent School District is located in east-central Oneida County and includes 5 schools. The high school, middle school, and one elementary school are located in Holland Patent Village; the two other elementary schools are located in the villages of Barnveld and Stitville.

The quality of Oneida County's water supply had been questioned for several years. In late August 1976, prior to the cluster of appendectomies, the Commissioner of Health in Oneida County declared that the Holland Patent Village water was inadequately treated and should be boiled before consumption. Many Holland Patent residents ignored the warning and continued to use unboiled village water. Other residents used well water or spring water. All three Holland Patent schools relied on village water, as did the high school kitchen, which prepared lunches for all 5 district schools.

QUESTION 1: Appendicitis is not a reportable disease. How might you determine whether this cluster represents an epidemic?

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Part II

Review of Appendectomies at Five Area Hospitals

In an attempt to document the existence of an epidemic, the investigating team reviewed records of patients who had undergone appendectomies at the 5 major hospitals serving Oneida County. Specifically, the investigators reviewed the charts of all persons 18 years of age or younger who had had an appendectomy during the period September 1974 through November 1976. In addition, they reviewed the operating room logs for September, October, and November, 1976 at each hospital. They obtained information from each hospital chart on the patient's age, sex, place of residence, date of operation, pre- and postoperative diagnosis, operative finding, and pathologic diagnosis.

Patients were classified by pathologic diagnosis into one of three categories: appendicitis, normal appendix, or lymphoid hyperplasia of the appendix. Those who had had an appendectomy as part of another operation were excluded from the tabulation. Patients were also classified by school district residence.

The number of appendectomies performed at the 5 area hospitals by month of operation is provided in Table 1. Figure 1 gives cases by date of onset.

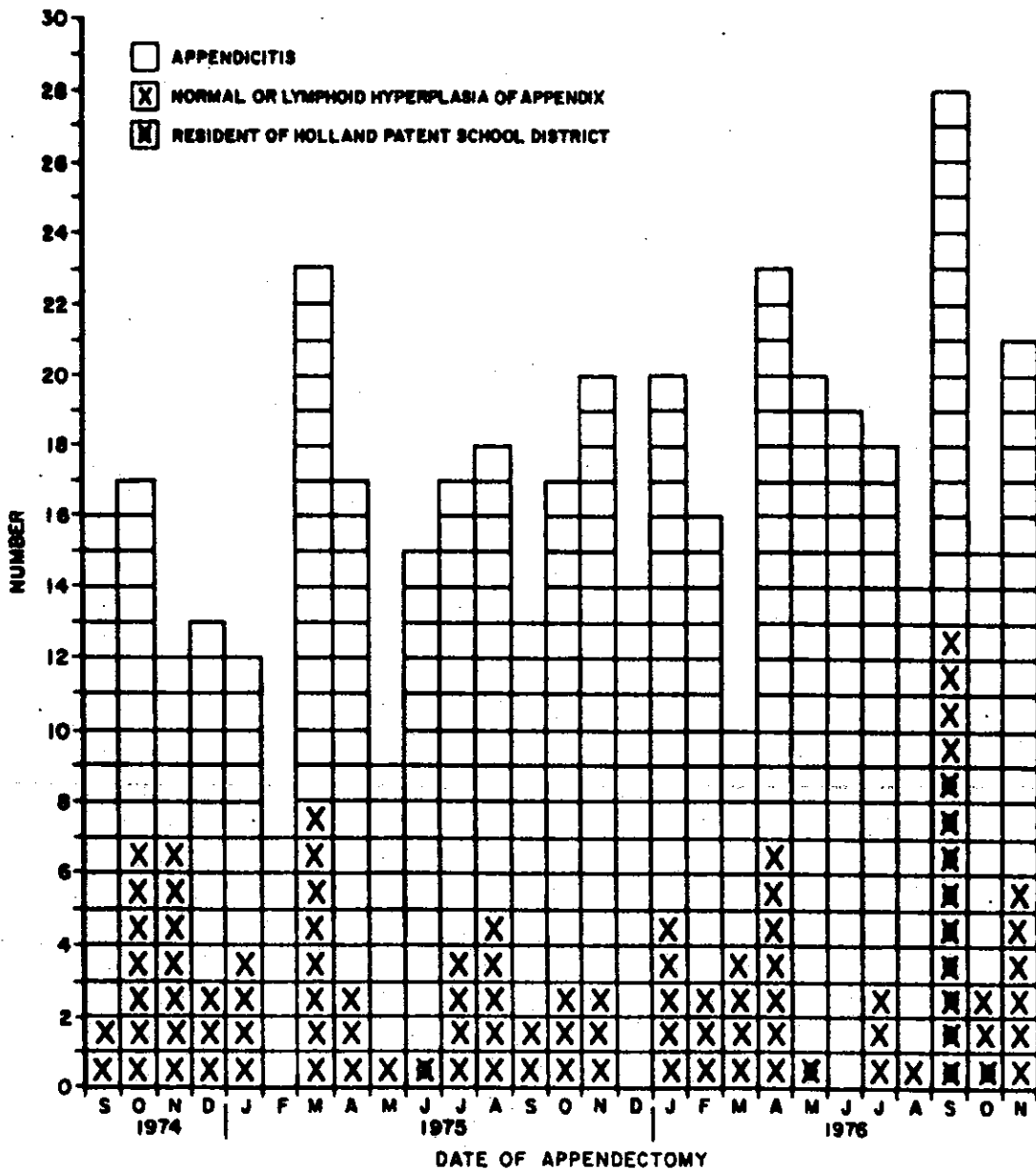
QUESTION 2. Interpret the data presented in Table 1 and Figure 1.

