Centers for Disease Control and Prevention
Epidemiology Program Office
Case Studies in Applied Epidemiology
No. 941-707

Surveillance for *E. coli* O157:H7 — Information for Action

Student' Guide

Learning Objectives
After completing this case study, the participant should be able to:

- ☐ Discuss the process and criteria for placing a disease or condition on a state or national notifiable disease list;
- ☐ List the categories of information that should be included in a surveillance instrument;
- ☐ Summarize and interpret surveillance data;
- ☐ Recognize difficulties in balancing public health concerns with consumer and industry considerations in emerging issues.

This case study is based on surveillance and investigation activities of the Oregon Health Division between 1986 and 1995. The investigation described in the second half of the case study has been published in the following reference:

Keene WE, Hedberg K, Herriott DE, Hancock DD, et al. A prolonged outbreak of *Escherichia coli* O157:H7 infections caused by commercially distributed raw milk. J Infect Dis 1997;176:815-818.

This case study is largely derived from another study, "An Outbreak of *E. coli* O157:H7 Associated with Raw Milk," developed in 1994 by Julie R. Crom (Animal and Public Health Inspection Service US Department of Agriculture) and Richard C Dicker, MD, MSc (CDC). This case study was developed in 1998 by Richard C. Dicker. Substantial background information, reviews, and suggestions were provided to both case studies by:

William Keene, PhD, MPH; Fred Hoesly, MD, MPH; and Katrina Hedberg, MD, MPH (Oregon Health Division); Donald Herriott, DVM, MPH (USDA, APHIS, VS, Salem, OR); and Thomas Gomez, DVM (USDA, APHIS, VS, [CDC], Atlanta, GA)

Current version updated in 2007 by Julie Magri with input from the 2007 EIS Summer Course case study instructors.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

PART I

Dateline: 1986. Infection with *Escherichia coli* O157:H7 was first recognized as a cause of human illness in 1982, when 26 persons in Oregon and 21 persons from Michigan developed bloody diarrhea after eating hamburgers contaminated with the organism. Both outbreaks were associated with restaurants of the same fast-food chain. In 1986 three patients in eastern Washington State were diagnosed with *E. coli* O157:H7 after being hospitalized with hemorrhagic colitis and subsequent thrombotic thrombocytopenic purpura. An epidemiologic investigation linked these three cases and 37 others in the same community to a local restaurant that had served ground beef, the suspected vehicle of transmission. This outbreak was found to be part of a statewide increase in *E. coli* O157:H7 cases. Infections among nursing home residents and in patients with hemolytic uremic syndrome (HUS) were seen across the state, and an increase in sporadic cases of hemorrhagic colitis was noted at a Seattle health maintenance organization.

Question 1: Health departments use public health surveillance to keep track of diseases that affect the public's health. What is public health surveillance?

Question 2: What is the difference between *active* and *passive* surveillance systems? When might you use each?

Each State has a list of diseases of public health importance that must be reported to the health department when diagnosed by a health care provider. Given the information on the previous page, public health officials in Washington and Oregon considered adding E. coli infection to their lists of notifiable diseases.

Question 3: What criteria would you use in deciding whether to add *E. coli* O157:H7 infection (or any other condition) to the reportable disease list in your State?

Question 4: What is the process for making a disease reportable? What are the alternatives?

Question 5: Assuming you would like to make *E. coli* O157:H7 infection a reportable disease in Oregon, what information must you specify in the regulation or statute?

Question 6: Assuming that you will add it to the reportable disease list in your state, what categories of information would you collect on an initial one-page disease report form?

PART II

Dateline: 1/1/93. By 1993, *E. coli* O157:H7 (O157) has been recognized as an important foodborne pathogen that can cause serious illness. Numerous outbreaks across the country have been attributed to ground beef, roast beef, water, apple cider, and unpasteurized milk. Human infection occurs primarily through ingestion of food or water contaminated with bovine fecal material, but person-to-person transmission also occurs. The organism can survive for extended periods in water, meat stored at subfreezing temperatures, soil, and acidic environments, but can be destroyed by thorough cooking or pasteurization.

Patients infected with O157 typically present with severe abdominal cramps, bloody diarrhea, and low grade fever. Children and the elderly are at greatest risk for complications such as hemorrhagic colitis, hemolytic uremic syndrome, and death.

