A Multifocal Outbreak of Hepatitis A Traced to Commercially Distributed Lettuce

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Abstract: From February 1 through March 20, 1988, 202 cases of hepatitis A were reported in and around Jefferson County, Kentucky. The epidemic curve indicated a common-source exposure. However, there was no apparent single source of exposure from a restaurant, or community gathering; nor was there a geographic clustering by residence. Cases were mainly adults 20–59 years old (89 percent); 51 percent were female. A case-control study using neighborhood controls found that factors associated with hepatitis A were: having eaten downtown (odds ratio [OR] = 4.0) and having dined at any one of three restaurants (OR = 21.0). Case-control studies of patrons of two of these restaurants found that eating green salad was strongly associated with acquiring hepatitis A: OR = 11.6 and OR = 4.4. The three implicated restaurants accounted for 71 percent of the cases. All three restaurants were supplied by the same fresh produce distributor; however, investigation suggested that contamination most likely occurred prior to local distribution. This outbreak of hepatitis A is the first in the United States apparently associated with fresh produce contaminated before distribution to restaurants, and raises important public health issues regarding the regulation of fresh produce. (*Am J Public Health* 1990; 80:1075–1080.)

Introduction

In 1988, 26,600 cases of hepatitis A were reported in the United States.[1] During 1983–88 the incidence of reported cases of hepatitis A increased from 9.2 to 10.9 per 100,000 population, representing the first increase in hepatitis A in more than a decade.[1–3] An estimated 1,000 cases are associated with suspected food- or water-borne outbreaks of hepatitis A each year.[3]

Previous investigations of common-source food-borne outbreaks of hepatitis A have described unifocal outbreaks in which a single location of food consumption (such as a restaurant) was the site of the outbreak; generally, a food handler, recently infected with hepatitis A virus (HAV) and working at that site, was implicated as the source of contamination of the food.[4–6] There have also been reports of outbreaks involving more than one restaurant; however, a food handler was implicated as the source of contamination at each restaurant.[4,7] The major multifocal food-borne outbreaks of hepatitis A due to the contamination of food before distribution to a restaurant have involved shellfish harvested from contaminated bays.[8,9] Reports from the United Kingdom have suggested that certain commercially processed foods (such as frozen raspberries) may have been associated with the transmission of HAV.[10,11]

This is the first report of a hepatitis A outbreak in the United States associated with unprocessed fresh produce contaminated before distribution to restaurants.

Methods

From February 1 through March 20, 1988, a widespread outbreak of hepatitis A affected 202 residents of Jefferson County, Kentucky (1986 intercensal population estimate, 681,066) and the surrounding area. The Louisville-Jefferson County Board of Health, the Kentucky Department of Health, and the Centers for Disease Control initiated a series of investigations to determine the risk factors for the transmission of HAV.

Case Identification

A case was defined as a person who had onset of an illness compatible with viral hepatitis from February 1 through March 20, 1988, and either a positive serologic test for immunoglobulin M (IgM) antibody to HAV (IgM anti-HAV) or a physician diagnosis of hepatitis A. Cases were ascertained through reports by physicians to the Louisville City-Jefferson County Health Department. Serologic testing for IgM anti-HAV was performed by private and hospital-based laboratories in Louisville. All cases were interviewed by telephone to obtain demographic information, date of onset and clinical course of illness, work location, and place of residence.

Community Food and Water Exposure Study

Because the epidemic curve indicated a common source of exposure, a case-control study using neighborhood controls was performed to identify the location of the common source of food or water in the community. A random sample of cases who resided in Jefferson County were matched with controls by neighborhood and by age within 10 years. One control who lived within 10 houses in either direction from each case was selected randomly by using a reverse telephone directory. Eligible controls had no history of hepatitis; no undiagnosed illness during February or March, with any two of the following symptoms: jaundice, nausea, vomiting, and abdominal discomfort; no receipt of immune globulins within the past six months; and no household or sexual contact with a person with hepatitis A since January 15, 1988. Cases and controls were interviewed by telephone to obtain demographic information, history of food and water exposures at home and work, and exposures at restaurants, stores, parties, and community gatherings during January 15–31.