Table 1
 Number of Appendectomies Performed On Persons 18 Years or Younger
 at Five Hospitals, By Month and Pathologic Diagnosis,
 Oneida County, NY, September 1974 - November 1976

Year and Month	Confirmed Appendicitis	Normal or Lymphoid Hyperplasia		Total # of Appendectomies	Percent with Normal or Lymphoid Hyperplasia
		Nonresident*	Resident		
<u>1974</u>					
Sept.	14	2	0	16	12.5%
Oct.	10	7	0	17	41.2%
Nov.	5	7	0	12	58.3%
Dec.	10	3	0	13	23.1%
<u>1975</u>					
Jan.	8	4	0	12	33.3%
Feb.	7	0	0	7	0.0%
Mar.	15	8	0	23	34.8%
Apr.	14	3	0	17	17.6%
May	8	1	0	9	11.1%
June	14	0	1	15	6.7%
July	13	4	0	17	23.5%
Aug.	13	5	0	18	27.8%
Sep.	11	2	0	13	15.4%
Oct.	14	3	0	17	17.6%
Nov.	17	3	0	20	10.0%
Dec.	14	0	0	14	0.0%
<u>1976</u>					
Jan.	15	5	0	20	25.0%
Feb.	13	3	0	16	18.8%
Mar.	6	4	0	10	40.0%
Apr.	16	7	0	23	30.4%
May	19	0	1	20	5.0%
June	19	0	0	19	0.0%
July	15	3	0	18	16.7%
Aug.	13	1	0	14	7.1%
SUBTOTAL	303	75	2	380	20.3%
Sep.	15	4	9	28	46.4%
Oct.	12	2	1	15	20.0%
Nov.	15	6	0	21	28.6%
SUBTOTAL	42	12	10	64	34.4%
TOTAL	345	87	12	444	22.3%

* Persons who do not reside in the Holland Patent School District

Figure 1
 Appendectomies at 5 Oneida County Hospitals,
 September 1974 - November 1976



* IN PERSONS 18 YEARS OR YOUNGER

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Part III

Summary of Appendectomies at Five Area Hospitals

During the "base-line" 24-month period between September 1974 and August 1976, 77 (20%) of 380 persons who underwent appendectomies had a normal appendix or lymphoid hyperplasia (mean 3.2 per month). Among Holland Patent residents, only 2 underwent appendectomies for non-inflamed appendices.

During September 1976, 28 appendectomies were performed, the greatest number of appendectomies in any month during the review period. Of the 28, 13 (46%) were categorized as normal appendix or lymphoid hyperplasia, the second highest monthly percentage of non-inflamed appendices. Nine Holland Patent residents underwent appendectomies for non-inflamed appendices.

In October and November 1976 the number of appendectomies and the proportion without appendicitis were close to base-line values.