In 1990, Oregon added *E. coli* O157:H7 to its reportable disease list. Oregon requires reporting by health care providers, health care facilities, and laboratories. The Laboratories must also send isolates to the State Laboratory.

Question 7: What attributes characterize a good surveillance system?

You are an epidemiologist assigned to the Oregon Health Division, and are responsible for reviewing surveillance data on a regular basis.

Question 8: What basic descriptive epidemiology would you like to see to characterize the occurrence of *E. coli* O157:H7 in Oregon?

PART III

Following are several tables of *E. coli* O157:H7 surveillance data collected in Oregon from August 1990 through December 1992.

Table A: *E. coli* O157:H7 cases by year (ONSETYY) and month (ONSETMM) of onset, Oregon, 1990-1992

	ONSETYY			
ONSETMM	90	91	92	Total
1	-	2	1	3
2	-	2	2	4
3	-	2	7	9
4	-	5	5	10
5	-	1	12	13
6	-	10	25	35
7	2	26	41	69
8	14	28	17	59
9	19	15	19	53
10	12	13	7	32
11	5	6	9	20
12	7	1	11	19
Total	59	111	156	326

Question 9: Graph the data in Table A and interpret.

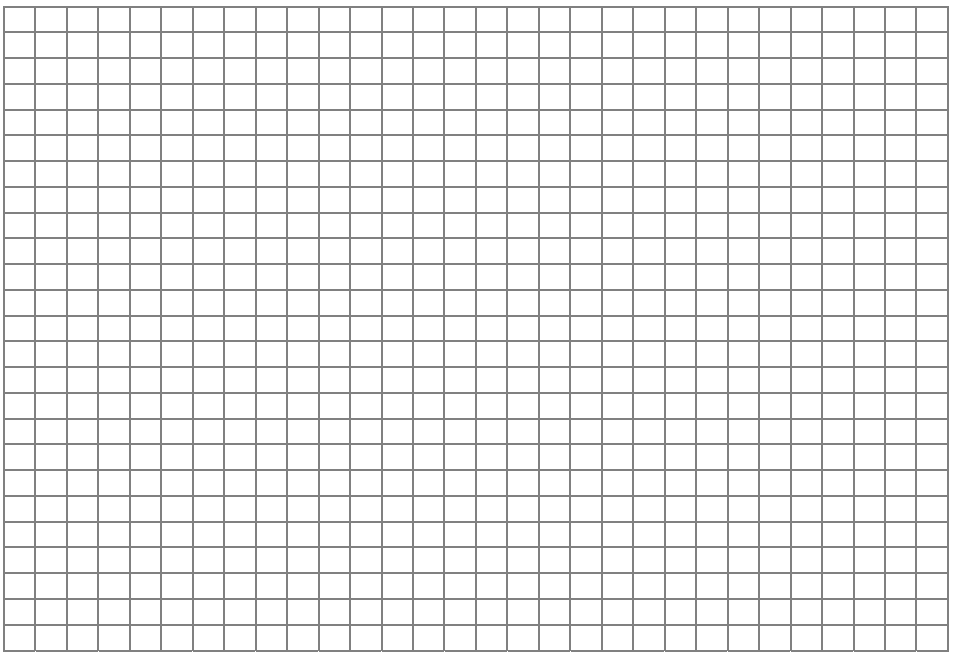
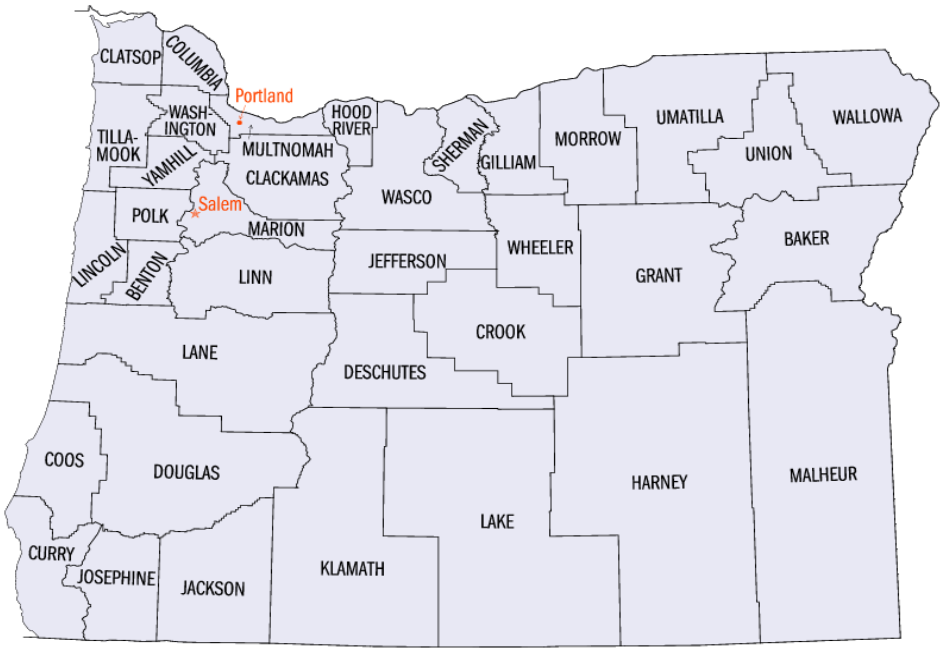