Restaurant Food Exposure Studies

Because the neighborhood study found that eating at any one of three restaurants was associated with acquiring hepatitis A, two of the restaurants (A and B) were selected as sites for the investigation of the source of HAV. Restaurants

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A and B were selected because they accounted for most of the cases, and no case had patronized both restaurants. Restaurant A, located in a downtown professional district, was primarily a lunch business, serving sandwiches, chef salads, and soup. Restaurant B, located in the outskirts of the city, was primarily a dinner restaurant, with standard American fare and a salad bar.

The period of risk of exposure at these restaurants was considered to be January 15–31, one month (the average incubation period for HAV) preceding the period of peak case incidence (February 15–28). Evaluation of the dates of exposure of patrons who ate only once at one of these restaurants (A or B) and ate at no other restaurants in Jefferson County during the month preceding their illness confirmed that January 15–23 was the period of high risk.

For each restaurant study, eligible cases and controls had dined at the designated restaurant (A or B) during January 15–31; controls also had to meet the four eligibility criteria described for controls in the neighborhood study. For the study of restaurant A patrons, unmatched controls were randomly selected from a list of coworkers of each case. For restaurant B, controls were meal companions of the cases. Telephone interviews of cases and controls obtained demographic information and history of food consumption, including the frequency of eating particular foods.

Investigating the Source of Contamination

Based on the results of the restaurant studies, which implicated fresh produce obtained from a single local distributor, the Food and Drug Administration traced the source of shipments of food received by the distributor. In collaboration with the Louisville-Jefferson County Board of Health, the Louisville Water Company evaluated the water supply system.

Statistical Methods

In the community case-control study, exact confidence limits for the odds ratios were calculated by using standard procedures for the binomial distribution.[12] MCSTRAT (a procedure in Statistical Analysis Systems), which is designed for matched case-control data, was used to estimate the variances of the odds ratios in multivariate analysis.[13] For the restaurant case-control studies, variances for the odds ratios were estimated by using the method described by Cornfield.[12]

Results

Outbreak

From February 1 through March 20, 1988, 202 reported cases of hepatitis A met the case definition; 99 percent were tested and confirmed as IgM anti-HAV positive. Cases included 172 Jefferson County residents, and 30 others who had histories of exposures in Jefferson County during the last two weeks in January.

During the 13 months preceding the epidemic, only 12 cases of hepatitis A had been reported in Jefferson County. During the epidemic, there was no increase in the number of cases reported in any of the surrounding counties in Kentucky or Indiana, except for the cases who had known exposures in Jefferson County.

The epidemic curve, with a sharp peak and most of the cases occurring within the two-week period, suggested a common-source exposure (Figure 1). There was no apparent single source of exposure from a restaurant or community gathering and no geographic cluster by location of residence; only seven families had more than one case. Cases clustered

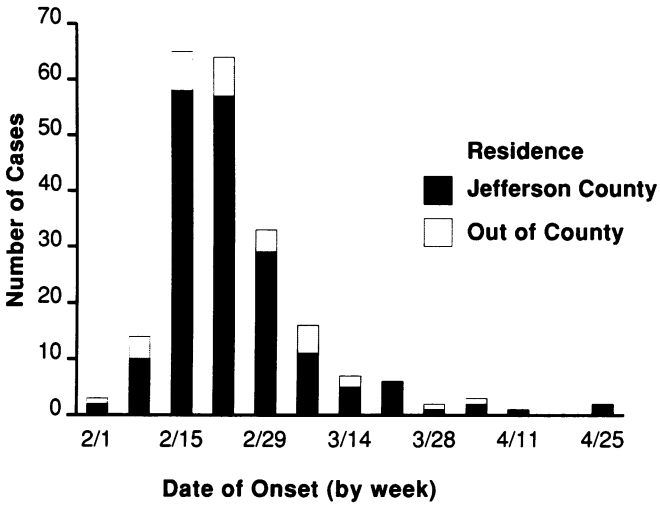

FIGURE 1—Hepatitis A Cases by Date of Onset of Symptoms, Jefferson County, Kentucky, February 1–April 30, 1988

by work location, with 33 percent of the cases working in the downtown area.

Of the cases residing in Jefferson County, the mean age was 38 years (range: 1 to 75 years), 89 percent were 20 to 59 years old, and 51 percent were female. The overall attack rate was 25 cases per 100,000 residents of Jefferson County. The highest attack rate was for adults 20 to 59 years old (40 cases per 100,000 persons), with the highest age-specific attack rate occurring among persons 40 to 49 years old (62 cases per 100,000). Of the 172 cases, 91 percent were jaundiced and 23 percent were hospitalized. HAV infection may have contributed to two deaths (for a case-fatality ratio of 1 percent), including a 60-year-old man who required a liver transplant five months after the onset of illness and died two months later, and a 53-year-old man with a history of alcohol abuse, who died three weeks after onset of illness.

