Molecular Epidemiology of Foodborne Hepatitis A Outbreaks in the United States, 2003

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Background. Molecular epidemiologic investigations can link geographically separate foodborne hepatitis A outbreaks but have not been used while field investigations are in progress. In 2003, outbreaks of foodborne hepatitis A were reported in multiple states.

Methods. Case-control studies were conducted in 3 states. Hepatitis A virus was sequenced from serologic specimens from individuals associated with outbreaks and from individuals concurrently ill with hepatitis A in nonoutbreak settings in the United States and Mexico.

Results. Case-control studies in Tennessee (TN), North Carolina (NC), and Georgia (GA) found green onions to be associated with illness among restaurant patrons (TN: odds ratio [OR], 65.5 [95% confidence interval [CI], 8.9–482.5; NC: OR, 2.4 [95% CI, 0.3–21.9]; GA: OR, 20.9 [95% CI, 3.9–110.3]). Viral sequences from TN case patients differed by 2 nt, compared with those from case patients in NC and GA. A third sequence, differing from the TN and GA/NC sequences by 1 nt, was identified among case patients in a subsequent outbreak in Pennsylvania. Each outbreak sequence was identical to ≥1 sequence isolated from northern Mexican resident(s) with hepatitis A. The sources of green onions served in restaurants in TN and GA were 3 farms in northern Mexico.

Conclusions. Ongoing viral strain surveillance facilitated the rapid implementation of control measures. Incorporation of molecular epidemiologic methods into routine hepatitis A surveillance would improve the detection of hepatitis A outbreaks and increase our understanding of hepatitis A epidemiology in the United States.

In the United States, hepatitis A virus (HAV) is transmitted primarily by person-to-person contact, but the source of infection for ~50% of reported cases is not identified. Foodborne outbreaks are recognized as the source of infection for <5% of reported cases. However, this proportion may be an underestimate, because routine surveillance may not detect cases related to foodborne transmission, and cases may accrue gradually or be dispersed among a number of public health jurisdictions [1].

Incorporation of molecular subtyping methods into surveillance has greatly improved detection of outbreaks and helped to define the epidemiology of other foodborne pathogens [2]. Molecular epidemiologic studies of hepatitis A, which combine HAV sequencing and traditional epidemiologic approaches, have been used to define the distribution of HAV strains and to clarify retrospectively whether case patients who were part of suspected multifocal foodborne outbreaks might be linked [3–16]. However, viral sequencing is time consuming and not widely available, and it has not previously been integrated into an ongoing epidemiologic investigation of a hepatitis A outbreak.

Hepatitis A is a reportable disease in the United
States. In September 2003, hepatitis A outbreaks were reported to the Centers for Disease Control and Prevention (CDC) from state health departments in Tennessee (TN), North Carolina (NC), and Georgia (GA). In each state, preliminary investigations suggested clustering of reported cases among patrons of 3 specific, unrelated restaurants. To investigate the outbreaks and determine their source(s), we conducted a molecular epidemiologic investigation that included separate case-control studies in each state and the simultaneous molecular characterization of HAV strains from identified cases. We further compared viral types from outbreak-related case patients in each state, as well as those from individuals identified in a subsequent foodborne outbreak that occurred in Pennsylvania (PA) [17] in October 2003, with viral types collected from individuals with hepatitis A identified through ongoing surveillance efforts in the United States and Mexico.

METHODS

Outbreak Investigation

Case definition. A case patient was defined as a person with onset of an acute illness with clinical symptoms consistent with hepatitis A between 3 August and 11 October 2003 and serologic evidence of acute infection (IgM antibody to HAV).

Case finding. Local and state health departments notified health-care providers and the public of the outbreaks by issuing press releases to local media and through physician and public-health reporting networks. Cases were identified from reports by laboratories and physicians to local health departments. As the investigations proceeded, health departments in other states were informed of the outbreaks and investigation findings by means of health advisories on the Epidemic Information Exchange network.

Case-control studies. Separate case-control studies were conducted in each state concurrently with the identification of hepatitis A cases. Case patients who met the above case definition and who ate in restaurant A, B, or C during the 2–6 weeks before illness onset were contacted for participation in the studies. Control subjects were identified by asking case patients to list names of persons with whom they had eaten at the indicated restaurant (concurrent dining companions) and/or from credit card receipts of patrons dining during the same time period.