Table B: *E. coli* O157:H7 cases by year of onset and county, Oregon, 1990-1992

	ONSETYY			
COUNTY	90	91	92	Total
BAKER	0	1	0	1
BENTON	1	4	11	16
CLACKAMAS	7	11	21	39
COLUMBIA	1	2	5	8
COOS	0	0	1	1
DESCHUTES	2	0	0	2
DOUGLAS	2	4	4	10
GRANT	0	0	2	2
JACKSON	1	0	4	5
JEFFERSON	0	0	2	2
JOSEPHINE	0	0	1	1
LANE	6	9	16	31
LINCOLN	2	1	1	4
LINN	4	4	5	13
MALHEUR	3	0	1	4
MARION	9	8	10	27
MULTNOMAH	11	36	41	88
POLK	1	1	3	5
UMATILLA	1	0	3	4
WASCO-SHER	0	2	1	3
WASHINGTON	7	26	19	52
YAMHILL	1	2	5	8
Total	59	111	156	326

Map: Oregon Counties



Question 10: Summarize the data in Table B and interpret.

Table C: *E. coli* O157:H7 cases by year of onset and 10-year age group, Oregon, 1990-1992

	ONSETYY			
AGE10	90	91	92	Total
0 TO 9	10	35	39	84
10 TO 19	10	11	31	52
20 TO 29	8	19	20	47
30 TO 39	7	14	10	31
40 TO 49	5	8	13	26
50 TO 59	6	8	14	28
60 TO 69	4	8	15	27
70 TO 79	6	5	8	19
80 TO 89	2	3	3	8
90 TO 99	0	0	3	3
990 TO 999	1	0	0	1
Total	59	111	156	326

Table D: *E. coli* O157:H7 cases by sex and 10-year age group, Oregon, 1990-1992

	SEX		
AGE10	F	M	Total
0 TO 9	42	42	84
10 TO 19	24	28	52
20 TO 29	22	25	47
30 TO 39	15	16	31
40 TO 49	17	9	26
50 TO 59	15	13	28
60 TO 69	11	16	27
70 TO 79	8	11	19
80 TO 89	2	6	8
90 TO 99	2	1	3
990 TO 999	1	0	1
Total	159	167	326

Table E: *E. coli* O157:H7 cases by year of onset and single year of age for those under age 11 years, Oregon, 1990-1992

	ONSETYY			
AGE	90	91	92	Total
0	1	0	2	3
1	3	6	6	15
2	2	6	6	14
3	3	5	4	12
4	0	6	6	12
5	1	3	3	7
6	0	3	4	7
7	0	2	5	7
8	0	0	2	2
9	0	4	1	5
10	1	0	7	8
Total	11	35	46	92

Table F: Population of all ages, all races, both sexes by age, Oregon, 1990 (n=2,842,321)

Age (yrs)	Population	% of N
0-4	205,649	7.23
5-9	208,902	7.34
10-14	200,742	7.06
15-19	191,070	6.72
20-24	189,859	6.67
25-29	212,127	7.46
30-34	239,715	8.43
35-39	250,218	8.80
40-44	223,537	7.86
45-49	165,811	5.83
50-54	128,860	4.53
55-59	115,362	4.05
60-64	120,704	4.24
65-69	122,332	4.30
70-74	101,583	3.57
75-79	78,200	2.75
80-84	49,383	1.73
85+	38,267	1.34

