A Multistate Outbreak of Oyster-Associated Gastroenteritis: Implications for Interstate Tracing of Contaminated Shellfish

Scott F. Dowell, Carmela Groves, Kathryn B. Kirkland, Helen G. Cicirello, Tamie Ando, Qi Jin, Jon R. Gentsch, Stephan S. Monroe, Charles D. Humphrey, Catherine Slemp, Diane M. Dwyer, Rebecca A. Meriwether, and Roger I. Glass

Epidemic Intelligence Service, Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Department of Environment, Health, and Natural Resources, Raleigh, North Carolina; Department of Health and Mental Hygiene, Baltimore, Maryland

In November 1993, clusters of gastroenteritis in six states following oyster consumption were investigated to identify common features, and stool samples were obtained to identify a pathogen. Efforts were made to account for all potentially contaminated oysters using harvest tags and the interstate recall system. Consumption of oysters was associated with illness in 10 clusters; no other food was implicated. A Norwalk-like virus was detected by electron microscopy in 9 of 18 samples and by reverse transcription–polymerase chain reaction in 20 of 26 samples from 6 clusters. Nucleotide sequences of a 123-bp fragment from all specimens were identical, consistent with a common source outbreak. Implicated oysters were harvested from the Louisiana coast between 9 and 12 November. Although some were recalled and destroyed, most oysters harvested from the area during this time remain unaccounted for. Current regulations and commercial practices need to be revised to permit thorough tracing and recall of contaminated oysters and to improve control of future epidemics.

The consumption of fecally contaminated shellfish has long been associated with outbreaks of illness caused by enteropathogens, including *Vibrio cholerae* O1 [1], other *Vibrio* species [2], *Salmonella* species [3], *Plesiomonas* species [4], hepatitis A virus [5], and small round-structured viruses (SRSVs), such as Norwalk virus [6–13]. Most of the commonly eaten shellfish, including oysters [7, 14], clams [13], cockles [15], and limpets [16], have served as vehicles for transmission of infectious microorganisms. Norwalk-like viruses have been the most common agents identified in outbreaks of oyster-associated gastroenteritis [6–13].

A series of outbreaks associated with the consumption of raw oysters occurring in the 19th and early 20th centuries, including one in 1855 that led to the deaths of several "highly esteemed" citizens of New York from cholera [17], a typhoid fever outbreak at Wesleyan College in Connecticut in 1894, and a typhoid epidemic in 1924–1925, which led to the development of the National Shellfish Sanitation Program (NSSP) [1]. This cooperative program involving the US Food and Drug Administration (FDA), state regulatory agencies, and the shellfish industry is charged with controlling the quality and safety of shellfish shipped in interstate commerce. Recommendations, such as limiting harvests to areas with clean water (<14 fecal coliforms/100 mL of H_2O), depurating harvested shellfish to reduce bacterial counts below the market guideline (230 coliforms/100 g of meat), and requiring tags with the location and date of harvest on all boxes of shellfish sold to allow back-tracing of contaminated lots and identification of contaminated beds, have all addressed the continuing problem of shellfish safety [18].

In November 1993, the Centers for Disease Control and Prevention (CDC) received reports of 23 clusters of acute gastroenteritis from six states; some of these clusters had been linked by the Louisiana Department of Health to the consumption of Louisiana oysters [19]. We investigated these outbreaks to confirm the vehicle of transmission, to identify the source of contamination, and to help direct a recall of oysters that was instituted by several states and the FDA. We used recently developed polymerase chain reaction (PCR)–based methods for the detection of Norwalk virus [20] to identify the etiologic agent and sequence analysis of PCR products to examine whether these geographically widespread clusters had a common source. We report here the results of epidemiologic and laboratory investigations in Maryland, North Carolina, Mississippi, Texas, and Pennsylvania. The clusters in Louisiana and investigation of the implicated oyster bed are the subject of a separate report [19].

Materials and Methods

Identification of outbreaks. On 17 November 1993, the state health departments of Louisiana, Maryland, and Mississippi reported a total of seven clusters of gastroenteritis to the Viral

Received 21 October 1994; revised 4 January 1995.

Presented in part: 43rd Annual Epidemic Intelligence Service Conference: A Multistate Oyster-Associated Outbreak: The Maryland Experience, Atlanta, 18–22 April 1994.

Correspondence: Dr. Scott Dowell, Mailstop G17, Centers for Disease Control and Prevention, 1600 Clifton Rd., N.E., Atlanta, GA 30333.