Review of Hospitalized Cases from Holland Patent School District

Because the data indicated an excess of normal surgically removed appendices in the Holland Patent School District residents during September 1976, the investigators attempted to identify additional cases by conducting a second review of hospital records which focused on children from that district who were hospitalized between September 1 and November 30. They broadened the case definition to include children with the discharge diagnoses of appendicitis, mesenteric adenitis, or regional enteritis instead of only children who had undergone appendectomies. They identified thirty-three cases, and found that of the children who had had appendectomies, pathologic diagnoses were without exception stated as normal or lymphoid hyperplasia of the appendix.

Of the 33 children who met the case definition, 23 (70%) had onsets of illness occurring the 6-day interval from September 23 through September 28 (see Figure 2). Twenty-three (70%) were males. The mean and median ages were 11.2 years and 13.0 years, respectively. Cases were seen in students from all five district schools, with hospitalization rates ranging from 3.1 to 19.8 per 1000 students per school. The overall hospitalization rate for the district was 12.4 per 1,000 students. Of the 27 with dates of onset during September, 13 underwent appendectomies; none of the 6 with dates of onset in October underwent surgery. Signs and symptoms did not differ between those children who underwent surgery and those who did not.

The distribution of clinical manifestations of illness among the 33 children is shown in Table 2.

QUESTION 3. What other information on time, place, and person would you like to have in order to describe this outbreak more fully?

Table 2
 Frequency of Signs and Symptoms Among Children Hospitalized for
 Appendicitis, Mesenteric Adenitis, and Regional Enteritis,
 Oneida County, NY, September - November, 1976

<u>Sign/Symptom</u>	<u>Number</u> (n = 33)	<u>Percent of Total</u>
Fever	32	97.0%
Abdominal pain	32	97.0%
Fever and abdominal pain	31	93.9%
Diarrhea	10	30.3%
Skin rash	7	21.2%
Back pain	4	12.1%
Joint pain	3	9.1%

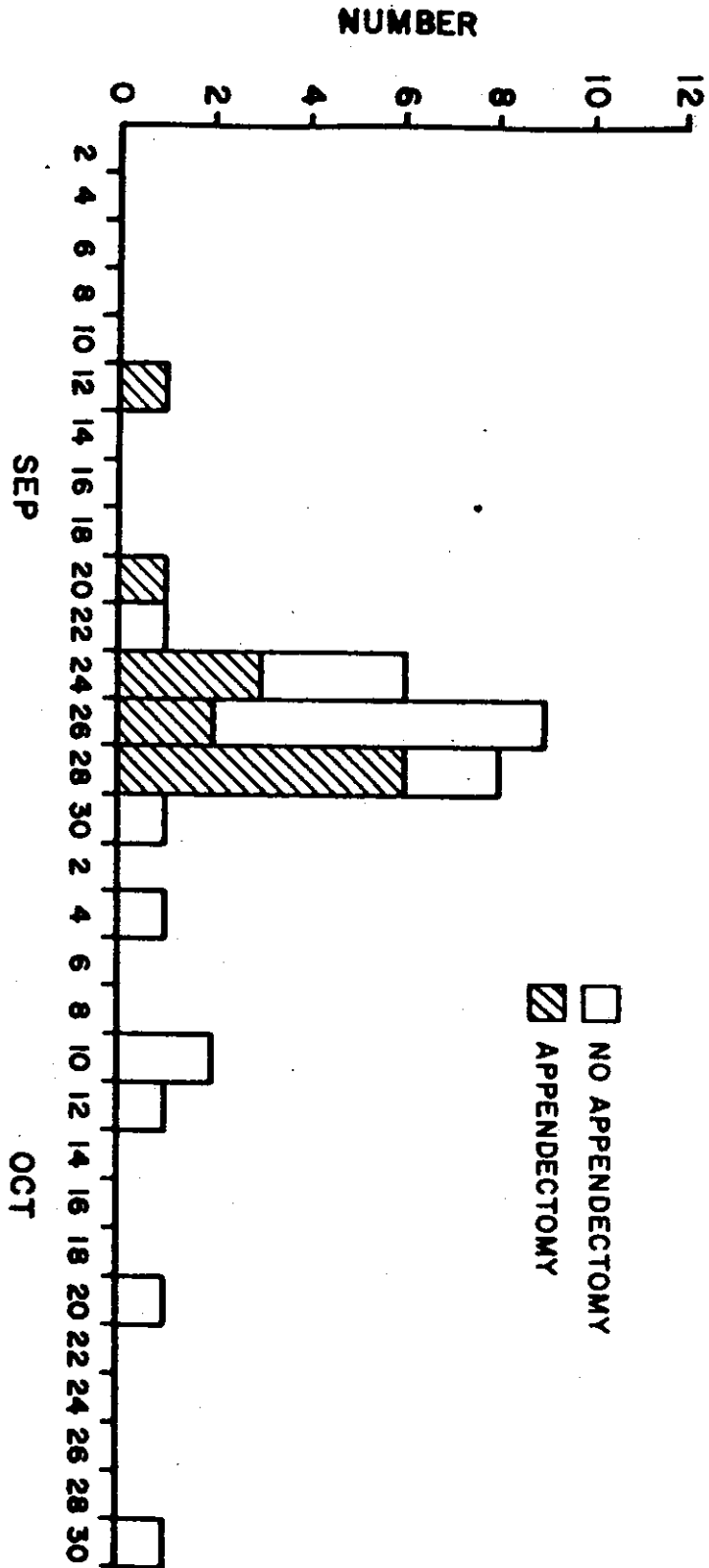
The working hypothesis at this point is that an outbreak of gastrointestinal infections caused by Yersinia enterocolitica has occurred. (The positive cultures in the four index cases, the rarity of Y. enterocolitica in normal bowel flora, and the knowledge that it may produce an appendicitis-like illness implicate it as the probable pathogen in this outbreak.) In view of the previous history of a contaminated water supply in Holland Patent Village, the water is a highly suspect vehicle.

