Typhoid Fever Outbreak Associated With Frozen Mamey Pulp Imported From Guatemala to the Western United States, 2010

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Background. Fifty-four outbreaks of domestically acquired typhoid fever were reported between 1960 and 1999. In 2010, the Southern Nevada Health District detected an outbreak of typhoid fever among persons who had not recently travelled abroad.

Methods. We conducted a case-control study to examine the relationship between illness and exposures. A case was defined as illness with the outbreak strain of Salmonella serotype Typhi, as determined by pulsed-field gel electrophoresis (PFGE), with onset during 2010. Controls were matched by neighborhood, age, and sex. Bivariate and multivariate statistical analyses were completed using logistic regression. Traceback investigation was completed.

Results. We identified 12 cases in 3 states with onset from 15 April 2010 to 4 September 2010. The median age of case patients was 18 years (range, 4–48 years), 8 (67%) were female, and 11 (92%) were Hispanic. Nine (82%) were hospitalized; none died. Consumption of frozen mamey pulp in a fruit shake was reported by 6 of 8 case patients (75%) and none of the 33 controls (matched odds ratio, 33.9; 95% confidence interval, 4.9). Traceback investigations implicated 2 brands of frozen mamey pulp from a single manufacturer in Guatemala, which was also implicated in a 1998–1999 outbreak of typhoid fever in Florida.

Conclusions. Reporting of individual cases of typhoid fever and subtyping of isolates by PFGE resulted in rapid detection of an outbreak associated with a ready-to-eat frozen food imported from a typhoid-endemic region. Improvements in food manufacturing practices and monitoring will prevent additional outbreaks.

Typhoid fever is a life-threatening illness caused by infection with Salmonella enterica serotype Typhi. Although endemic in many developing regions of the world, typhoid fever is less prevalent in the United States, and >75% of reported US cases are associated with international travel [1–3]. Humans are the only source of and reservoir for Salmonella Typhi; persons become infected through ingestion of contaminated food and water. Most outbreaks of typhoid fever occur from ingestion of food or water contaminated with fecal matter, often from an asymptomatic carrier. Between 1960 and 1999, 60 outbreaks of typhoid fever were reported in the United States; 54 (90%) were domestically acquired, accounting for 957 total cases and 4 deaths [4, 5]. An outbreak in Florida in 1998–1999 was linked to imported frozen mamey fruit pulp from Guatemala, where typhoid fever is endemic [6]. We investigated an
outbreak of domestically acquired typhoid fever in the western United States during 2010.

**METHODS**

**Outbreak Identification**

In June 2010, the Southern Nevada Health District (SNHD) detected 2 cases of *Salmonella* serotype Typhi infection in the Las Vegas area with an indistinguishable pulsed-field gel electrophoresis (PFGE) pattern (XbaI: JPPX01.0064, BlnI: JPPA26.0198) — the outbreak strain. This PFGE pattern was posted to PulseNet [7], the national molecular subtyping network for foodborne bacterial disease surveillance. Three isolates of the outbreak strain were subsequently identified in California. The SNHD notified the Nevada Department of Health, which contacted the Centers for Disease Control and Prevention (CDC) and other states about their investigation. To promote case finding, public health alerts were sent to public health agencies and clinicians via the Epidemic Information Exchange, a Web-based communications tool for sharing health surveillance information. The outbreak pattern was compared with the PFGE pattern of isolates from the outbreak in 1998–1999 [6].

**Hypothesis Generation**

States conducted initial hypothesis-generating interviews. The CDC conducted open-ended hypothesis-generating phone interviews, using a modified structured guide for eliciting information about foods consumed and food preferences. SNDH visited homes to interview case patients’ families and catalogue food products in the home.

**Analytic Evaluation**

**Case Definition and Identification**

A case was defined as illness with onset from 1 January 2010 to 30 September 2010, in a person whose specimen yielded *Salmonella* serotype Typhi matching the outbreak strain. Cases were identified through PulseNet.