Table G: Population of all ages, all races, both sexes by county, Oregon, 1990 (n=2,842,321)

	County	Population	% of N		County	Population	% of N
1	MULTNOMAH	583,887	20.54	19	CLATSOP	33,301	1.17
2	WASHINGTON	311,554	10.96	20	MALHEUR	26,038	0.91
3	LANE	282,912	9.95	21	UNION	23,598	0.83
4	CLACKAMAS	278,850	9.81	22	WASCO	21,683	0.76
5	MARION	228,483	8.03	23	TILLAMOOK	21,570	0.75
6	JACKSON	146,389	5.15	24	CURRY	19,327	0.67
7	DOUGLAS	94,649	3.32	25	HOOD RIVER	16,903	0.59
8	LINN	91,227	3.20	26	BAKER	15,317	0.53
9	DESCHUTES	74,958	2.63	27	CROOK	14,111	0.49
10	BENTON	70,811	2.49	28	JEFFERSON	13,676	0.48
11	YAMHILL	65,551	2.30	29	GRANT	7,853	0.27
12	JOSEPHINE	62,649	2.20	30	MORROW	7,625	0.26
13	COOS	60,273	2.12	31	LAKE	7,186	0.25
14	UMATILLA	59,249	2.08	32	HARNEY	7,060	0.24
15	KLAMATH	57,702	2.03	33	WALLOWA	6,911	0.24
16	POLK	49,541	1.74	34	SHERMAN	1,918	0.06
17	LINCOLN	38,889	1.36	35	GILLIAM	1,717	0.06
18	COLUMBIA	37,557	1.32	36	WHEELER	1,396	0.04

Question 11: Analyze these data by place and person, completing the tables below.

Table H: County-specific rates of E. Coli O157:H7 per 100,000 persons, Oregon

County	Population	1991	1992	2-Yr Avg
Baker	15,317	6.53	0.00	3.26
Benton	_____	_____	_____	_____
Clackamas	_____	_____	_____	_____
Columbia	37,557	5.33	13.31	9.32
Coos	60,273	0.00	1.66	0.83
Deschutes	74,958	0.00	0.00	0.00
Douglas	94,649	4.23	4.23	4.23
Grant	_____	_____	_____	_____
Jackson	146,389	0.00	2.73	1.37
Jefferson	13,676	0.00	14.62	7.31
Josephine	62,649	0.00	1.60	0.80
Lane	282,912	3.18	5.66	4.42
Lincoln	38,889	2.57	2.57	2.57
Linn	91,227	4.38	5.48	4.93
Malheur	26,038	0.00	3.84	1.92
Marion	228,483	3.50	4.38	3.94
Multnomah	_____	_____	_____	_____
Polk	49,541	2.02	6.06	4.04
Umatilla	_____	_____	_____	_____
Washington	_____	_____	_____	_____
Yamhill	65,551	3.05	7.63	7.22
Wasco-Sherman	23,601	8.47	4.24	5.34
Statewide	**2,842,321**	**3.91**	**5.49**	**4.70**

Table I: Age-group-specific rates of E. Coli O157:H7 per 100,000 persons, Oregon

Age Group	Population	1991	1992	2-Yr Avg
0 to 4 years	_____	_____	_____	_____
5 to 9	_____	_____	_____	_____
10 to 19	_____	_____	_____	_____
20 to 29	401,986	4.73	4.98	4.85
30 to 39	489,933	2.86	2.04	2.45
40 to 49	389,348	2.05	3.34	2.70
50 to 59	_____	_____	_____	_____
60 to 69	_____	_____	_____	_____
70 to 79	_____	_____	_____	_____
80+	87,650	3.42	6.85	5.13
Total	**2,842,321**	**3.91**	**5.49**	**4.70**

Dateline: 4/19/93. All *E. coli* O157:H7 case reports in Oregon are investigated by county health department nurse-epidemiologists. The investigation includes an interview about recognized sources for *E. coli* O157:H7 infection. Nurses at the Multnomah County (which includes the city of Portland) health department noted that three recent cases had reported drinking raw milk within the nine days prior to disease onset. Suspecting a possible outbreak, they immediately notified the state epidemiologist.

Question 12: Calculate the expected number of cases in Multnomah County in April. (Hint: Should you use 1990 data?)