Because all 4 documented index cases were among children attending the Holland Patent schools, the possibility of an association between consumption of food or water at the schools and acquiring Y. enterocolitica should also be considered.

The investigators decided to conduct an epidemiologic study.

QUESTION 4. What type of epidemiologic study would you conduct?

Figure 2
 Children from 5 Schools Hospitalized With Abdominal Pain and Fever,
 By Date of Onset, September - October 1976



CHILDREN FROM 5 SCHOOLS HOSPITALIZED WITH ABDOMINAL PAIN AND
 FEVER, BY DATE OF ONSET, SEPTEMBER - OCTOBER 1976

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Part IV

Survey of Residents in Holland Patent Village

The Holland Patent Village water supply was initially suspected as a possible vehicle in the outbreak because of the well publicized inadequacies in its treatment. The investigators decided to conduct a survey of Holland Patent Village residents to identify additional non-hospitalized cases, to determine if illness was related to exposure to village versus well or spring water, and to determine if the outbreak involved village residents of all ages or only school-age children.

On October 21 and 22, field investigators attempted to visit every household. For each household resident, they obtained information on illness and exposure to various water sources, schools, and school lunches. When an adult respondent was not available at a household, the investigator revisited the home after working hours. Based on census population, the estimated questionnaire completion rate was 61%. Results are given in Table 3.

QUESTION 5. Using the data in Table 3, for those instances in which measures of association and statistical tests of significance might be applied, determine and calculate appropriate measures of association and statistical tests.

QUESTION 6. What epidemiologic conclusions would you draw from your results?

QUESTION 7. What are the limitations of the above survey design and its results?

Table 3
 Frequency of Selected Characteristics Among Survey Respondents,
 Holland Patent Village, 1976

<u>Characteristic</u>	<u># Ill*</u>	<u># Well</u>	<u>Total</u>	<u>% Ill</u>
TOTAL NUMBER	27	315	342	7.9%
Age				
≤ 5 yrs. of age	1	23	24	4.2%
6-18 yrs. of age	14	67	81	17.3%
≥ 19 yrs. of age	12	225	237	5.1%
Attended or worked in a school**	16	82	98	16.3%
Did not attend or work in a school**	11	213	224	4.9%
Ate in school cafeteria**	15	52	67	22.4%
Did not eat in school cafeteria**	1	26	27	3.7%
Used Holland Patent spring/well water	9	29	38	23.7%
Used Holland Patent village water	18	262	280	6.4%

* Abdominal pain and fever

** School contact = any district school, for Holland Patent residents

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Part V

Summary of Findings of Survey of Residents in Holland Patent Village

Onsets of illness characterized by fever and abdominal pain occurred among school children 6 through 18 years of age in Holland Patent Village from September 11 through October 10, 1976. Cases occurred among other residents of Holland Patent during September and October, but the attack rates were significantly lower than among school children.