**Case-Control Study**

A case-control study was performed on 4 August 2010. Case patients identified by the time of the study were enrolled. The questionnaire was based on a list of suspect foods derived from hypothesis-generating interviews. Patients were interviewed by telephone about exposure to foods in the 60 days before illness onset. This period was chosen because the incubation period for typhoid fever can be as long 60 days [8]. Controls were identified through computer-generated, randomized lists of telephone numbers that were matched to neighborhoods of case patients. We contacted well controls by phone and enrolled 3–5 controls for each case patient, matched by age group (4–17 and 18–40 years) and sex. A parent or guardian was interviewed for case patients or controls aged <18 years old. Controls were interviewed about the same 60-day period as the corresponding case patient.

**Case Exposure Questionnaire**

Case patients identified after the case-control study was completed were interviewed using the case exposure questionnaire.

**Statistical Analysis**

Data were entered into a Microsoft Access 2003 database (Microsoft) and analyzed using SAS 9.2 software (SAS Institute). Matched odds ratios (mORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression to measure associations between individual exposures and illness. Exposure variables found in the bivariate analysis to be significantly associated with case status (P < .1) were included in the multivariate model, using forward selection.

**Environmental and Traceback Investigations**

During visits to case patients’ homes, investigators from the SNHD collected food samples for testing. State and local public health agencies and the US Food and Drug Administration (FDA) visited grocery stores where case patients purchased food products in order to collect food samples. FDA collected information about brand, place of purchase, and packaging information for suspect food products. FDA conducted an on-site inspection of the plant in Guatemala, observed the food processing procedure, and collected environmental samples for testing.

**Processing Plant Employee Investigation**

The Guatemalan Ministry of Public Health and Welfare, in collaboration with the CDC, investigated whether any workers at the maney processing plant were carriers of *Salmonella* Typhi. All persons who currently worked at the processing plant were contacted; attempts were made to interview all employees who had direct or indirect contact with the implicated fruit using a standardized questionnaire. A stool specimen and serum sample were collected from each employee.

**RESULTS**

**Laboratory**

Stool and serum samples collected from plant employees were transported to the Guatemalan National Public Health Laboratory, where stool specimens were cultured for enteric bacteria. Serum samples were shipped on dry ice to CDC. The CDC determined typhoid carrier status using an indirect hemagglutination assay to quantify antibody titers to the Vi antigen of *Salmonella* Typhi. An elevated anti-Vi antibody titer suggests a chronic carrier state [9, 10].
In the United States, clinical laboratories send *Salmonella* strains isolated from ill persons to local and state public health laboratories for serotyping and subtyping by PFGE. These results are then reported to PulseNet; State and local public health laboratories and the FDA participated in the laboratory analyses of product samples and environmental investigations at retail locations where frozen mamey pulp milkshakes (*batidos*) were prepared for consumption.

**Case Finding**

Twelve case patients with illness onset between 15 April 2010 and 4 September 2010 were identified in Nevada, California, and Oregon. The outbreak PFGE pattern (XbaI: JPPX01.0064, *BlnI*: JPPA26.0198) is rare in the PulseNet database; only 15 human isolates were reported from 1 January 2000 to 31 December 2009. PulseNet Canada and PulseNet International did not report matching isolates. This outbreak pattern did not match the PFGE pattern of isolates from the outbreak in Florida in 1998–1999.

Eight patients were female (67%); the median age was 18 years (range, 4–48 years) (Table 1). Eleven patients (92%) self-reported Hispanic identity. Eleven patients with available clinical information reported high fever, with maximum temperatures >38.9°C. Eight (73%) reported headache, 10 (91%) reported malaise, 9 (82%) were hospitalized, and none died. In household contact testing, stool culture from the mother of an ill child was positive for *Salmonella* Typhi; she denied symptoms, suggesting that she was an asymptomatic carrier or a subclinical case.