Reprints: Dr. Roger Glass, Mailstop G04, Centers for Disease Control and Prevention, 1600 Clifton Rd., N.E., Atlanta, GA 30333.

The Journal of Infectious Diseases 1995;171:1497–503

0022-1899/95/7106-0015$01.00

Gastroenteritis Unit, CDC. In three of the clusters, the oysters were harvested from Grand Pass and contiguous areas of Cabbage Reef and Lake Borgne off the Louisiana coast. Information regarding these clusters was disseminated through notices to state epidemiologists, an FDA advisory to consumers, and press reports. Epidemiologists in North Carolina, Pennsylvania, Texas, and Florida also reported oyster-associated clusters of gastroenteritis. Oysters from the Grand Pass area beds are routinely distributed throughout the United States; in the week before closure, they had been distributed to at least 14 states.

Once it became apparent that all clusters might be linked to oysters harvested off the Louisiana coast during the second week of November, we made further efforts to identify other clusters that had gone unreported by tracing potentially contaminated oysters to their point of consumption.

Investigation of clusters of gastroenteritis. Ten clusters of illness were investigated: five in Maryland, two in North Carolina, and one each in Mississippi, Texas, and Pennsylvania. In seven of these clusters, we conducted cohort studies by obtaining a list of all persons who attended events where oysters were served and interviewing these persons by telephone or in person. Interviews were conducted using a standardized questionnaire covering demographic data, a complete list of menu items served at the event, and symptoms and timing of illness. Attack rates were calculated for specific food items. Fresh stool specimens were obtained within 72 h of illness, and blood samples were obtained within 5 days of illness and again 3–4 weeks after recovery.

A case was defined as a person who attended one of the events and became ill with vomiting or diarrhea (more than two loose stools a day) within 72 h of the event. Secondary cases were defined as household contacts who did not attend the event but had vomiting or diarrhea within 72 h of onset in a case-patient. Probable secondary cases were defined as those who attended the event, did not eat oysters, but developed illness >72 h after the event but within 72 h after onset of illness in a case-patient who was a household contact.

In three large gatherings, attended by >19,000 people, lists of attendees did not exist, and extensive case finding was thought to be impractical and unnecessary. For these events, we conducted case-control studies in which cases were identified by passive surveillance, and controls were friends who accompanied them to the event but remained well.

Additional specimens were collected from patients whose epidemiologic links to the contaminated oysters were uncertain. A gastroenteritis outbreak at a Maryland nursing home occurred at the same time as the oyster-associated outbreaks, raising the possibility of secondary spread from an oyster-associated case. A second group of specimens was received from patients with oyster-associated gastroenteritis, in which the origin of the oysters was initially unclear. Finally, specimens were received from one health department worker who became ill 24 h after packing but not eating the contaminated oysters and from a family member of one of the investigators who became ill 24 h after eating shucked oysters believed to be from safe harvest areas in Louisiana.

Tracing of oysters. Oysters are distributed in boxes that contain ~200 oysters each and are marked with an NSSP-approved tag showing the date and site of harvest. For each illness cluster, the restaurant or supplier of oysters was visited, and the boxes were traced back to the point of harvest, using harvest tags and shipping labels when available or invoices and accounting logs when tags were unavailable.

In addition, we attempted to use information collected by the state shellfish sanitation and FDA programs during their recall activities to trace the incriminated lots of oysters from the Grand Pass area forward through the system of suppliers to assess the completeness of the recall, to locate and destroy any remaining oysters, and to estimate the magnitude of the multistate outbreak.

Laboratory studies. Stool specimens collected in Cary-Blair media or buffered glycerol saline were tested for bacterial enteric pathogens, including *Salmonella*, *Shigella*, *Vibrio*, and *Campylobacter* species, by state or local laboratories. Larger-volume (25–100 mL) fecal specimens were stored at 4°C and examined by electron microscopy (EM) at CDC, using methods previously described [21]. Because SRSVs were observed in some of the specimens, those of adequate volume were tested for Norwalk virus and Norwalk-like viruses by reverse transcription (RT)–PCR [22]. When intensively stained bands were detected by RT-PCR, the PCR product was sequenced on an automated sequencer (ABI 373A; Applied Biosystems, Foster City, CA) [23], using the dideoxy nucleotide chain termination method of Sanger et al. [24].