Question 13: What can account for an increase in the number of cases reported to a surveillance system?

PART IV

Epidemiologists at the State Health Department reviewed all 1992 and 1993 *E. coli* O157:H7 case reports and identified three more persons among the 13 sporadic cases (not related to any recognized outbreak) who reported drinking Dairy A raw milk in the days before their onsets. The cases did not appear to share any other common exposures. All lived in the greater Portland area. Thus a total of 6 out of 13 sporadic cases reported drinking Dairy A brand raw milk, the only brand of raw milk sold in the Portland area. Additional (presumptive) cases were also reported among raw milk-drinking household members. The following table summarizes the 6 cases confirmed to date associated with Dairy A:

CITY	COUNTY	AGE	SEX	ONSET
Portland	Multnomah	61	F	12/19/92
Sandy	Clackamas	3	M	03/21/93
Portland	Multnomah	43	M	04/03/93
Sherwood	Washington	9	M	04/07/93
Portland	Multnomah	34	M	04/11/93
Portland	Multnomah	38	F	04/14/93

For comparison purposes, a review was done on all cases of salmonellosis in the Portland area 1992 and 1993. Raw milk consumption was not reported for any of these cases.

Question 14: In addition to the state and local health departments, what other agencies should be involved, and what are their roles? Who are the stakeholders in this situation? What concerns are they likely to raise?

PART V

Consultation with officials at the Food and Dairy Division of the Oregon Department of Agriculture (ODA) and with the USDA Animal and Plant Health Inspection Service (APHIS) Area Epidemiologist provided the following information:

The ODA Food and Dairy Division licenses raw milk dairies. There are five licensed cow dairies and one goat dairy in the state. In 1987, the FDA banned the distribution and sale of unpasteurized milk outside of the state in which it was produced. A recent FDA survey showed that intrastate raw milk sales are permitted in 27 states and raw milk was sold in at least 18 states in 1992. The 111 raw milk dairies in the U.S. constitute 0.06 percent of all dairies. It is estimated that raw milk sold to consumers consists of approximately 0.02 percent of the total milk production in the U.S.

Unpasteurized milk has been frequently implicated as a vehicle for many enteric infections, including campylobacteriosis and salmonellosis as well as O157 infection. Health food enthusiasts claim benefits result from drinking raw milk such as higher nutritive value and enhanced resistance to disease. While pasteurization does cause trivial decreases in thiamine, vitamin B_{12}, and vitamin C contents, human nutrition studies have shown no advantage of raw milk over pasteurized milk. No evidence exists in support of claims for disease resistance.

Dairy A has 132 cattle and produces 350 gallons of milk per day that is distributed through 35 retail outlets, including major supermarkets and numerous health food stores. It is the only supplier of bovine raw milk in the Portland area. In the early 1980s Dairy A was the apparent source of a small outbreak of campylobacteriosis, but this finding was not made public at the time.

The ODA inspects all dairies in Oregon six times per year and collects bulk milk samples approximately every six weeks. Herds are also required to be tested for brucellosis and tuberculosis once each year by an accredited veterinarian. Samples from the bulk tanks are tested for total bacterial count, *Salmonella*, milk fat percentage, added water, etc. In raw milk dairies, additional testing is done for fecal coliforms, but a maximum standard is not established and the numbers are strictly informational.

The mechanism by which raw milk becomes contaminated with O157 has not been documented; however fecal contamination associated with milking is presumed. Pathogen sources may include the farm environment, contaminated equipment used for milking, filtering, cooling, storing, and milk distribution, or infected farm workers. Preliminary evidence suggests that cattle transiently or sporadically shed O157 in their feces and that the excretion period ranges from hours to weeks. O157 is not known to cause clinical disease in cattle under natural conditions. Currently, not enough is known about the ecology of O157 in cattle to implement prudent, on-farm intervention measures to prevent future contamination.

Dateline: 4/20/93. Two epidemiologists including the Public Health Veterinarian from the Oregon Health Division and a sanitarian from the ODA Food and Dairy Division went to the dairy to inform the owner of the outbreak. While there, they collected swabs for culture from 30 manure piles near the milking area. Six raw milk samples were collected from the dairy and from several local distributors for testing and culture. Results from these preliminary tests will not be available for several days. Plans were made to do a complete herd test as soon as logistically possible.