**Hypothesis Generation**

Initial case patient interviews by state and local public health agencies showed that 5 (83%) of 6 patients interviewed reported no recent international travel. Eight open-ended hypothesis-generating phone interviews yielded a list of patients’ food preferences and common food exposures. All patients reported purchasing groceries at Hispanic-style grocery stores. The SNHD generated a list of common foods found in 2 case patients’ homes. Food exposures common to both patients included chicken, beef, rice, beans, tortillas, frozen shrimp, frozen fruit pulp, dry adobo seasoning, and yogurt. Both case patients had brand A frozen mamey pulp in their freezers.

**Case-Control Study**

Eight case patients and 33 matched controls were enrolled in the case-control study conducted on 4 August 2010. Four case patients had illness onset after completion of the case-control study. Bivariate analysis demonstrated that consumption of frozen mamey fruit pulp (*batidos*) in the 60 days before illness onset compared with none of the 33 controls. No other foods or beverages were significantly associated with illness. Consumption of mamey *batidos* remained significantly associated with illness (mOR, 11.6; 95% CI, 1.3–∞) when analysis was limited to 17 controls who self-reported Hispanic ethnicity. Hispanic ethnicity, shopping at Hispanic-style grocery stores or markets, consuming mamey *batidos*, and eating Mexican-style soft cheese (*queso fresco*) were included in the multivariable model. Consumption of mamey *batidos* was the only exposure that was independently associated with illness (Table 2).

**Case Patient Exposure to Mamey Batidos**

Of 11 case patients with available information, 8 (73%) reported consuming mamey *batidos* in the 60 days before illness onset. Five (63%) of these 8 recalled drinking *batidos* at home, prepared with brand A frozen mamey pulp. Of the remaining 3 case patients, 2 (67%) consumed mamey *batidos* made in a Hispanic-style market and 1 (33%) drank a mamey *batido* in a Hispanic-style restaurant; these case patients did not know the brand of the mamey pulp. The household contact who was stool culture-positive reported no consumption of or exposure to mamey *batidos*.

**Traceback Investigation**

State and local public health officials visited the 2 markets where case patients reported purchasing and drinking mamey *batidos*. One market reported using brand A frozen mamey pulp to prepare *batidos*; the other reported using brand B. Both brand A and brand B frozen mamey pulp are sold in 400-g (14-oz) vacuum-sealed packages. FDA notified the companies that sell brand A and brand B frozen mamey pulp, and, in August 2010, the companies issued voluntary recalls of brand A and brand B frozen mamey pulp products including pulp, fruit bars, and ice cream. Traceback investigation showed that the source of both brand A and brand B mamey pulp was a single processing plant in

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**Table 1. Demographic Characteristics of Case Patients With *Salmonella* Serotype Typhi Infection and Controls, Western United States, 2010**

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Case Patients (n = 12a)</th>
<th>Controls (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, No. (%)</td>
<td>8 (67)</td>
<td>20 (61)</td>
</tr>
<tr>
<td>Age, median (range), years</td>
<td>18 (4–48)</td>
<td>17 (6–40)</td>
</tr>
<tr>
<td>Hispanic ethnicity (self-reported), No. (%)</td>
<td>11 (92)</td>
<td>17 (52)</td>
</tr>
</tbody>
</table>

* Only 8 case patients were reported and included at the time of the case-control study.
Guatemala, which was owned and operated by a company different from those that sold mamey pulp in the United States. Freshly picked mamey fruit was shipped from local independent farms, allowed to ripen in a warehouse, and washed with chlorinated water before entering the processing plant. Employees cut the fruit in half and used utensils to scoop out the fruit. They loaded the fruit into a pulping machine and used a metal plunger to push it through the machine. Extruded pulp was loaded into a filling machine that placed it in heat-sealed 400-g bags. Plant staff stated that if a sample of a product lot indicated high microbial levels, this portion would be pasteurized. Pasteurization involved placing sealed bags of frozen pulp into a hot water bath and then refreezing them. The FDA observed that the pasteurization process was insufficient to eliminate pathogens. The mamey pulp was not reopened or repackaged before reaching retail locations.