Paired serum samples were tested for rises in IgG antibody to Norwalk virus using a recently described EIA with baculovirus-expressed antigen [25]. In two outbreaks, our investigation was delayed, so only single serum samples collected 7–21 days after the onset of symptoms were available. These specimens were tested for Norwalk virus–specific IgA, and the levels of IgA in this group were compared with those found in sera collected at the same time from persons living in the same area as one of the outbreaks (Baltimore) but who had not had recent gastroenteritis [25].

Results

Investigation of clusters of gastroenteritis. We investigated 10 clusters (from five states) associated with the consumption of oysters harvested in a small area off the Louisiana coast between 9 and 12 November 1993. The clusters were associated with events ranging from large festivals to family meals; 6 involved >20 people (table 1). No sporadic cases were reported. Some of the smaller clusters were detected among public health professionals aware of the ongoing investigation, including the illness in the family of one of the investigators.

Illness in all 10 clusters occurred within a 2-week period in mid-November (figure 1). Illness generally began 1–2 days after events where oysters were served. In addition, some secondary illness occurred within 2 weeks among family members who had neither attended the events nor eaten oysters.

In 5 clusters in which ≥10 ill people were interviewed, the

Table 1. Ten clusters of gastroenteritis associated with the consumption of Louisiana oysters, 1993.

State, county	Event	No. of attendees	No. of cases studied	Tagged origin of oysters*	Date of harvest
Maryland					
Talbot	Annual festival	~19,000	51†	GPA	9 Nov
Harford	Oyster roast	~120	16	GPA	9 Nov
Baltimore 1	Employee banquet	~180	4†	GPA	9 Nov
Baltimore 2	Fund-raiser	~400	15†	GPA	‡
Carroll	Family meal	12	3	GPA	12 Nov
Mississippi					
Harrison	Family meal	7	6	GPA	13 Nov§
North Carolina					
Cluster 1	Church supper	51	15	BB	8 Nov‖
Cluster 2	Church supper	21	12	GPA	18 Nov§
Pennsylvania					
Philadelphia	Snack	2	2	GPA	9 Nov
Texas					
Bexar	Restaurants	9	6	BB	9 Nov

* GPA = Grand Pass area, including Grand Pass, Cabbage Reef, Oyster Bayou, and Lake Borgne—all in same area off Louisiana coast; BB = Black Bay—separate area off Louisiana coast.

† Case-control studies; all others are cohort studies.

‡ Harvest tags were unavailable, but oysters were traced by invoices to distributor involved in other clusters (see figure 2).

§ Bought on this date; actual harvest date unknown.

‖ One of several Louisiana harvest tags recovered.

clinical presentations of patients were similar. Diarrhea was reported in 91% of all cases (range for individual clusters, 87%–100%), vomiting in 67% (range, 33%–80%), and fever in 44% (range, 33%–75%). The mean incubation time was 34 h (range, 31–39), and the mean duration of illness was 47 h (range, 32–59). Eight people were seen in hospital, and 1 required a 3-day stay to rule out appendicitis. No deaths were reported.

Association with oysters. Analysis of food-specific attack rates confirmed the preliminary impression that illness was associated with the consumption of oysters in all 10 outbreaks. In 8 clusters, illness was associated with eating raw oysters; in the other 2, steamed as well as raw oysters were implicated. This association of illness with oyster consumption was strong and consistent across all clusters, with an overall Mantel-Haenszel weighted odds ratio of 48 (95% confidence interval, 21–130; $P < .001$; table 2). No other food or beverage was independently associated with illness in any cluster.

In 1 outbreak, a waterfowl festival, illness was associated with consumption of oysters at one of five food stands serving oysters. This food stand served 12 boxes of Louisiana oysters prior to 2:30 P.M. and 6 boxes of Maryland oysters after 2:30 P.M. Saturday afternoon. This fact was not known to the consumers. Of 34 people who were ill and consumed a single meal at the food stand, all reported eating before 2:30 P.M., when the Louisiana oysters were served ($P < .001$, binomial distribution).

A weak dose-response relationship was detected in analysis of data combined from the 5 cohorts who ate only raw oysters; attack rates ranged from 40% among those who ate 1–5 oysters, 68% among those who ate 6–17 oysters, and 77% among those who ate ≥18 ($P = .16$, χ^2 test for linear trend). However, some persons reported illness after eating a single oyster, while others remained well after eating as many as 50. The overall attack rate of 62% did not vary significantly by age ($P = .76$, χ^2 test for homogeneity). Neither drinking beer (11/15 drinkers vs. 22/38 nondrinkers, $P = .3$) nor using cocktail sauce, which has an acid pH (4/7 who did vs. 28/45 who did not, $P = .6$), was protective. Among the 2 cohorts who attended events where both steamed and raw oysters were served, the attack rate for those who ate steamed oysters only was 54% and for those who ate both steamed and raw oysters was 56% ($P = .8$).