Staff at the Oregon Health Division calculated the probability of finding by chance alone that at least six of the thirteen cases would have consumed raw milk, assuming that no more than 1% of the population in the area are raw milk drinkers. They reported the result in their epidemiology newsletter as follows: "The probability that at least six out of thirteen cases would be brand A drinkers by chance alone, given a 1% exposure prevalence, is 0.00000000162 (or less than 1 in 500 million)."

Question 15: List the lines of evidence that suggest that raw milk from Dairy A is the source of this *E. coli* O157:H7 outbreak.

Question 16: After reviewing the lines of evidence you listed above, do you believe Dairy A's raw milk is the source (or at least a source) of *E. coli*?

Question 17: What actions might you take next (e.g., issue warning about raw milk, pull raw milk off shelves, require pasteurization of raw milk, close Dairy A, do more investigation, wait for lab results, etc.)?

PART VI

Dateline: 4/21/93. The Oregon Health Division went public. They issued a press release announcing that a cluster of six confirmed cases of *E. coli* O157:H7 in Portland area residents were linked to consumption of raw (unpasteurized) milk produced by Dairy A. At the same time, the Oregon Dept. of Agriculture announced a recall on Dairy A raw milk and arranged for the dairy's milk to be diverted temporarily to a nearby creamery for pasteurization.

Dateline: 4/26/93. Results from the fecal and milk sample tests all came back negative for O157. The Oregon Department of Agriculture lifted the recall.

The investigation became a hot topic in the local press.

Question 18: What would be your "SOCO" (Single Overriding Communication Objective) to the media? What other "spin" might the local media put on this story?

PART VII

Dateline: 5/93. The media portrayed the situation as the Government bullying a local businessman trying to make a living by selling a local product to informed local consumers. Letters to the Editor supported the dairy.

Meanwhile, a case was reported in a 73-year old man whose illness began on April 21. He had consumed raw milk form Dairy A.

Dateline: 6/93. Two sisters, one age 3 and the other age 9 months, were diagnosed with *E. coli* O157:H7 within a week of each other. The 3-year-old had consumed raw milk from Dairy A while visiting her grandmother on June 11 and 12. The 9-month-old had not consumed the milk, but was exposed to her sister. Samples of the implicated milk were tested at three separate labs but were found to be negative for O157.

After these new cases came to light, a meeting was convene with representatives of the Oregon Department of Agriculture, the Oregon Health Division, and the dairy's attorney. The parties agreed to test the milk every 2 weeks and perform 2 prevalence surveys of the herd. They also agreed that if the milk tested positive, a recall would be issued and pasteurization would be instituted. Animals testing positive for O157 would be removed from milk production.

Dateline: 7/19/93. A herd test was conducted on all 132 cattle on the premises. The testing found four animals in the milking herd positive for O157 (3% prevalence). The isolates from the positive animals matched the sub-typing on four of the previous human cases associated with the dairy.

Dateline: 8/24/93. Dairy A refused to allow a second herd test. No subsequent herd tests for O157 were permitted.

Oregon enacted an administrative rule requiring all unpasteurized milk to carry a warning label: *"This product has not been pasteurized... may contain disease-producing organisms"*.

Dateline: Spring 1994. A new cluster of O157 occurred involving three confirmed and four presumptive cases in three different families. As a result, ODA conducted a second herd test (by fecal swabs) at Dairy A. Two different subtypes isolated from the cases matched subtypes from at least two of the animals in the herd. The Oregon Health Division took the Dairy to court using a consumer protection statute that states "...cannot willfully spread an infectious disease." The court issued a restraining order preventing the dairy from selling raw milk.

Question 19: Consider the steps of a surveillance system (data collection, analysis, etc.) Which steps, if any, are traditionally the "weak links" in the system? How has the Oregon Health Division performed?

PART VIII - CONCLUSION

The Dairy sued to vacate the restraining order, arguing that the subtyping results came back three weeks after the people became ill so there is no evidence of "ongoing public health threat." Further, the sale of raw milk was legal in Oregon and the health department had not come up with standards that the Dairy could meet to be able to market their product.

The restraining order was not lifted. Nevertheless, the dairy continued to sell raw milk surreptitiously until October 1995, when a Department of Agriculture "sting" operation uncovered the sales. The dairy owner was fined and jailed for contempt of court. No Dairy-A-associated cases have been reported since June 1994.