Observations of the firm’s frozen fruit pulp operation uncovered numerous other problems, including failure to meet US food regulations for processing of juice and juice products [11]; insufficient monitoring of sanitation conditions; inadequate monitoring of the safety of the water that comes into contact with food or food contact surfaces; employee practices that could contribute to cross-contamination; lack of proper maintenance of hand washing, hand sanitizing, and toilet facilities;

Table 2. Bivariate Analysis of Exposures Among Case Patients With Salmonella Serotype Typhi Infection and Controls Participating in a Case-Control Study, Western United States, 2010

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Case Patients, No. (%) (n = 8)</th>
<th>Controls, No. (%) (n = 33)</th>
<th>mOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mamey <em>batido</em></td>
<td>6 (75)</td>
<td>0 (0)</td>
<td>33.9</td>
<td>4.9–∞</td>
</tr>
<tr>
<td>Hispanic ethnicity (self-reported)</td>
<td>8 (100)</td>
<td>17 (52)</td>
<td>14.9</td>
<td>1.8–∞</td>
</tr>
<tr>
<td>Hispanic grocery store</td>
<td>7 (88)</td>
<td>20 (61)</td>
<td>7.8</td>
<td>1.0–∞</td>
</tr>
<tr>
<td>Mexican-style soft cheese (queso fresco)</td>
<td>6 (75)</td>
<td>13 (41)</td>
<td>5.7</td>
<td>.8–∞</td>
</tr>
<tr>
<td><em>Pico de gallo</em></td>
<td>5 (63)</td>
<td>6 (18)</td>
<td>4.8</td>
<td>.9–32.7</td>
</tr>
<tr>
<td>Fresh fruit juice</td>
<td>8 (100)</td>
<td>22 (67)</td>
<td>4.7</td>
<td>.7–∞</td>
</tr>
<tr>
<td>Frozen fruit popsicles (paletas)</td>
<td>6 (75)</td>
<td>16 (52)</td>
<td>4.5</td>
<td>.5–240.7</td>
</tr>
<tr>
<td>Hispanic-style spice or bay leaves</td>
<td>7 (88)</td>
<td>20 (61)</td>
<td>4.5</td>
<td>.5–226.5</td>
</tr>
<tr>
<td>Fruit pulp</td>
<td>4 (50)</td>
<td>5 (16)</td>
<td>4.4</td>
<td>.7–31.5</td>
</tr>
<tr>
<td>Mexican-style cream (crema)</td>
<td>5 (63)</td>
<td>7 (23)</td>
<td>4.0</td>
<td>.7–26.7</td>
</tr>
<tr>
<td>Mexican bread</td>
<td>4 (50)</td>
<td>8 (25)</td>
<td>3.4</td>
<td>.5–25.7</td>
</tr>
<tr>
<td>Hispanic-style <em>horchatas</em> (rice drink)</td>
<td>5 (63)</td>
<td>13 (39)</td>
<td>2.9</td>
<td>.4–34.2</td>
</tr>
<tr>
<td>Tortillas</td>
<td>8 (100)</td>
<td>27 (82)</td>
<td>2.2</td>
<td>.3–∞</td>
</tr>
<tr>
<td>Fresh or frozen shrimp</td>
<td>5 (63)</td>
<td>14 (42)</td>
<td>1.9</td>
<td>.3–12.9</td>
</tr>
<tr>
<td>Guacamole</td>
<td>5 (63)</td>
<td>18 (55)</td>
<td>1.5</td>
<td>.2–11.6</td>
</tr>
<tr>
<td>Ground beef</td>
<td>7 (88)</td>
<td>27 (82)</td>
<td>1.5</td>
<td>.1–74.8</td>
</tr>
<tr>
<td>Fruit-flavored ice cream</td>
<td>3 (38)</td>
<td>11 (33)</td>
<td>1.1</td>
<td>.1–6.6</td>
</tr>
<tr>
<td>Jalapenos or spicy peppers</td>
<td>2 (25)</td>
<td>11 (33)</td>
<td>.7</td>
<td>.1–4.6</td>
</tr>
<tr>
<td>Shaved-ice (raspados)</td>
<td>1 (13)</td>
<td>9 (27)</td>
<td>0.4</td>
<td>0–3.4</td>
</tr>
<tr>
<td>Salsa</td>
<td>3 (38)</td>
<td>26 (79)</td>
<td>0.1</td>
<td>0–7</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; mOR, matched odds ratio.

a Case patients were questioned about exposures during the 60 days before illness onset; controls were questioned about exposures during the same 60 days as the respective case patient.

b Only 8 case patients were reported and included at the time of the case-control study.