Tracing of oysters. In all 10 clusters, the implicated oysters were harvested from Louisiana coastal waters. For 8 of 10 clusters, the oysters could be traced to a single harvest area. This was the same harvest area implicated by investigation of oyster-related outbreaks of gastroenteritis in Louisiana [19]. From 4 of 5 Maryland events, we could trace the oysters back through a complex network of retailers, Maryland wholesalers, Maryland distributors, large shippers and packers, and Louisiana distributors, to the Grand Pass area (figure 2). In the fifth cluster (Baltimore 2), the trail stopped with a large shipper who supplied oysters to another outbreak-associated event. Three of the 5 non-Maryland events were linked to oysters from the Grand Pass area by harvest tags. The clusters in Texas and 1 cluster in North Carolina

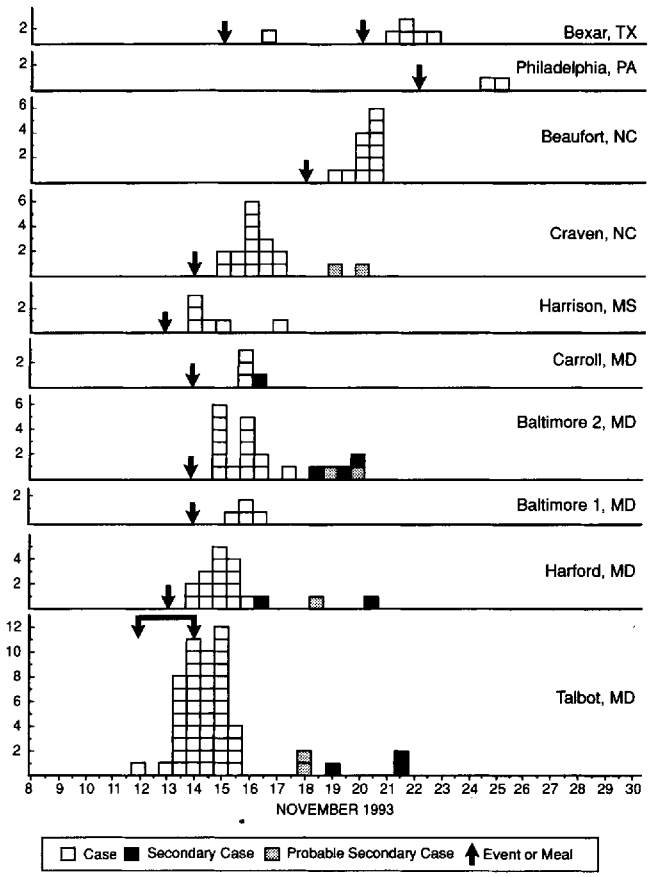

Figure 1. Epidemic curves from 10 clusters of gastroenteritis associated with Louisiana oysters. Case was defined as person who attended event and became ill with vomiting or diarrhea (>2 loose stools/day) within 72 h of event. Secondary cases were household contacts who did not attend event but had vomiting or diarrhea within 72 h of onset in case-patient. Probable secondary cases were those who attended event, did not eat oysters, but developed illness >72 h after event but within 72 h of onset of illness in case-patient who was household contact.

were linked to oysters from Black Bay, a harvest area near the Grand Pass area and worked by some of the same oyster gatherers.

In contrast to the success in tracing the implicated oysters backward to the harvest area, forward tracing of the ~23,000 boxes of oysters harvested from the implicated area in the 4-day period was largely unsuccessful. Inspectors could document which merchants had Grand Pass oysters confiscated or destroyed but could not account for most of the Grand Pass oysters harvested. Most state shellfish programs do not routinely collect information about the number of oysters or boxes destroyed during a recall or about the number of potentially contaminated boxes received and distributed prior to notification of the recall. Of the five states in which we conducted investigations, three instituted voluntary recalls in which licensed shellfish shippers were notified of the potentially contaminated oysters, and two relied on information released by the FDA and the state of Louisiana for alerting merchants and consumers. One of the five states contacted packing houses and some retailers in addition to licensed shippers, but none had detailed records available accounting for the potentially contaminated oysters in their state.