Dateline: 1995. In response to this and another outbreak, legislation to outlaw the retail sale of raw milk in Oregon was introduced in 1995. It died in committee.

Dateline: 1997. The owner closed the dairy and sold the property to a developer for a substantial sum.

REFERENCES

Surveillance

1. Carter AO. Setting priorities: The Canadian experience in communicable disease surveillance. MMWR Supplement 1992;41:79-84.

2. Centers for Disease Control. Guidelines for evaluating surveillance systems. MMWR 1988;37(S5): 1-18.

3. Teutsch SM, Churchill RE, eds. Principles and practice of public health surveillance. New York: Oxford University Press, 1994.

***E. coli* O157:H7**

4. Keene WE, Hedberg K, Herriott DE, Hancock DD, et al. A prolonged outbreak of *Escherichia Coli* O157:H7 infections caused by commercially distributed raw milk. J Infect Dis 1997;176:815-818.

5. CDC. Update: Multistate outbreak of *Escherichia coli* O157:H7 infections from hamburgers - Western United States, 1992-1993. MMWR 1993;42:258-263.

6. Griffin PM, Tauxe RV. The epidemiology of infections caused by *Escherichia coli* O157:H7, other enterohemorrhagic *E. coli*, and the associated hemolytic uremic syndrome. Am J Epidemiol 1991;13:60-98.

Raw Milk

7. Potter ME; Kaufmann AF; Blake PA et al. Unpasteurized milk - the hazards of a health fetish. JAMA 1984; 252:2048-52.

Appendix 1 - Solution to Binomial Problem

(From text of Part V: "The probability that at least 6 out of 13 cases would be brand A drinkers by chance alone, given a 1% exposure prevalence, is 0.00000000162 (or less than 1 in 500 million)."

$$\sum_{x=i}^{N}\left(\frac{N!}{x!(N-x)!}\right)p^{x}(1-p)^{N-x}$$

where N = total number of observations (13)
x = i = all possible values from 0 to N
p = prevalence in population

To determine probability of at least 6 out of 13, add the probabilities for $x \geq 6$.

Prob (x=0)	=	$13!/0!13! \times 0.01^{0} \times 0.99^{13}$	=	1×0.877521	= 0.878
Prob (x=1)	=	$13!/1!12! \times 0.01^{1} \times 0.99^{12}$	=	13×0.008863	= 0.115
Prob (x=2)	=	$13!/2!11! \times 0.01^{2} \times 0.99^{11}$	=	78×0.000089	= 0.00698
Prob (x=3)	=	$13!/3!10! \times 0.01^{3} \times 0.99^{10}$	=	$286 \times 9.0 \times 10^{-7}$	= 2.59×10^{-4}
Prob (x=4)	=	$13!/4!9! \times 0.01^{4} \times 0.99^{9}$	=	$715 \times 9.1 \times 10^{-9}$	= 6.53×10^{-6}
Prob (x=5)	=	$13!/5!8! \times 0.01^{5} \times 0.99^{8}$	=	$1287 \times 9.2 \times 10^{-11}$	= 1.19×10^{-7}
Prob (x=6)	**=**	$\mathbf{13!/6!7! \times 0.01^{6} \times 0.99^{7}}$	**=**	$\mathbf{1716 \times 9.3 \times 10^{-13}}$	**=** $\mathbf{1.60 \times 10^{-9}}$
Prob (x=7)	**=**	$\mathbf{13!/7!6! \times 0.01^{7} \times 0.99^{6}}$	**=**	$\mathbf{1716 \times 9.4 \times 10^{-15}}$	**=** $\mathbf{1.62 \times 10^{-11}}$
Prob (x=8)	**=**	$\mathbf{13!/8!5! \times 0.01^{8} \times 0.99^{5}}$	**=**	$\mathbf{1287 \times 9.5 \times 10^{-17}}$	**=** $\mathbf{1.22 \times 10^{-13}}$
Prob (x=9)	**=**	$\mathbf{13!/9!4! \times 0.01^{9} \times 0.99^{4}}$	**=**	$\mathbf{715 \times 9.6 \times 10^{-19}}$	**=** $\mathbf{6.87 \times 10^{-16}}$
Prob (x=10)	**=**	$\mathbf{13!/10!3! \times 0.01^{10} \times 0.99^{3}}$	**=**	$\mathbf{286 \times 9.7 \times 10^{-21}}$	**=** $\mathbf{2.78 \times 10^{-18}}$
Prob (x=11)	**=**	$\mathbf{13!/11!2! \times 0.01^{11} \times 0.99^{2}}$	**=**	$\mathbf{78 \times 9.8 \times 10^{-23}}$	**=** $\mathbf{7.64 \times 10^{-21}}$
Prob (x=12)	**=**	$\mathbf{13!/12!1! \times 0.01^{12} \times 0.99^{1}}$	**=**	$\mathbf{13 \times 9.9 \times 10^{-25}}$	**=** $\mathbf{1.29 \times 10^{-23}}$
Prob (x=13)	**=**	$\mathbf{13!/13!0! \times 0.01^{13} \times 0.99^{0}}$	**=**	$\mathbf{1 \times 1.0 \times 10^{-26}}$	**=** $\mathbf{1.00 \times 10^{-26}}$