Case patients and control subjects in each study were interviewed using a standardized questionnaire. Information collected included sociodemographic data, the date of onset of hepatitis symptoms (such as fever, aches, nausea/vomiting, diarrhea, yellow skin/eyes, dark urine, stomach pain, light-colored stool, and loss of appetite), and out-of-state and international travel. Participants were asked about menu items (and garnishes) consumed from the indicated restaurant during the study period. Specific ingredients were associated with menu items by use of restaurant recipe books. Exclusion criteria for control subjects included a history of jaundice, hepatitis, receipt of hepatitis A vaccine, or recent (August–September 2003) symptoms of fatigue and dark urine.

Viral sequencing. Serum samples were collected from case patients in TN, GA, and NC and were sent to the CDC’s Division of Viral Hepatitis Molecular Epidemiology Laboratory (Atlanta, GA) for HAV RNA isolation, amplification, and sequencing. Serum samples were also collected from case patients in a subsequent hepatitis A outbreak in PA [17]. MagNA Pure LC RNA Isolation Kits I (Roche Molecular Biochemicals) and a MagNA Pure LC Instrument (Roche Applied Science) were used for HAV RNA extraction. A 315-nt segment of HAV at the VP1-2a junction was amplified by nested reverse-transcription polymerase chain reaction (RT-PCR), as described elsewhere [4]. RT-PCR amplicons were purified and sequenced using Big Dye Terminator 3 (Applied Biosystems) with an ABI 3100 sequencer.

Statistical analysis. Odds ratios (ORs) were used to measure the strength of associations in the case-control studies, and 95% confidence intervals (CIs) were calculated with SPSS software (version 11), using the Mantel-Haenszel statistic [18]. P < .05 was considered to indicate statistical significance. In the TN case-control study, a logistic-regression model was constructed to control for exposures to multiple food ingredients.

Molecular Surveillance

Case finding. In addition to serum specimens collected from case patients in outbreak-related settings, serum specimens were collected from individuals with hepatitis A who were identified by state and local health departments after a national announcement was made of an apparent multistate hepatitis A outbreak. State and local health departments were encouraged to submit specimens from individuals with hepatitis A onset between September and December 2003 and no typical risk factors for hepatitis A (i.e., contact with another case patient, international travel, illicit drug use, or being a man who has sex with men [MSM]) were encouraged. Viral sequences from these case patients were compared with those obtained from persons with hepatitis A onset between January 2002 and August 2003 who were identified through an ongoing population-based surveillance project in 6 US counties (the Sentinel Counties Study of Acute Viral Hepatitis) [4] and an ongoing jaundice surveillance project conducted in the US-Mexico border region [19].

Sequence analysis Preliminary sequence analysis was performed with Sequence Analysis and Sequence Navigator software (Applied Biosystems). Further sequences analysis was performed with the Accelrys GCG (version 10.3; Genetic Computer Group). Sequence alignments were made using the GCG Pileup program. The genetic distance was calculated by use of the uncorrected distance algorithm within the distances program in GCG. Sequence analysis by different methods showed similar clustering of sequences. Final tree construction was based on
unweighted pair group method with arithmetic mean (UPGMA) algorithms [20].

RESULTS

Outbreak Investigation

Descriptive epidemiology. Between 3 August and 11 October 2003, 73 hepatitis A cases among residents of metropolitan Knoxville were reported to the Tennessee Department of Public Health (figure 1A), 16 cases were reported to the Buncombe County, NC, Department of Public Health (figure 1B), and 333 were reported to the Georgia Division of Public Health (figure 1C). The peak dates of illness onset in TN were 1 week earlier than those in NC and GA.

No cases of hepatitis A had been reported among residents of metropolitan Knoxville, TN, or Buncombe County, NC, from January through July 2003. In interviews with case patients in TN, 65 (89%) of 73 reported having eaten at restaurant A during the 2–6 weeks before symptom onset. In NC, 12 (75%) of 16 case patients reported having eaten at restaurant B during the 2–6 weeks before symptom onset.

