A Large Food-borne Outbreak of Group A Streptococcal Pharyngitis in an Industrial Plant: Potential for Deliberate Contamination

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Abstract

Contamination of food with streptococci could present with unusual outbreaks that may be difficult to recognize in the early stages. This is demonstrated in a large food-borne outbreak of streptococcal pharyngitis that occurred in 2003 in a factory in Israel. The outbreak was reported to the public health services on July 2 and an epidemiologic investigation was initiated. Cases and controls were interviewed and throat swabs were taken. An estimated 212 cases occurred within the first 4 days, the peak occurring on the second day. There was a wave of secondary cases during an additional 11 days. The early signs were of a respiratory illness including sore throat, weakness and fever, with high absenteeism rates suggesting a respiratory illness. As part of a case-control study, cases and controls were interviewed and throat swabs taken. Illness was significantly associated with consumption of egg-mayonnaise salad (odds ratio 4.2, 95% confidence interval 1.4–12.6), suggesting an incubation period of 12–96 hours. The initial respiratory signs of food-borne streptococcal pharyngitis outbreaks could delay the identification of the vehicle of transmission. This could be particularly problematic in the event of deliberate contamination.

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Food-borne outbreaks caused by streptococcal infections have been associated mostly with social events or have occurred in military and confined settings [1-10]. The possible use of streptococci for deliberate outbreaks cannot be excluded since the organism is easily obtainable, can be introduced simply into the food, and can cause considerable disabling illness. In addition, streptococci are resilient to the environment and replicate in food with relative ease; moreover, secondary spread by droplets is common [1]. Several incidences of deliberate contamination of food have been documented [11-14]. The most notorious was that of the salmonellosis outbreak that occurred in 1984 in Oregon in the United States [13], where salads in restaurants were deliberately contaminated with Salmonella typhimurium by an extremist group and at least 751 people were affected. In another incident, 12 laboratory workers became ill after another worker deliberately contaminated food with Shigella dysenteriae type 2 [12].

While pathogens involved in outbreaks of food-borne disease generally produce gastrointestinal symptoms, the signs and symptoms of streptococcal infections are typical of respiratory infections [3]. Thus, a food-borne route of infection would be low on the index of suspicion. The situation may be further complicated by the fact that secondary spread is through droplet infection. In this paper we describe a food-borne outbreak of streptococcal pharyngitis in a large industrial plant and evaluate the implications for deliberate outbreaks.

The outbreak

On the morning of 2 July 2003 the physician of a large industrial plant, which manufactures for both the civilian and the military sectors, notified the district health officer that since the previous evening, 50 workers had visited the clinic with complaints of headache, sore throat and fever. By noon the report was updated to 100 workers with the same complaints. Officials at the district health department started a preliminary investigation on the same day; viral agents, such as influenza and adenovirus, were the prime suspects. Twenty nasopharyngeal swabs and blood samples were sent for evaluation to the Central Virology Laboratory of the Israel Ministry of Health. On the morning of July 3, the physician updated his report to include 180 workers, and by noon he reported that a large number of workers were absent from work on that day. On Friday, July 4, active surveillance at a community clinic identified seven cases from the same factory. Physical examination revealed exudative pharyngitis. Pharyngeal swabs were sent for analysis at the Ministry of Health streptococcal reference laboratory. On July 5, all these swabs were found to be positive to hemolytic streptococci.

On July 6 the possibility of a food-borne outbreak was considered. On that day, the kitchen was inspected, the staff was interviewed and their hands were examined. Nasopharyngeal swabs and food samples were sent for microbiologic analysis. Microbiologic analysis of food samples consumed before July 2 could not be carried out since samples of meals served be-
before July 2 were not available (according to the Ministry’s regulations, food samples are to be kept for 48 hours).

Methods
Laboratory methods
Nasopharyngeal swabs were cultured on sheep blood agar and characteristic beta-hemolytic colonies were checked for resistance to Bacitracin. Group identification was performed by agar precipitation (Lancefield method). The group A Streptococcus isolates were further typed by T agglutination to determine the T type. For emm typing the emm gene was amplified by polymerase chain reaction, and the product of the amplification was subjected to restriction fragment-length polymorphism analysis. Those isolates that yielded a distinct pattern, as well as a representative subset of the isolates that yielded an identical pattern, were sequenced.