Table 3. Exposure Variables Included in the Multivariate Model, Using Forward Selection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Other Exposure</th>
<th>Mamey Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic ethnicity</td>
<td>mOR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Conditional degenerate distribution</td>
<td>7.3</td>
<td>.7–∞</td>
</tr>
<tr>
<td>Shopping at Hispanic-style grocery stores or markets</td>
<td>0.5</td>
<td>0–∞</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; mOR, matched odds ratio.
and failure to provide adequate screening or protection against pests.

**Laboratory and Environmental Testing**
The SNHD collected packages of brand A frozen mamey pulp, 2 open and 1 unopened, from 3 case patients’ homes. Culture of 1 unopened package of brand A frozen mamey pulp yielded *Salmonella enterica* subspecies *diarizonae* serotype 60:r:e:n,z15. State and local public health agencies and the FDA collected samples from both markets. Cultures of all samples from homes and markets were negative for *Salmonella Typhi*. Culture of product obtained from the processing plant, labeled as pasteurized, yielded a non-Typhi *Salmonella* that was not serotyped.

**Processing Plant Employee Investigation**
From 15 November to 22 November 2010, we interviewed and obtained serum and stool samples from 37 persons currently working at the factory; 33 (89%) had contact with fruit. Among those with fruit contact, 10 (30%) selected fruit, 3 (9%) washed fruit, 9 (27%) processed fruit, and 7 (21%) packaged fruit. No stool cultures yielded *Salmonella* or *Shigella*. All 33 serum samples from the factory employees tested negative for antibodies to the Vi antigen of *Salmonella Typhi*.

**DISCUSSION**

We report the largest outbreak of domestically acquired typhoid fever in the United States in >10 years. Epidemiologic and traceback investigations strongly implicated imported frozen mamey pulp as the vehicle, resulting in a nationwide recall of frozen mamey pulp by the 2 companies. The same product from the same processing plant was also implicated in a typhoid fever outbreak in Florida in 1998 [6]. After that outbreak, the plant received training in sanitation practices, and it was recommended that the plant implement pasteurization, which was reportedly being done as of June 2001 [6]. To our knowledge, no subsequent inspections of the plant have been conducted since the current investigation identified numerous processing problems. The identification of these problems resulted in a ban on imported pulp products from this plant that will remain in effect until FDA regulations are met.

Because *Salmonella Typhi* is rare in the United States, it is often not considered in the differential diagnosis for sustained fever, particularly in patients who lack travel history to typhoid-endemic regions. Persons with typhoid fever usually have sustained high fever ≥38.9°C [12]. Symptoms can also include headache, malaise, abdominal pain, and loss of appetite. Unlike nontyphoidal *Salmonella* infections, infection with *Salmonella Typhi* commonly causes constipation rather than diarrhea in adults. Healthcare providers should consider obtaining blood cultures from patients with unexplained sustained high fever, despite lack of travel history outside the United States.

Mamey pulp is vulnerable to contamination because its production involves hand manipulation at multiple process points. Contamination could have been introduced during harvest or transport. The deficient conditions in the processing plant suggest that contamination may have been introduced by a worker who was a convalescent or chronic asymptomatic carrier of *Salmonella Typhi*. Alternatively, contamination may have been introduced through fecal contamination of the water supply to the plant. Within the processing plant, multiple opportunities existed for cross-contamination and distribution of bacteria to large volumes of pulp. The subsequent heating of packaged pulp was insufficient to pasteurize the product. Although serologic testing of plant employees was negative for *Salmonella Typhi*, it is possible that a previous or current employee was a carrier or a carrier who had been treated. Based on our investigation, the firm routinely manufactured and exported unpasteurized frozen mamey pulp to the United States and did not implement procedures to control potential contamination. Though cultures of suspected food samples were negative for *Salmonella Typhi*, the presence of nontyphoidal *Salmonella* from previously unopened product indicates that fecal contamination occurred during the food production process.