The sum of probabilities for x = 6 through x = 13 = 1.62×10^{-9}, or 0.00000000162.

Note that, with an expected value of 1 in 100, the probability of x=0 (0.878) plus the probability of x=1 (0.115) add up to 0.99. Therefore, any observed value of 2 or greater has a p-value less than 0.01.

Appendix 2 - Case Definitions Used in Public Health Surveillance

Shiga toxin-producing *Escherichia coli* (STEC), 2005 Case Definition

Clinical description

An infection of variable severity characterized by diarrhea (often bloody) and abdominal cramps. Illness may be complicated by hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP); asymptomatic infections also may occur and the organism may cause extraintestinal infections.

Laboratory criteria for diagnosis

Isolation of Shiga toxin-producing Escherichia coli from a clinical specimen. Escherichia coli O157:H7 isolates may be assumed to be Shiga toxin-producing. For all other E. coli isolates, Shiga toxin production or the presence of Shiga toxin genes must be determined to be considered STEC.

Case classification

Suspect: A case of postdiarrheal HUS or TTP (see HUS case definition), or identification of Shiga toxin in a specimen from a clinically compatible case without the isolation of the Shiga toxin-producing E. coli.

Probable:

- A case with isolation of E. coli O157 from a clinical specimen, without confirmation of H antigen or Shiga toxin production,

OR

- A clinically compatible case that is epidemiologically linked to a confirmed or probable case,

OR

- Identification of an elevated antibody titer to a known Shiga toxin-producing E. coli serotype from a clinically compatible case.

Confirmed: A case that meets the laboratory criteria for diagnosis. When available, O and H antigen serotype characterization should be reported.

Comment

For users of the legacy National Electronic Telecommunications System for Surveillance (NETSS), laboratory-confirmed isolates are also reported via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. The National Electronic Disease Surveillance System (NEDSS) or NEDSS compatible systems will eventually replace PHLIS and NETSS; users of NEDSS or compatible systems which report to CDC should not report via PHLIS.
Both asymptomatic infections and infections at sites other than the gastrointestinal tract, if laboratory confirmed, are considered confirmed cases that should be reported.

http://www.cdc.gov/epo/dphsi/casedef/shiga_current.htm

Hemolytic Uremic Syndrome, Post-diarrheal, 1996 Case Definition

Clinical description

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thrombocytopenic purpura (TTP) also is characterized by these features but can include central nervous system (CNS) involvement and fever and may have a more gradual onset. Most cases of HUS (but few cases of TTP) occur after an acute gastrointestinal illness (usually diarrheal).

Laboratory criteria for diagnosis

The following are both present at some time during the illness:

- Anemia (acute onset) with microangiopathic changes (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear and
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., greater than or equal to 1.0 mg/dL in a child aged less than 13 years or greater than or equal to 1.5 mg/dL in a person aged greater than or equal to 13 years, or greater than or equal to 50% increase over baseline)

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not less than 150,000/mm3, other diagnoses should be considered.

Case classification

Probable:

- An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding 3 weeks

OR

- An acute illness diagnosed as HUS or TTP, that a) has onset within 3 weeks after onset of an acute or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed

Confirmed: an acute illness diagnosed as HUS or TTP that both meets the laboratory criteria and began within 3 weeks after onset of an episode of acute or bloody diarrhea

Comment

Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as postdiarrheal HUS.

http://www.cdc.gov/epo/dphsi/casedef/hemolyticcurrent.htm