Case-control study
Both sick and healthy workers from respective departments were interviewed from July 6 to July 9 in order to conduct a case-control study. Before the final diagnosis was reached, a case was defined as an employee with fever, chills and clinically purulent pharyngitis diagnosed from June 30. Afterwards, a further definition included only workers who had culture-proven group A streptococcal throat infection. A structured questionnaire was used to collect demographic data, clinical signs and symptoms, and food consumption data. Information from the menus for June 29 to July 3 was used to list the food to which the employees were exposed. The questionnaires were completed by the workers themselves. During that time, nasopharyngeal swabs were also taken and sent to the Ministry of Health streptococcal reference laboratory.

Statistical analyses
Odds ratios and 95% confidence intervals were computed for the association between consumption of certain food items and clinical illness in the case-control study. Data were analyzed using SAS software.

Results
Although a large number of workers were reported to be absent from work during the outbreak, we identified 259 cases, meeting the criteria of the preliminary case definition used in the study. Since the outbreak affected only a portion of the employees, and meals at the factory are served in several dining rooms, it was not possible to determine the actual number of workers exposed.

A total of 562 workers (233 cases, 197 controls and 132 food workers) completed questionnaires on signs and symptoms of the illness. Partial data were available for another 26 cases. Data on time of disease onset reported in the questionnaires were used to construct the epidemic curve shown in Figure 1. There was an initial rapid increase to a peak on the second day. This was followed by a rapid decline, followed by a second wave for an additional 11 days.

Primary cases were defined as patients who reported the onset of disease on or before July 3, i.e., within 72 hours of the time of presentation of the first case. Those who presented on or after July 4 were regarded as secondary cases. Figure 2 demonstrates the distribution of the clinical symptoms and signs among the primary cases. The most common symptoms were fever (78.3%), sore throat (93.1%) and weakness (84.3%).

Table 1 presents the distribution of the streptococcal isolates...
**Discussion**

We describe a large food-borne outbreak of streptococcal pharyngitis. Early indications suggested that an infection spread by the respiratory route caused this large outbreak. However, during the outbreak, food and water were also considered as possible sources for common exposure. The possibility of deliberate food contamination was also raised. However, in this case there was no evidence among the food handlers of recent new personnel or any other employee's leaving suddenly following the incident, to support this possibility.

No food samples from the start of the outbreak were available for microbiologic analysis from the time when patients started to appear in the factory clinic. Thus, food involvement in the current outbreak is supported by strong indirect evidence. This included the identical isolates from the primary cases and the food workers, and the findings of a case-control study conducted in the factory. Egg salad was the food item most implicated with the outbreak. In food-borne outbreaks of streptococcal pharyngitis, contamination of the hands with respiratory secretions is an important means of infecting the food [2]. As found in the current study during inspection of the factory kitchen, although disposable gloves were available, gloves were not worn by the food handlers. Thus, contamination of the hands, also in this outbreak, could not be ruled out as the source of infection.

The documented role of egg salad in food-borne outbreaks of Group A streptococcal infection [2] makes egg salad a good choice as a substrate for deliberate contamination of food. In combination with the relative high temperatures prevalent in the summer, it could yield a heavy bacterial load. In addition, no sophisticated procedures would be needed to disseminate the inoculum among the diners. Since secondary spread of streptococcal pharyngitis is generally via respiratory droplets [1], the inoculum among the diners. Since secondary spread of streptococcal pharyngitis is generally via respiratory droplets [1], it strengthens the attractiveness of Group A Streptococcus for bioterrorism. In this study, 49 secondary cases were documented, comprising 24% of the primary cases. Person-to-person transmission is probably largely underestimated, due to the difficulty in identifying cases outside of the industrial plant where the primary outbreak occurred. Clearly, if streptococcal infection is not suspected, effective treatment will be delayed and the potential for secondary spread increases.

Early detection of the outbreak and rapid identification of the causative agent are essential for mitigating the effects of a possible bioterrorist event [15]. In this outbreak, its explosive nature, the fact that it was limited to the industrial plant itself, and the availability of healthcare services at the plant made early detection relatively simple. Less than 48 hours after exposure to the infected food items the plant physician notified the regional public health officer about unusual morbidity. However, in more widespread scenarios of food-borne outbreaks, such as that of Oregon in 1984 [13] where ten restaurants were involved, identifying and associating apparently isolated events would be more problematic. People dining in restaurants would have fewer social or working relations and they would seek medical advice at different clinics. In addition, had the outbreak occurred in winter, it would have been more difficult to identify.