Attack rates among residents of Holland Patent were found to be associated with attendance at or work in one of the district schools. Among residents with such school contact, attack rates were also associated with eating in the school cafeterias. A statistically significant difference in attack rates was observed between residents drinking well or spring water as compared with residents drinking village water. Among the 38 residents using well or spring water, 9 cases occurred. Of these 9 cases, 6 were in school children. The village water supply could not be implicated as the source of infection in light of the low attack rate among users (6.4%) and the fact that there was no increase in rates of illness with increasing consumption of water. The attack rate among residents who boiled their home water was not significantly different from the attack rate among residents drinking unboiled water.

Holland Patent School District Case-Control Study

The Holland Patent survey suggested that illness was associated with attending one of the Holland Patent district schools. Therefore, the investigating team decided to look for potentially important exposures within the schools by doing a case-control study. They compared the 33 hospitalized children from the Holland Patent schools with well controls matched for age, sex, and class in school. At least one case came from each of the 5 Holland Patent schools. One case was eliminated from the study because he had moved prior to the investigation. On October 24, the investigating team interviewed each child and his parents by telephone to gather information on the child's water, food, and milk exposures at the school subsequent to September 1, 1976.

QUESTION 8. Do you agree with the investigators' decision to select controls matched for age, sex, and class?

Exposure history data for the matched pairs are provided in Table 4.

QUESTION 9. Calculate the appropriate measure of association and test of statistical significance for each exposure listed in Table 4.

QUESTION 10. For which of the exposures is there a strong association with illness? For which of the exposures is there a statistically significant association with illness?

QUESTION 11. Do these data prove the vehicle of the outbreak?

QUESTION 12. What additional information might you seek to identify further the source of the outbreak and mode of transmission?

Table 4
 Summary of School Exposure Histories of Matched Pairs
 from Holland Patent School District Case-Control Study,
 Oneida County, NY, September - October, 1976

<u>Exposure</u>	Case Exposed?	Control Exposed?		<u>Measure of Association</u>	<u>Test of Significance</u>
		Yes	No		
Ate school lunches	Yes	14	12		
	No	5	1		
Drank milk	Yes	23	6		
	No	3	0		
Drank white milk	Yes	12	8		
	No	7	5		
Drank chocolate milk	Yes	12	14		
	No	4	2		
Drank water (1st 2 weeks of school)	Yes	18	3		
	No	6	0		
Drank water from the shower	Yes	1	3		
	No	2	18		
Drank water from the bathroom	Yes	0	1		
	No	1	20		
Drank water from the water fountain	Yes	7	2		
	No	12	5		
Ate fish fry	Yes	7	6		
	No	11	7		
Attended HS Football Game (Sept. 18)	Yes	0	3		
	No	4	22		
Ever traveled south of the Mason-Dixon line	Yes	1	4		
	No	1	27		

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PART VI - CONCLUSION

Dairy Investigation

After chocolate milk was epidemiologically implicated as the vehicle in this outbreak, 4 cartons each of chocolate and white milk from the high school cafeteria were cultured. One carton of chocolate milk yielded Yersinia enterocolitica O:8 N2W1, the same strain found in 38 ill persons.

Dairy A was the exclusive supplier of milk to the Holland Patent schools. Almost all of Dairy A's chocolate milk was produced for consumption at the schools.

Most of the milk processed at Dairy A came from its own herd of 60 cows, but the Dairy also purchased additional milk from the local milk cooperative. The Dairy A cows were mechanically milked. The raw milk was piped to a holding tank in the adjacent dairy plant, then once a day the milk was bulk pasteurized, homogenized, cooled, and packaged in 8-ounce cardboard cartons.