In GA, a total of 383 hepatitis A cases had been reported statewide from January through August 2003 (~10 cases weekly), similar to the number reported during the same time period in previous years [21, 22]. Interviews with 127 case patients with disease onset in September indicated that 12 (9%) had exposure to a single restaurant (restaurant C) during the 2–6 weeks before symptom onset. Two smaller clusters of case patients who reported having eaten at 2 other restaurants were also identified (restaurants D and E).

Investigations in all 3 states examined the possibility of transmission from an infected food handler. Seven food handlers from restaurant A and 1 food handler from restaurant B were identified among case patients with disease onset that was simultaneous with those of other patients. No other food handlers with recent infection were identified.

Case-control studies: TN. Of the 65 eligible case patients in Knoxville, TN, 57 (88%) were enrolled in the case-control study. Eight case patients were excluded, as a result of refusal to participate in the study (3), no recall of food history (2), or our inability to contact them (3). Of the 240 potential control subjects contacted, 204 (85%) were eligible and agreed to participate. Of these, 17 worked at restaurant A, 73 were dining companions of case patients, and 114 were individuals identified from credit card receipts.

Sixty-three percent of case patients and 59% of control subjects were female; 86% of case patients and 90% of control subjects were white. The median age was 41 years for case patients and 37 years for control subjects. Sex, age, and race were not associated with illness.

Of 83 menu items, 3 were significantly associated with illness (chicken salad: OR, 7.9 [95% CI, 1.9–32.6]; potato soup: OR, 3.38 [95% CI, 1.7–6.6]; potato skins: OR, 3.05 [95% CI, 1.4–6.7]), but no single menu item was consumed by >37% of case patients. The only common ingredients contained in all 3 menu items were green onions and cheese. Nine specific ingredients were significantly associated with illness in univariate analysis: green onions, cheese, romaine lettuce, chicken, chopped lettuce, mushrooms, carrots, leaf lettuce, and roma tomatoes (table 1). Of the case patients, 56 (98%) reported consumption of green onions, compared with 94 (46%) of the control subjects. In a logistic-regression model, consumption of green onions was the only significant exposure associated with illness (OR, 64.4 [95% CI, 8.6–480.5]).

Case-control studies: NC and GA. In NC, all 12 eligible case patients and 34 control subjects were enrolled in the case-control study. Of the case patients, 11 (92%) reported consumption of food items containing green onions at restaurant B, compared with 28 (82%) of the control subjects (OR, 2.4 [95% CI, 0.3–21.9]). Nearly all menu items contained green onions.

In GA, 11 (92%) of 12 eligible case patients (1 could not be contacted) and 62 control subjects were enrolled in the case-control study. Nine (82%) of the case patients and 11 (18%) of the control subjects reported consumption of food items containing green onions at restaurant C (OR, 20.9 [95% CI, 3.9–110.3]).
**Viral sequencing.** HAV RNA was detected in 28 (90%) of 31 serum samples collected from patrons or employees of restaurant A in TN. All positive specimens were of a single sequence type (sequence A). In GA, 136 (80%) of 169 specimens received were HAV RNA positive; 122 (90%) of these were of a single, distinct sequence (sequence B), which differed from sequence A by 2 nt. Sequence B was found in all 5 specimens available from individuals who reported having eaten at restaurant C. Of the remaining GA residents with sequence B, limited risk-factor and food-history information was available, and no common exposure was identified. Sequence B was also identified from 10 specimens available from NC, all of which were from individuals who reported having eaten at restaurant B. One hundred seventy specimens from case patients who resided in 3 states (PA, Ohio [OH], and West Virginia [WV]) and were associated with a restaurant-related hepatitis A outbreak in western PA [17] had an identical sequence (sequence D), which differed from both sequence A and sequence B by 1 nt.

**Food and Drug Administration (FDA) traceback investigation.** A traceback investigation of green onions from restaurant A in TN and restaurant C in GA was conducted by the FDA. The investigation determined that the green onions implicated in the TN and GA outbreaks were grown in the same region of northern Mexico. Two farms were identified as potential suppliers of the green onions delivered to restaurant A, and a single different farm was identified as the supplier of green onions to restaurant C. Green onions were grown, packaged, and packed on ice at the source farms and were delivered to restaurants A and C without intermediate repacking or re-icing. Inspection of the farms revealed poor sanitation and inadequate hand-washing facilities, among other problems [23].