Community Food and Water Exposures

In the study of community food and water exposures, 30 neighborhood case-control pairs were interviewed. A comparison of cases and their matched controls indicated that 70 percent of the pairs had similar levels of income and education, and all were White and non-Hispanic.

Exposures associated with acquiring hepatitis A in univariate analysis included (Table 1) working downtown (odds ratio [OR] = 5.0), having eaten downtown (OR = 4.0), having dined at any one of three (A, B, or C) restaurants (OR = 21.0), and having eaten salad at any restaurant (OR = 6.0). Two of the three implicated retaurants were located downtown. The association between acquiring hepatitis A and having dined at these three restaurants persisted when results were adjusted separately for history of work downtown, and for potential confounders (e.g., income and education).

Restaurant Food Exposures

Restaurant A: In the study of patrons of restaurant A, 38 (100 percent) of the eligible cases were interviewed, and 36 fellow office workers were interviewed as controls. The study found that eating green salad was associated with an 11.6-fold increased risk of acquiring hepatitis A (Table 2). Consumption of other foods was not associated with an increased risk of disease. The risk of acquiring hepatitis A increased as the frequency of consumption of green salads increased from a

TABLE 1—Neighborhood Study of Community Food and Water Exposures

Exposure	% Cases exposed (n = 30)	% Controls exposed (n = 30)	Matched odds ratio	95% confidence interval
Patronize restaurants				
A, B, or C	77	10	21.0	3.4, 832.3
A	30	0	∞	2.0, ∞
B	33	7	9.0	1.2, 399.0
C	23	3	∞	1.1, ∞
Work downtown	40	13	5.0	1.1, 46.6
Eat downtown	47	17	4.0	1.1, 21.7
Eat salad at any restaurant	83	50	6.0	1.3, 49.0
On public water supply	100	97	∞	—
Patronize grocery store 1	70	73	0.8	0.1, 4.2
Patronize grocery store 2	30	23	1.4	0.4, 5.3
Drink water at workplace	77	70	1.5	0.4, 7.2
Use ice machine at work	37	23	1.7	0.6, 5.6

TABLE 2—Restaurant A: Study of Food Exposures

Food Consumed	(%) Cases exposed	(%) Controls exposed	Odds ratio	95% confidence interval
Green salads	32/38 (84)	11/35 (31)	11.6	3.4, 42.8
Soup	26/38 (68)	20/36 (56)	1.7	0.6, 5.0
Prepared salads	16/38 (42)	13/36 (36)	1.3	0.5, 3.7
Iced drinks	9/38 (24)	11/36 (31)	0.7	0.2, 2.2
Sandwich	22/38 (58)	32/36 (89)	0.2	0.04, 0.7
Dressing (if ate salad)	26/32 (81)	11/11 (100)	0.0	0.0, 2.7
Garnish on sandwich (among nonsalad eaters)	6/6 (100)	13/24 (54)	∞	0.8, ∞
Green salads, or garnish on sandwich	38/38 (100)	24/36 (67)	∞	0.0, ∞

1.0-fold risk for those never ordering salad, to an 8.0-fold risk for those sometimes ordering salad, to an 18.0-fold risk for those always ordering salad ($p < .001$, Mantel-Haenszel trend test).

Among those not eating salad, there was an association between disease and consumption of a sandwich with a lettuce or a tomato garnish ($p = .046$). All cases ordered either a green salad or a sandwich with a garnish. The high correlation between ordering a lettuce and a tomato garnish on a sandwich (.74) precluded analysis of the risk of disease associated with a single vegetable.

Restaurant B: In the study of patrons of restaurant B, 48 (100 percent) of the eligible cases and 43 controls were interviewed. Results indicated that eating salad from the salad bar was associated with a 4.4-fold risk of infection and that ordering either the salad bar or a tossed salad with a main dish was associated with a 6.7-fold risk of disease (Table 3). No other menu item was associated with increased risk.