Chocolate milk was produced by adding thick chocolate syrup to pasteurized milk in an open vat in a 1:10 proportion. The milk and chocolate syrup were mixed by hand with a perforated metal stirring rod. After mixing, the prepared chocolate milk was mechanically packaged in cartons.

Chocolate and white milk were delivered in an unrefrigerated truck to the schools each day. Milk was not dated and stock was rotated by the delivery men.

Chocolate syrup was purchased in 5-gallon and #10 cans from a supplier in upstate New York. The syrup manufacturer routinely heated all syrup ingredients at 185° F for at least 15 minutes before the final product was sealed in cans. The manufacturer routinely cultured batches of syrup and had no history of bacterial contamination. No deficiencies in the plant's processing techniques were identified by FDA inspectors.

Inspection of the dairy's pasteurization records, co-op milk purchase records, and inquiries about changes in operating procedures before the epidemic period were not revealing.

The extended family who owned and operated Dairy A was composed of 10 persons, including 5 adults who worked in the dairy. Four family members became ill with abdominal complaints in August and September 1976. One man who cared for and milked the cows became ill with abdominal and right-sided flank pain in early August 1976. He underwent an exploratory laparotomy, and a normal appendix and a Meckels diverticulum were removed. An IVP was consistent with a renal stone.

Two preschool children and the wife of the man in charge of the dairy plant operation became ill in late September 1976. None had contact with the local schools but all drank chocolate milk. One of the children, a 3-year-old girl, underwent appendectomy for abdominal pain and fever on September 30. At operation she was found to have mesenteric lymph node enlargement with microscopic follicular hyperplasia, and the appendix showed marked lymphoid hyperplasia but no evidence of suppuration. The other child and their mother had abdominal pain, fever, and diarrhea in early October. Stool cultures from both children were positive for Y. enterocolitica 0:8 N2W1.

In late October, rectal and blood cultures were obtained from 4 of the family members involved in the dairy operation, including the man who was ill in August. Cultures were also obtained from numerous farm animals, the stirrer used in mixing the chocolate milk, chocolate syrup, water sources supplying the farm, and rodent droppings from the pigpen and feed shack. A rat trapped in the farm's pigpen had Y. enterocolitica serotype 0:13 Nilehn biotype. Cultures of raw milk obtained in November yielded a Yersinia serotype 0:6, 30 N1W1 in 1 sample and 0:8 N1W1 in another. The epidemic strain (0:8 N2W1) was not found in any of the cultures obtained on the farm except from the 2 preschool children who lived on the farm.

Summary and Conclusions

The clinical syndrome of abdominal pain and fever among children ill in the epidemic period is typical of the usual manifestations of Yersinia infection in this age group. The spectrum of clinical syndromes associated with Yersinia infection has been described in large studies from Europe: gastroenteritis occurs most frequently in infants, abdominal pain mimicking appendicitis most often in children and young adults, and arthritis and other non-suppurative sequelae of infection in older adults. Suppurative infection and septicemia occur in all age groups, although the latter has been reported most frequently in patients with severe underlying illness.

The syndrome of right lower quadrant pain mimicking appendicitis has been associated with a variety of pathologic findings confined typically to the ileocecal region: Namely, mesenteric adenitis, appendicitis, grossly normal appendix with areas of focal ulceration, and inflammation of the terminal ileum or some combination of these. All of these findings were observed in the group of patients who had appendectomies in this outbreak.

The overall attack rate for abdominal pain and fever of 100° F or greater was 11% and was lower than that observed in previous outbreaks involving schools in which 12% to 47% were reported ill. A rigid case definition may have kept the attack rate in this outbreak low. In approximately 1/3 of culture-proven cases, the patients had diarrhea, a rate similar to those in other outbreaks involving school children. The appendectomy case rate in this outbreak was 6%; in the other outbreaks from which similar information was available, 1.5%–9.5% of cases had appendectomies. In a previously reported interfamilial outbreak of 16 cases, 2 patients died; in this and other school-related outbreaks, there have been no fatalities.

The incubation period of gastroenteritis or abdominal pain from Yersinia infection is not known. In an outbreak of gastroenteritis among Canadian school children, possibly caused by Y. enterocolitica, the incubation period was between 3-5 days. In person-to-person outbreaks, incubation periods have ranged from 3 days to approximately 2 weeks. Laboratory surveillance of Y. enterocolitica specimens from humans and animals demonstrate a seasonal predilection for cold weather months from fall to spring.