**Molecular Surveillance**

Hepatitis A viral sequences from case patients identified through outbreak investigations (in TN, GA, NC, and PA), from sporadic hepatitis A cases (occurring between September and December 2003) with no reported risk factor identified through increased outbreak-related surveillance, from individuals with hepatitis A detected through ongoing surveillance in 6 US counties (Sentinel Counties Study), and from an ongoing US-Mexico Border Infectious Disease Surveillance (BIDS) project were compared with one another (figure 2). Overall, 106 distinct sequences from 594 individuals were identified; 101 (95%) distinct sequences from 587 (99%) individuals were genotype IA, and the rest were genotype IB. Of those in genotype IA, 57 (56%) distinct sequences from 478 (81%) individuals grouped into a single cluster, X. All sequences in this cluster were &gt;96% similar (or differed from one another by &lt;=11 nt). Smaller clusters of similar viral sequences differed from sequences in cluster X by &gt;=17 nt.

**Cluster X.** Cluster X included viral sequences from all individuals identified from northern Mexico (BIDS project), as well as from all individuals associated with outbreaks in TN, GA, NC, and PA. Three distinct outbreak sequences were identified (A, B, and D). Sequence A was found among 28 restaurant A patrons in TN, 1 restaurant A patron from GA, and 20 individuals from northern Mexico. This sequence was also found in serum specimens from 5 other individuals (4 from TN) who reported no link to restaurant A (table 2).

Sequence B was found in 122 GA residents, 10 NC residents, and 1 individual from northern Mexico. Twenty-one residents of 9 other states were also found to have sequence B virus. Eighteen of these individuals were available for interview. Ten reported travel to GA during the incubation period in mid-August 2003, whereas 8 reported no travel to GA or NC and no typical risk factors for hepatitis A.

The third outbreak sequence, sequence D, was found in specimens from 170 individuals from 3 states (PA, OH, and WV) who were associated with a foodborne hepatitis A outbreak in western PA [17]. Sequence D was also found in specimens from 15 Mexico residents. Four individuals in 3 other states not

### Table 1. Comparison of consumption of selected food items by case patients and control subjects who ate at restaurant A between 1 and 31 August 2003, Knoxville, Tennessee.

<table>
<thead>
<tr>
<th>Food Item</th>
<th>Case patients (n = 57)</th>
<th>Control subjects (n = 204)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green onion</td>
<td>56 (98)</td>
<td>94 (46)</td>
<td>65.5 (8.9–482.5)</td>
</tr>
<tr>
<td>Cheese</td>
<td>55 (96)</td>
<td>153 (75)</td>
<td>9.2 (2.2–38.9)</td>
</tr>
<tr>
<td>Mushroom</td>
<td>6 (11)</td>
<td>4 (2)</td>
<td>5.9 (1.6–21.6)</td>
</tr>
<tr>
<td>Romaine lettuce</td>
<td>42 (74)</td>
<td>104 (51)</td>
<td>2.7 (1.4–5.2)</td>
</tr>
<tr>
<td>Chicken</td>
<td>40 (70)</td>
<td>101 (50)</td>
<td>2.4 (1.3–4.5)</td>
</tr>
<tr>
<td>Leaf lettuce</td>
<td>39 (68)</td>
<td>96 (47)</td>
<td>2.4 (1.3–4.5)</td>
</tr>
<tr>
<td>Chopped lettuce</td>
<td>36 (63)</td>
<td>87 (43)</td>
<td>2.3 (1.3–4.2)</td>
</tr>
<tr>
<td>Carrots</td>
<td>36 (63)</td>
<td>87 (43)</td>
<td>2.3 (1.3–4.2)</td>
</tr>
<tr>
<td>Roma tomato</td>
<td>32 (56)</td>
<td>82 (40)</td>
<td>1.9 (1.1–3.5)</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval; OR, odds ratio.