Patrons of restaurant B were interviewed about the consumption of specific food items from the salad bar; however, no single item could be implicated. The high degree of correlation between ordering two given items from the salad bar precluded further analysis of the risk associated with a single salad bar item. Among those eating salad, salad dressing was not associated with increased risk of infection.

Tracing the Source of Contaminated Fresh Produce

During January 15–30, 71 percent of the cases reported exposures at any one of the three implicated restaurants. The peak of the epidemic curve associated with each of these restaurants occurred the same week. Three of the reported cases were food handlers at restaurant A, and one was a food handler at restaurant B; however, the dates of onset of illness among these employees were within the main part of the epidemic curve, not consistent with transmission to their customers, and the employees did not work at other restau-

TABLE 3—Restaurant B: Study of Food Exposures

Food consumed	Cases exposed* n (%)	Controls exposed* n (%)	Odds ratio	95% confidence interval
Salad bar	40/48 (83)	23/43 (53)	4.4	1.5, 12.8
Salad bar or tossed salad	43/46 (93)	28/41 (68)	6.7	1.6, 32.6
Fish	4/45 (9)	3/40 (8)	1.2	0.2, 7.4
Seafood	3/44 (7)	4/41 (9)	0.7	0.1, 3.9
Meat	25/44 (57)	25/37 (68)	0.6	0.2, 1.7

*If a respondent did not answer a question, the respondent was excluded from analysis for that exposure.

rants. The remainder of the employees at restaurant A were tested and were negative for IgM anti-HAV.

The epidemiologic studies implicated salad as the vehicle of transmission, and results of the study at restaurant A suggested that either lettuce or tomatoes were the contaminated produce. Lettuce was considered the most probable vehicle of transmission because all the implicated types of salads contained lettuce, and because lettuce, as compared with other produce such as tomatoes, is harder to clean thoroughly by rinsing. Since all three of the implicated restaurants served iceberg lettuce, and two of the three restaurants served only iceberg lettuce, the suspected vehicle was iceberg lettuce.

All three restaurants were supplied by the same local fresh produce distributor. (Less than 5 percent of food service establishments in Jefferson County were supplied by the implicated distributor.) At the implicated distributor, no hepatitis A cases were identified among the workers, and the handling of produce was minimal. Produce was generally not unpacked from the crates in which it was shipped and not washed or processed. Therefore, contamination most likely occurred before local distribution.

Shipments of iceberg lettuce that would have been received by the local distributor in Louisville January 11–16 were traced to four domestic suppliers; however, no information was available regarding the farm source of lettuce provided by these suppliers. Just before the outbreak in January of 1988, the importation of Mexican iceberg lettuce increased 10-fold[14] because of drought in the Summer of 1987 in the United States (Figure 2). Mexican iceberg lettuce was observed in Louisville by local United States Department of Agriculture (USDA) inspectors during the last two weeks in January (J. Sullivan, Louisville-Jefferson County Board of Health, personal communication, March 1988). However, there is no information available to determine if Mexican imported produce was received by the local distributor or its suppliers.

Investigation of the Water System

The results of bacteriologic sampling of the water distribution system were within normal limits during the months of January and February 1988. No relationship was found between the geographic distribution of cases and the water distribution system or events such as water company construction, repair, and unusual flow disturbances.

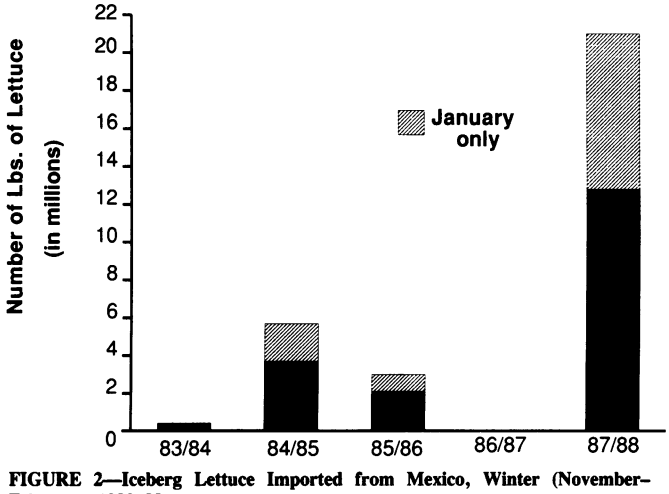

FIGURE 2—Iceberg Lettuce Imported from Mexico, Winter (November–February: 1983–88
SOURCE: Agricultural Marketing Service, US Department of Agriculture

Discussion

This common-source outbreak of hepatitis A was unusual in that there was no single source of exposure from a restaurant or community gathering, nor was there geographic clustering by neighborhood. The epidemic curve, with a sharp peak and most of the cases occurring within a two-week period, indicated a common source of exposure. The age distribution (88 percent of the cases in adults 20 to 59 years old) was atypical of community person-to-person spread and suggested that the persons primarily affected by the epidemic were a "working" cohort.