The ecology of Y. enterocolitica, its reservoirs, and patterns of transmission to man are poorly understood. Domestic and wild animals have been identified as carriers of the organism; infections in sub-human primates, chinchillas, dogs, and other animals have been described. Abattoir surveys have demonstrated a 5% prevalence of Yersinia enterocolitica colonization in pigs; because of the predominance of serotype 3 in pigs it has been proposed that they may be the primary reservoir for human infection in Japan, Europe, and Canada where serotype 3 is the most frequently isolated human strain. However, the only documented reports of human illness associated with animal contact has been with dogs.

Many different serotypes have been found in water from lakes, streams, and potable sources, although frequently they have been non-pathogenic serotypes. Waterborne infection has been documented by culture in a reported human case from New York state.

Y. enterocolitica has been isolated from raw beef, poultry, fish, vacuum packed meat, shellfish, milk, and ice cream. The potential for foodborne illness with Y. enterocolitica is apparent. Although milk has previously been suggested as a possible vehicle of transmission, this is the first outbreak of yersiniosis in which food has been documented by culture as the vehicle. Although pathogenic strains have previously been isolated from food, serotype 0:8, the most commonly identified serotype in the United States, has not been isolated from non-human sources other than water and dogs. Knowledge of the reservoirs for these serotype is incomplete. Serotype 5 is the next most frequently reported serotype in the United States, and its presence in 2 persons from the villages involved in the outbreak probably reflects endemic transmission. Serotype 0:6,30, found in isolates of raw milk, has previously been found in raw milk.

The epidemiologic investigation clearly indicated that consumption of chocolate milk sold by Dairy A was associated with the epidemic illness. The cultures of chocolate milk obtained in mid-October, approximately 3 weeks after the apparent common-source outbreak, yielded Y. enterocolitica of the same epidemic serotype. This suggests that contamination of chocolate milk was either continuous or occurred at multiple points in time. Additional evidence that risk of illness was continuing comes from the shape of the epidemic curve in the absence of evidence of secondary transmission and if one assumes an incubation period of less than 2 weeks. Following the peak in late September, cases continued to occur over the next several weeks. It is possible that small numbers of the organism were present in the milk during most of September and October, and that during the epidemic period a larger inoculum caused clinical illness in a large number of persons. The infective dose required for human infection is not known.

The presence of illness and isolation of the epidemic serotype from residents of a nearby village (Remsen) suggests that the school in that village may also have been involved in the outbreak. The school also serves chocolate milk processed at Dairy A. A door-to-door survey in Remsen failed to identify a high attack rate in school-age children, although Remsen Village residents with school contact who ate in the school cafeteria appeared to be at increased risk of illness. Remsen school students were not studied systematically. Most likely, low rates of infection in Remsen schools were present, but due to variations of inoculum, handling or storage of milk in the 2 systems, the milk served in the Remsen school did not contain enough organisms to cause epidemic illness.

The epidemiologic investigation and the absence of the epidemic serotype in cultures of white milk suggested that contamination of the milk occurred after pasteurization. The opportunity for contamination of the chocolate milk was present when chocolate syrup was mixed in by hand in an open vat. Improper cleaning of the vat or ladle or indirect contamination of the milk or syrup during mixing could have occurred. The source of the epidemic strain of the dairy plant is unknown. Y. enterocolitica 0:8 N2W1 was isolated on the premises of the farm from only 2 family members who became ill late in the epidemic period.

CONTROL MEASURES

The dairy owners voluntarily ceased production of chocolate milk after the New York State Health Department informed them that their chocolate milk had been implicated epidemiologically as the vehicle in the outbreak. State agricultural officials have increased the frequency of their routine inspections of the plant and culturing of milk specimens. The dairy will institute terminal pasteurization of milk before chocolate milk is marketed again.

The outbreak appeared to have waned prior to cessation of distribution of the implicated chocolate milk. Surveillance by the school nurses, town physicians, local hospitals, and an Oneida County Public Health nurse indicated that the epidemic illness did not recur in November and December.