1326 • JID 2005:192 (15 October) • Amon et al.
Figure 2. Comparison of hepatitis A virus (HAV) sequences among individuals with hepatitis A from northern Mexico (Border Infectious Disease Surveillance [BIDS] Project), 2002–2003; outbreak-related surveillance, October–December 2003; and 6 US Sentinel Counties Study sites, January 2002–August 2003. Nos. in parentheses indicate the no. of samples with an identical sequence identified from the same surveillance source. Bars are color coded according to the source of the sample or, for samples identified through sentinel counties surveillance, by the reported hepatitis A risk factors. Multicolored bars indicate, by the size of each colored segment, the proportion of individuals with an identical sequence reporting a hepatitis A risk factor or with no identified risk factors. Abbreviations of countries of travel outside of North America are as follows: EC, Ecuador; IND, Indonesia; PHI, Philippines; VEN, Venezuela. X represents a cluster of sequences >96% similar to one another. MSM, man who has sex with men.
Table 2. Sources and distribution of cluster X hepatitis A virus sequences.

<table>
<thead>
<tr>
<th>Source</th>
<th>Cluster X non–A, B, D (n = 73)</th>
<th>Sequence A (n = 54)</th>
<th>Sequence B (n = 154)</th>
<th>Sequence D (n = 197)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outbreak surveillance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TN</td>
<td>0</td>
<td>32</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PA/OH/WV</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>170</td>
</tr>
<tr>
<td>NC</td>
<td>0</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GA</td>
<td>0</td>
<td>122</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>21</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>US Sentinel Counties</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Mexico (BIDS)</td>
<td>42</td>
<td>20</td>
<td>1</td>
<td>15</td>
</tr>
</tbody>
</table>

NOTE. Data are the no. of specimens. BIDS, Border Infectious Disease Surveillance; GA, Georgia; NC, North Carolina; OH, Ohio; PA, Pennsylvania; TN, Tennessee; WV, West Virginia.

bordering PA were found to have sequence D virus: of these, 2 reported household contact with individuals with hepatitis A who had recently visited Mexico, and 1 had visited Mexico during the incubation period. From the Sentinel Counties Study, 8 other individuals were identified with a viral sequence matching sequence D. Five of these individuals had no identified risk factor for hepatitis A, 2 reported travel to Mexico/Guatemala, and 1 was an MSM.

In addition to those who matched the 3 outbreak sequences, 42 Mexico residents, 8 individuals with hepatitis A who were identified through outbreak-associated surveillance, and 23 individuals with hepatitis A who were identified through the Sentinel Counties Study had viral sequences that grouped in cluster X. None of the 8 individuals identified through outbreak-related surveillance reported any hepatitis-related risk factors. Among those individuals identified in the Sentinel Counties Study, 10 of the 12 with identified risk-factor information reported travel to Mexico or Guatemala during the disease incubation period.

Additional sequences. Sequences that did not form a part of cluster X consisted of 44 sequences from 109 individuals, including 84 from individuals with hepatitis A who were identified in the Sentinel Counties Study and 25 from individuals with hepatitis A who were identified through increased outbreak-related surveillance. In this part of the dendrogram, viral sequences largely grouped into clades according to 3 identified risk factors: individuals reporting drug use, MSM behavior, and foreign travel outside of North America.

**DISCUSSION**

Defining the disease burden and epidemiology of foodborne hepatitis A in the United States is challenging. Foodborne transmission is hard to recognize, for several reasons [24]. Hepatitis A cases are underreported, and many infections, especially among children, are unrecognized because typical symptoms of hepatitis A are not present. In addition, hepatitis A has a long incubation period, viral contamination can be focal, and the virus remains viable in the environment for weeks, resulting in cases being both geographically and temporally dispersed. The results of the present investigation demonstrate the benefits of incorporating molecular epidemiologic methods into ongoing foodborne hepatitis A outbreak investigations and routine hepatitis A surveillance. Separate case-control studies conducted in the 3 states with outbreaks in September and October 2003 indicated an association between illness and consumption of green onions, as did a subsequent study in PA in November 2003 [17]. However, the relationships between these outbreaks were unclear. Viral sequencing demonstrated that 4 geographically separate but temporally related outbreaks (in TN, NC, GA, and PA) represented at least 3 distinct events. Sequencing efforts also helped to define the scope of the outbreaks by quickly distinguishing outbreak-related from non–outbreak-related cases in 16 other states, thus providing reassurance that a larger, unrecognized outbreak was not being missed. Finally, a comparison of the outbreak sequences with sequences from cases identified through routine hepatitis A surveillance in the United States and Mexico supported traceback results and provided evidence of sporadic unrecognized foodborne transmission in the United States.