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**Table 1. Distribution of streptococcal isolates by group in a food-borne outbreak of streptococcal pharyngitis in Israel in 2003**

<table>
<thead>
<tr>
<th>Total Swabs</th>
<th>Streptococcal group</th>
<th>No isolate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Primary cases, not taking antibiotics</td>
<td>90</td>
<td>46</td>
</tr>
<tr>
<td>(51.1)</td>
<td>(1.1)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Primary cases, taking antibiotics</td>
<td>112</td>
<td>3</td>
</tr>
<tr>
<td>(2.7)</td>
<td>(0.9)</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>197</td>
<td>15</td>
</tr>
<tr>
<td>(7.6)</td>
<td>(1.5)</td>
<td>(2.0)</td>
</tr>
<tr>
<td>Healthy food workers</td>
<td>132</td>
<td>9</td>
</tr>
<tr>
<td>(6.8)</td>
<td>(0.8)</td>
<td>(1.5)</td>
</tr>
</tbody>
</table>

The values in parentheses are percentages

**Table 2. Case-control study to evaluate exposure to egg salad in a food-borne outbreak of streptococcal pharyngitis in Israel in 2003**

<table>
<thead>
<tr>
<th>Have you consumed egg salad?</th>
<th>Cases*</th>
<th>Controls</th>
<th>Cases – group A Streptococcus proven**</th>
<th>Controls – non-group A Streptococcus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>42</td>
<td>4</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>90</td>
<td>36</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>132</td>
<td>40</td>
<td>28</td>
<td>36</td>
</tr>
</tbody>
</table>

* OR 4.2, 95% CI 1.4–12.6  
** OR 14.0, 95% CI 1.6–120.0

by group for primary cases, healthy controls, and food workers. Microbiologic data were available for 202 primary cases, and for all the controls and food workers enrolled in the study. For primary cases, results were segregated by use of antibiotics. The respective percentages of isolates found to be positive for group A Streptococcus for primary cases not taking antibiotics, primary cases taking antibiotics, healthy controls and food workers were 51.1%, 2.7%, 7.6% and 6.8% respectively. Most of the group A Streptococci isolates were of the same T type 3/13/B3264, 12 (95.9%, 73.3%, 88.9% for the primary cases, controls and food workers, respectively), and all except one were type emm22.

For the case-control study, only 132 primary cases and 40 controls who fully completed the food consumption part of the questionnaire were included. The strongest association with streptococcal pharyngitis was consumption of the egg salad served at lunch on June 30 (OR 4.2, 95% CI 1.4–12.6) [Table 2]. For laboratory-confirmed cases the odds ratio was 14.0 (95% CI 1.6–120.0). A significant association was also found for turkey schnitzel served at the same meal (OR 2.8, 95% CI 1.03–7.8). Considering that lunch time on June 30 was the time when exposure took place, the incubation period for this outbreak ranged from less than 24 hours to about 3 days.

OR = odds ratio  
CI = confidence interval
Conclusions
To the best of our knowledge, this outbreak is one of the largest food-borne streptococcal pharyngitis described. Both the relative ease with which large numbers of workers were infected and the impact on the function of the plant emphasize the need to include streptococci as a potential category B bioterrorist agent. Therefore, food items liable to be implicated in food bioterrorism should be monitored carefully.

References

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I have often wondered how it is that every man loves himself more than all the rest of men, but yet sets less value on his own opinion of himself than on the opinion of others
Marcus Aurelius (121-180 BC), Roman emperor and philosopher

Capsule
An up- and down-regulator
The liver is a key controller of fuel utilization, and insulin acts to inhibit hepatic gluconeogenesis and activate lipogenesis, thereby preventing excessive glucose release during the fed state. Phosphatidylinositol 3-kinase (PI3K) is a mediator of insulin signaling and is a dimer of a catalytic subunit (p110) and a regulatory subunit (p85). Phosphatidylinositol (3,4,5)-trisphosphate (PIP3), the product of PI3K, is metabolized by the lipid phosphatase PTEN. Taniguchi et al. created a liver-specific knockout of the p85 subunit in mice and found that, contrary to expectations, these mice showed increased liver responsiveness to insulin and had lower circulating glucose, free fatty acids, and triglyceride concentrations than wild-type littermates. Muscle and adipose glucose utilization was also increased in the knockout mice. Although the knockout mice showed decreased hepatic PI3K activity and decreased levels of the p110 subunit (p85 stabilizes p110), insulin produced a prolonged elevation in hepatic PIP3 and a higher activation of Akt, a kinase regulated by PIP3, as compared to wild-type mice. The increase in PIP3 appeared to be due to decreased PTEN activity in the livers of the knockout mice, suggesting that p85 regulates not only the production of PI3P but also its metabolism. Proc Natl Acad Sci USA 2006;103:12093
Eitan Israeli