Case-control studies found that the outbreak was due to contaminated salad served by several restaurants. Because serum specimens of controls were not tested, it is possible that some controls may have been immune or asymptomatic cases. For this possibility to have accounted for the observed associations, there would have to have been an association between exposure, and either immunity or expression of illness. However, without such an assumption (for which there is no basis), the presence of immune controls or asymptomatic cases would tend to produce a conservative estimate of the associations observed.

This is the first report of an outbreak of hepatitis A in the United States associated with a vegetable product which was contaminated prior to distribution to restaurants. At least three restaurants were involved in the outbreak, each accounting for no more than one-third of the cases. Foodhandlers at the restaurants were unlikely to have been the source of the epidemic for two reasons. First, no index case was identified at any of the restaurants. Although serosurveys were not performed at all restaurants, most (76–97 percent) of HAV infections among adults are symptomatic.[14] Second, because the epidemic curve was unimodal, it was unlikely that foodhandlers at each restaurant could have accounted for transmission of HAV to their clientele. Contamination of the produce most likely occurred before local distribution to the restaurants, as there was no hepatitis A case identified among the workers, and there was minimal handling of produce at the local distributor which supplied the three restaurants.

The most likely vehicle of transmission was iceberg lettuce; however, the exact farm source of contaminated lettuce could not be determined. There was no evidence of concurrent outbreaks in the United States associated with lettuce contaminated before local distribution, and the focal nature of the outbreak suggested that either a limited supply of lettuce grown in the United States or imported lettuce had been contaminated. During the peak period of importation in January 1988, Mexican lettuce accounted for only 1 percent of the total US consumption,[15] with any single grower accounting for a small fraction of the total. Contamination of the produce may have occurred in the fields from contaminated water used for growing or irrigation, or from the use of night soil (excrement removed from a cesspool or privy and used as fertilizer). Alternatively, contamination may have occurred during the shipping process if riders were transported in the back of the truck with the produce.

Lettuce contaminated before distribution to food-service facilities also has been associated with two recent large epidemics of shigellosis.[16,17] In these outbreaks, contamination was believed to have occurred in the field or a

warehouse,[16] and in a food-processing plant.[17] Laboratory studies have demonstrated the survival of HAV (in feces) and *Shigella* (in a variety of nonacidic foods) for several weeks at 25 °C.[18,19] These outbreaks underscore the importance of proper sanitation facilities, and good hygiene of workers at each step of the food handling chain.

The timing of the marked increase in imported lettuce in relation to this outbreak, which was associated with fresh produce contaminated before local distribution, raises public health concerns regarding the regulation of imported fresh produce. The purity of water supply used in growing, availability of sanitation facilities to workers, and possible use of night soil by foreign lettuce growers, have not been determined. Imported lettuce is not routinely examined for evidence of fecal contamination at the port of entry to the United States. Imported unprocessed lettuce is exempt from US Customs requirements to label the country of origin on the imported article itself.[20] Although the country of origin must be marked on the outermost container of lettuce that reaches the ultimate purchaser,[20] containers such as supermarket bins and rubberbands holding fresh produce are not subject to marking; if produce should reach the ultimate purchaser without a container, there is no requirement to display the country of origin (M. Amernick, Esq., US Customs, personal communication, October 1989).

Moreover, because there are no federal requirements to label the name of the farm on either imported or domestic lettuce that reaches the ultimate purchaser, and because more than one farm can supply any supplier, it may be impossible to trace lettuce to the growing site during an outbreak, as was the case in this epidemic.

During 1983–88, for the first time in over a decade, there has been a nationwide increase in reported cases of hepatitis A[1–3]; the cause of the increase is not known. This multifocal epidemic of hepatitis A is the first report of an outbreak in the United States associated with a vegetable contaminated before distribution to restaurants, and raises important public health concerns regarding the regulation of both domestic and imported fresh produce.

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