Laboratory studies. Stool samples were available from 6 of the 10 clusters and were negative for bacterial pathogens, including *Salmonella*, *Shigella*, *Vibrio*, and *Campylobacter* species. SRSVs were seen by EM in 9 (50%) of 18 specimens and in at least 1 sample from each of 4 clusters. Of 26 stool samples, 20 (77%), including specimens from all 6 clusters, were positive by RT-PCR (table 3).

In each of the 6 clusters positive by RT-PCR, the PCR products were sequenced to determine if the clusters could be traced to a common strain (figure 3). Sequences obtained from fecal specimens collected from patients in Maryland, Mississippi, North Carolina, and Texas were identical, consistent with a genogroup I SRSV [23], and were distinct from all Norwalk-like strains previously examined in our laboratory. This was the same sequence found in specimens from concurrent Grand Pass oyster-related outbreaks in Louisiana [19].

Of the additional specimens from patients not clearly linked to the outbreak, the sequence from the family member who ate shucked oysters was identical to the outbreak strain, while the sequence from specimens collected in the oyster-associated outbreak in Florida [26], the Maryland nursing home, and the person who packed the implicated oysters were all distinct from the outbreak strain and from each other.

Serologic test results from case-persons in 8 of the 10 clus-

Table 2. Exposure to oysters among ill and well persons in 10 clusters of gastroenteritis.

	Ill		Well		
Cluster	*n*	% who consumed oysters	*n*	% who consumed oysters	OR (95% CI)
Talbot, MD	51	88	51	10	69 (17–313)
Harford, MD	16	81	74	20	17 (4–89)
Baltimore 1, MD	4	100	8	25	Undefined
Baltimore 2, MD	15	87	8	25	20 (1.6–404)
Carroll, MD	3	100	9	11	Undefined
Harrison, MS	6	100	0	—	—
Cluster 1, NC	15	100	36	50	Undefined
Cluster 2, NC	12	100	9	44	Undefined
Philadelphia, PA	2	100	0	—	—
Bexar, TX	6	100	3	0	Undefined
Totals	130	92	198	24	48 (21–130)*

NOTE. OR = odds ratio, CI = confidence interval.
* Mantel-Haenszel weighted odds ratio.

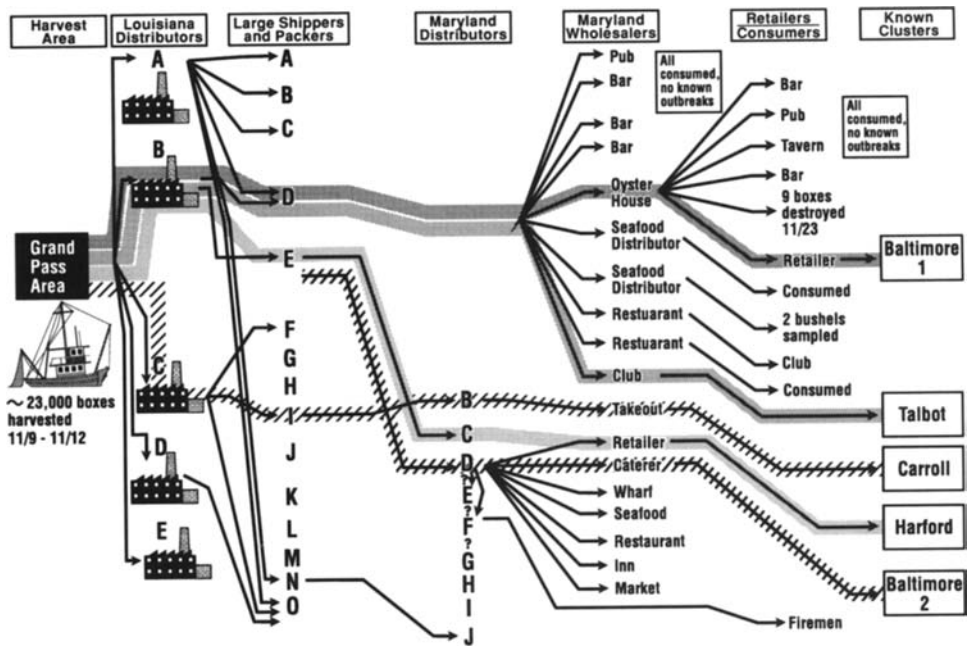

Figure 2. Results of backward tracing of oysters implicated in 5 clusters of gastroenteritis in Maryland. Oysters from clusters (at right) were traced through network of retailers, wholesalers, distributors, and shippers by use of harvest tags, shipping invoices, and sales logs. Four of 5 clusters were traced to Grand Pass area off Louisiana coast; fifth (Baltimore 2) was traced only as far as large Louisiana shipper.