This case-control study demonstrated a strong association between illness and consumption of mamey *batidos*. Three case patients, aged 5–9 years, did not report consumption of mamey pulp products. Notably, because we interviewed only 1 primary caregiver per child, children’s food histories may have been incomplete if they were fed by multiple caregivers and given mamey by someone other than the interviewee. Given that case patients and controls were questioned about food consumption over a long period, they may have eaten products containing frozen mamey pulp and forgotten. Some may have consumed mamey unknowingly as an ingredient in another dish. In addition, some case patients may have become infected through contact with another person who had consumed mamey and was either asymptomatic or a convalescent carrier. To the extent that these case patients’ exposures to mamey were underreported, the resulting bias would be toward the null. Finally, though rare in the PulseNet database, this outbreak strain was not unique to this outbreak and had been identified from 15 other cases during the previous decade. Thus, it is possible that the 3 cases without reported mamey exposure in fact became ill through another unidentified exposure.

Two aspects of the study design may have introduced bias. First, the long incubation period for typhoid fever and lag time from onset of illness to reporting of cases meant that most subjects were questioned about food exposures that occurred ≥1–2 months before the interview. If case patients, who were
interviewed multiple times by telephone and, in some instances, in the home, recalled exposures more accurately than controls, who were interviewed only once, the resulting recall bias may have led to overestimation of the association of exposures with illness. However, this bias would be expected to affect any exposure; the fact that only mamey was associated with illness suggests that the association is not due solely to bias. Second, to avoid overmatching, controls were not matched by ethnicity. This aspect of the study design probably introduced a degree of confounding by ethnicity. However, 2 strategies to control such confounding, including only Hispanic controls in the bivariate analysis and controlling for Hispanic ethnicity in the multivariate analysis, showed that exposure to mamey batidos alone was strongly associated with illness.

Obtaining food histories and information about other exposures from patients with typhoid fever can be difficult because the incubation period can be as long as 60 days. Home visits were a useful tool for hypothesis generation and collection of suspect foods in this investigation. Patients did not identify consuming mamey batidos until home visits conducted by the SNHD epidemiologists identified brand A frozen mamey pulp in the freezers of 3 case patients’ homes.

This outbreak was initially detected through PulseNet [7], which allows comparison of enteric organisms over large geographic areas. PulseNet is a powerful tool to enable early detection of foodborne disease outbreaks, before localized outbreaks develop, thus preventing many possible cases.

The continued trend toward centralized production and global distribution of foods has important implications for food safety. The safety of foods imported into the United States depends on the food safety systems of other countries. In recent years, numerous outbreaks of enteric diseases, such as cyclosporiasis, salmonellosis, staphylococcal food poisoning, and cholera, have involved imported food [13–16]. The outbreak reported here was recognized because typhoid fever can be very severe; however, many illnesses caused by imported foods are likely to go undetected or unreported. This outbreak highlights the need for collaboration of public health and regulatory agencies between countries to maintain food safety across borders. The FDA Food Safety Modernization Act (Public Law 111–353), enacted in 2010, includes provision for such regulations to promote food safety of imported foods [17].

As a result of this outbreak, a contaminated imported food product was recalled and will not be imported into the United States until the company has demonstrated to the FDA full compliance with all applicable food safety regulations, including the mandatory juice and juice products requirements and procedures to prevent further violations of the Federal Food, Drug, and Cosmetic Act. Importantly, this outbreak underscores the role of increased oversight of proper food production processes for both imported and domestically produced foods for the prevention of typhoid fever and other foodborne disease outbreaks.

Notes

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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