Viral sequencing was also critical to control efforts. The molecular characterization of HAV sequences obtained from case patients involved in the outbreak in PA was completed before the results from the case-control study in PA were available. These additional findings prompted public health authorities and the FDA to initiate immediate traceback and control measures, including informing consumers of the potential risk from eating uncooked green onions through an advisory and press release and, ultimately, an import bulletin prohibiting the entry of green onions from 4 Mexican farms [23].

Additional focal outbreaks might have been expected, because green onions grown in northern Mexico were distributed throughout the United States in the fall of 2003. Nonetheless, despite public health alerts, extensive media coverage, and intensified surveillance activities nationwide, no additional related
clusters of hepatitis A cases were identified. However, at least 10 case patients in 5 states had viral sequences that matched sequence A, B, or D; had no identified risk factors; and reported no travel to TN, GA, NC, or PA. Four additional case patients in TN had viral sequences identical to the outbreak sequence (sequence A) but reported no exposure to restaurant A.

The presence of an outbreak sequence in apparently unrelated cases might indicate that these sequences were circulating elsewhere in the United States. Alternatively, these case patients might have been exposed to contaminated green onions (1) in a setting where relatively few susceptible individuals were exposed or (2) from shipments that had only minimal or focal contamination. Similarly, the large number of case patients in GA who shared the outbreak strain could be an indication of hepatitis A cases resulting from either focal or low-level contamination of widely distributed green onions. The investigation in GA, as well as those in other states, was limited by incomplete information about whether persons with hepatitis A ate green onions during the incubation period. An analysis of green onion distribution in GA during the incubation period revealed a common supplier for the 3 restaurants with identified clusters, and an overlapping concentration of cases and green onion distribution in central and northern GA [25]. These findings illustrate the need for thorough epidemiologic data to explain molecularly related cases.

Cocirculation of different viral sequences was seen in a single outbreak associated with the consumption of raw shellfish [26], and small genetic differences in HAV sequences were seen among exposed case patients in an outbreak associated with contaminated produce [4]. However, we found that a single food item (green onions) related to outbreaks in 4 states represented 3 separate outbreaks, as is supported by the difference in peak onset dates of illness in each outbreak and by traceback investigations indicating different farm sources for the implicated green onions in GA, TN, and PA. The small nucleotide differences between the TN and GA/NC sequences were supported by extended sequencing of the entire VP1 gene (nt 2172–3288) of 26 specimens (authors’ unpublished data). The close similarity of viral sequences that we found in the 78 individuals with hepatitis A residing in northern Mexico infected over a 2-year period also supports the idea that distinct but closely related hepatitis A viruses were circulating in northern Mexico and were separately responsible for the contamination of the main agricultural export crop in that region.

In 1993, during the investigation of a large, multistate outbreak of hemolytic uremic syndrome caused by ground beef contaminated with *Escherichia coli* O157:H7, the identification of an outbreak strain by use of pulsed-field gel electrophoresis was a critical component in understanding the epidemiology of the outbreak [27]. Demonstrating the utility of this relatively new technique in an outbreak investigation spurred efforts to develop and integrate subtyping methods into state public health laboratories and ongoing national surveillance for bacterial foodborne diseases. During the past decade, these molecular epidemiologic techniques have enabled investigators to recognize previously unsuspected common exposures among foodborne illness cases scattered across the United States [2]. The investigations of foodborne hepatitis A reported here have shown the benefits of applying this approach to hepatitis A surveillance. Incorporation of viral sequencing into routine hepatitis A surveillance would improve the detection of outbreaks, help to relate sporadic hepatitis A cases that are associated with unidentified risk factors to recognized outbreaks, improve estimates of the disease burden due to foodborne hepatitis A, and increase our understanding of the epidemiology of hepatitis A in the United States.

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References