ters provided consistent evidence that the outbreak was due to recent infection with a Norwalk-like virus (table 3). Of 25 paired serum samples tested from 6 clusters, 15 had a ≥4-fold rise in IgG antibody, and at least 1 individual in each cluster had a ≥4-fold rise in IgG. In the remaining 2 clusters, Norwalk-specific IgA levels in single sera from 9 of 14 cases but only 3 of 10 controls were >200 U (P = .09).

Oysters sampled from six lots linked to illness in 3 of the clusters were free of significant contamination by fecal coliforms, and no enterococci, *Clostridium perfringens*, or male-specific bacteriophage were detected in tests done at FDA.

Table 3. Laboratory evidence associating 10 clusters of gastroenteritis with a single strain of Norwalk-like virus.

Cluster	Serology	EM (SRSV)	RT-PCR	Sequence 1
Talbot, MD	5/10*	1/4	7/10	2/2
Harford, MD	4/6*	2/8	5/8	3/3
Baltimore 1, MD	2/2*	3/3	3/3	2/2
Baltimore 2, MD	5/7†	—	—	—
Carroll, MD	1/2*	—	—	—
Harrison, MS	—	—	1/1	1/1
Cluster 1, NC	4/7†	—	—	—
Cluster 2, NC	2/3*	3/3	3/3	2/2
Philadelphia, PA	1/2*	—	—	—
Bexar, TX	—	—	1/1	1/1
Totals	15/25*	9/18	20/26	11/11

NOTE. Data are no. positive/no. tested. EM, electron microscopy; SRSV, small round-structured viruses; RT-PCR, reverse transcription–polymerase chain reaction.

* Paired sera: 4-fold rise in IgG.

† Single sera: IgA >200 units (3/10 controls also had high levels of IgA).

Attempts to detect Norwalk virus in these oysters by using RT-PCR are ongoing.

Discussion

This multistate outbreak of Norwalk virus gastroenteritis was traced by epidemiologic investigation, commercial oyster tags, and genetic analysis to the consumption of oysters harvested at a common source. The 130 ill persons from five states identified in our investigation probably represent a small proportion of the total number of persons affected. It is likely that many persons failed to link their illness to oysters

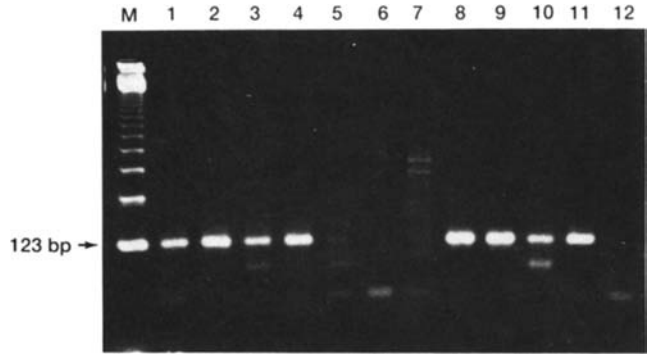

Figure 3. UV-illuminated agarose gel showing 123-bp polymerase chain reaction product from 8 fecal specimens from 3 clusters of gastroenteritis associated with Louisiana oysters. By lane: M, mass marker; 1–3, North Carolina; 4 and 5, Maryland; 6, astrovirus; 7, rotavirus; 8–10, Maryland; 11, Norwalk prototype; 12, water control. 3% agarose gel with 0.5 μg of ethidium bromide/mL was run at 140 V for 90 min.

or to report it to the health department. About 23,000 boxes (~4,600,000 oysters) were harvested from the implicated beds over the 4-day period and distributed rapidly through a complex nationwide seafood distribution system to retailers in at least 14 states. If the remaining oysters were contaminated and eaten raw or inadequately cooked and an average of 12 oysters was consumed per individual (the median from these 10 clusters), >300,000 people would have been exposed, of whom as many as 186,000 may have become ill (attack rate, 62%).

The NSSP requirement to keep harvest tags from boxes of oysters for 90 days after sale allowed us to trace the oysters back to the harvest area in 9 of 10 outbreaks. However, our investigation would have been more complete and the recall of potentially contaminated oysters more effective if oysters could have been traced forward from the Grand Pass area to the consumer. The location of most of the 23,000 boxes of potentially contaminated oysters could not be determined quickly or completely, despite efforts by FDA, state health departments, and CDC. Inspectors focused on notifying seafood merchants and confiscating existing shellfish stock and not on documenting the number of oysters destroyed or the location of contaminated oysters already sold.

Since shellfish may be shucked, frozen, and sold at a later date, contaminated oysters may be available to consumers for months following outbreaks such as this. In a large outbreak of Norwalk gastroenteritis in Australia, for example, 2 further clusters of illness occurred 6 months after the original clusters and were associated with consumption of frozen oysters from the same lot [7]. The illness in the family members of one of our investigators after eating shucked oysters from a jar further illustrates this risk.

The ability to forward trace oysters and identify the source of shucked oysters in the jar may prevent such cases. However, among the five states we investigated, only one state shellfish program contacted shucking or packing houses about the recall. Improved methods for forward tracing of contaminated shellfish were proposed by FDA in 1994 as the Hazard Analysis Critical Control Point regulations. This plan would place primary responsibility for ensuring the safety of shellfish on the industry, would require processors to maintain permanent records of each lot sold, and would allow for increased federal oversight, including the seizure and destruction of any untagged shellfish. Other proposals to require the labeling of shucked oysters with their point of origin are being considered for inclusion in the NSSP (Creasey R, FDA, personal communication).

Molecular epidemiology with sequence analysis was helpful in defining the extent of this outbreak. It enabled us to distinguish nonoutbreak cases in instances in which the epidemiologic links were unclear and to link unequivocally cases from many states, highlight the potential for continued illness from shucked oysters, and indicate that the outbreak included Texas, all based on sequence analysis of a single common outbreak strain.

Currently, it is impossible to ensure the safety of shellfish, the largest source of protein consumed raw. NSSP regulations concerning the maximum levels of fecal coliforms permitted in oyster meat provide an imperfect proxy measure for contamination with viruses. In this outbreak, the oysters had acceptably low levels of fecal coliforms but were apparently contaminated with Norwalk virus. The finding of true viral contamination in the absence of fecal coliform indicators and the implications for control of viral outbreaks have been noted [1]. Techniques such as PCR, which could make it possible to screen for viruses in addition to bacteria and thus provide greater protection from contaminated shellfish, clearly need to be used. Enforcement of existing NSSP regulations and simplification of tracing and recall may also decrease the risk from contaminated shellfish.

In summary, backward tracing of oysters to their site of harvest combined with sequence studies of virus isolates confirmed that oysters from a common harvest bed caused a large multistate outbreak of gastroenteritis. The current recall system should be carefully evaluated to determine its efficacy in preventing oysters from reaching consumers, and efforts should be made to improve forward tracing and thorough recall of contaminated shellfish.

Acknowledgments

We thank Scott Rippey, Robert Creasey, Kevin Calci, William Burkhardt, Tom Billy, Fred Shenk, George Hoskin, Dick Dees, Ed Steele, and David Dressel (FDA); Sarah Stine and John O'Connor (CDC); Linda Pollock (Mississippi Department of Health); Beverly Ray (Texas Department of Health); Debra Koenig (Philadelphia Regional Office of FDA); and local health department personnel in Maryland, North Carolina, Mississippi, Texas, and Pennsylvania for help with investigations of outbreaks in their states and Mel Kohn, Tom Farley, Louise McFarland, and others in Louisiana for sharing the results of their thorough investigations.

References

1. Richards GP. Outbreaks of shellfish-associated enteric virus illness in the United States: requisite for development of viral guidelines. J Food Protect **1985**;48:815–23.
2. Lowry PW, McFarland LM, Peltier BH, et al. *Vibrio* gastroenteritis in Louisiana: a prospective study among attendees of a scientific congress in New Orleans. J Infect Dis **1989**;160:978–84.
3. Lumsden LL, Hasseltine HE, Leak JP, Veldee MV. A typhoid fever epidemic caused by oyster-borne infection. Public Health Rep Suppl **1925**;50:1–102.
4. Holmberg SD, Wachsmuth IK, Hickman-Brenner FW, Blake PA, Farmer JJ III. *Plesiomonas* enteric infections in the United States. Ann Intern Med **1986**;105:690–4.
5. Mason JO, McLean WR. Infectious hepatitis traced to the consumption of raw oysters: an epidemiologic study. Am J Hyg **1962**;75:90–111.

6. Kaplan JE, Gary GW, Baron RC, et al. Epidemiology of Norwalk gastroenteritis and the role of Norwalk virus in outbreaks of acute nonbacterial gastroenteritis. Ann Intern Med **1982**;96:756–61.
7. Murphy AM, Grohmann GS, Christopher PJ, Lopez WA, Davey GR, Millsom RH. An Australia-wide outbreak of gastroenteritis from oysters caused by Norwalk virus. Med J Aust **1979**;2:329–33.
8. Grohmann GS, Greenberg HB, Welch BM, Murphy AM. Oyster-associated gastroenteritis in Australia: the detection of Norwalk virus and its antibody by immune electron microscopy and radioimmunoassay. J Med Virol **1980**;6:11–9.
9. Gunn RA, Janowski HT, Lieb S, Prather EC, Greenberg HB. Norwalk virus gastroenteritis following raw oyster consumption. Am J Epidemiol **1982**;115:348-51.
10. Gill ON, Cubitt WD, McSwiggan DA, Watney BM, Bartlett CLR. Epidemic of gastroenteritis caused by oysters contaminated with small round structured viruses. Br Med J **1983**;287:1532–4.
11. Morse DL, Guzewich JJ, Hanrahan JP, et al. Widespread outbreaks of clam- and oyster-associated gastroenteritis. Role of Norwalk virus. N Engl J Med **1986**;314:678–81.
12. Sekine S, Okada S, Hayashi Y, et al. Prevalence of small round structured virus infections in acute gastroenteritis outbreaks in Tokyo. Microbiol Immunol **1989**;33:207–17.
13. Truman BI, Madore HP, Menegus MA, Nitzkin JL, Dolin R. Snow mountain agent gastroenteritis from clams. Am J Epidemiol **1987**;126:516–25.
14. Kawamoto H, Hasegawa S, Sawatari S, et al. Small, round structured viruses (SRSVs) associated with acute gastroenteritis in Gifu, Japan. Microbiol Immunol **1993**;37:991–7.
15. Appleton H, Buckley M. Virus-like particles in winter vomiting disease. Lancet **1977**;19:409–11.
16. Watson RW, Smelsey SO, Clark MH, Cassidy EJ. Typhoid fever outbreak associated with shellfish from Portugal. California Morbid **1976** May 28;20:1.
17. Ingersoll E. The history and present condition of the fishery industries. The oyster industry. Tenth Census of the United States. Washington, DC: Department of the Interior, **1881**:124.
18. Guzewich JJ, Morse DL. Sources of shellfish in outbreaks of probable viral gastroenteritis: implications for control. J Food Protect **1986**;49:389–94.
19. Kohn MA, Farley TA, Ando T, et al. A large outbreak of Norwalk virus gastroenteritis associated with eating raw oysters: implications for maintaining safe oyster beds. JAMA **1995**;273:466–71.
20. Ando T, Monroe SS, Gentsch JR, Jin Q, Lewis DC, Glass RI. Detection and differentiation of antigenically distinct small round-structured viruses (Norwalk-like viruses) by reverse transcription–PCR and Southern hybridization. J Clin Microbiol **1995**;33:64–71.
21. Khan AS, Moe CL, Glass RI, et al. Norwalk virus–associated gastroenteritis traced to ice consumption aboard a cruise ship in Hawaii: comparison and application of molecular-based assays. J Clin Microbiol **1994**;32:318–22.
22. Moe CL, Gentsch J, Ando T, et al. Application of PCR to detect Norwalk virus in fecal specimens from outbreaks of gastroenteritis. J Clin Microbiol **1994**;32:642–8.
23. Ando T, Mulders MN, Lewis DC, Estes MK, Monroe SS, Glass RI. Comparison of the polymerase region of small round structured virus strains previously classified in three antigenic types by solid-phase immune electron microscopy. Arch Virol **1994**;135:217–26.
24. Sanger F, Nicklen S, Coulson AR. DNA sequencing with chain-terminating inhibitors. Proc Natl Acad Sci USA **1977**;74:5463–7.
25. Monroe SS, Stine SE, Jiang XI, Estes MK, Glass RI. Detection of antibody to recombinant Norwalk virus antigen in specimens from outbreaks of gastroenteritis. J Clin Microbiol **1993**;31:2866–72.
26. Centers for Disease Control and Prevention. Viral gastroenteritis associated with consumption of raw oysters—Florida, 1993. MMWR Morbid Mortal Wkly Rep **1994**;43:446–9.