Outbreak report

OUTBREAK OF DOMESTICALLY ACQUIRED TYPHOID FEVER IN LEIPZIG, GERMANY, JUNE 2004

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In June 2004, three confirmed cases of typhoid fever were reported to the health authorities in Leipzig, Germany. The patients had been admitted to hospital with unexplained fever and otherwise mild symptoms. All were members of the same pony club, none had been abroad. A retrospective cohort study among pony club members was performed to identify the source of infection. A suspected case was defined as unexplained fever $\geq 38.5^{\circ}\text{C}$ over three or more days since 1 May 2004. Additional positive serology defined a probable case and *Salmonella* Typhi isolation from blood or stool cultures a confirmed case. All hospitals, paediatricians and general practitioners in Leipzig and surroundings were contacted to identify additional cases. In total, six cases were identified, all among pony club members: four confirmed, including the three originally reported cases, one probable and one suspected. The only exposure common to all cases during the probable time of infection was consumption of sandwiches with herb dressing from a snack bar on 25 or 26 May (May 25: RR=5.7; 95% CI 0.9-37.9; both days: RR= , P=0.007). Foods and workers from the snack bar tested negative. However, one worker, not previously registered with the health authorities, was identified during a site visit. It cannot be excluded that further unregistered individuals worked at the snack bar between May and June 2004. Despite intense case-finding activities, no further cases were identified among the population. The most likely vehicle in this outbreak was sandwiches with herb dressing, though the source of contamination remains unknown. Even without history of travel to endemic countries, physicians should consider typhoid fever when managing patients with unexplained fever.

Introduction

Typhoid fever is a systemic infection caused by the human-specific pathogen *Salmonella enterica* serovar Typhi. Asymptomatically infected individuals may develop chronic carriage and shed bacteria in the stool for months or even years. Infection is usually acquired by ingestion of contaminated food or water. In industrially developed countries, domestically acquired infections are rare and usually associated with travel to endemic regions.

Typhoid fever is a notifiable disease in Germany. Between 59 and 88 cases of typhoid fever have been reported annually since 2001. Of these, more than 85% were related to travel abroad. On 30 June 2004, three microbiologically confirmed cases of *S. Typhi* infection were reported to the local health authorities in Leipzig, Germany. The three patients had been admitted to hospital with unexplained fever and relatively mild symptoms lasting approximately two weeks. Extensive questioning showed they had not been abroad nor had they had contact to travellers returning from endemic

countries in the previous six months, and that all three patients were members of a club owning and managing a pony farm. Thus, local transmission was considered, possibly ongoing and extending beyond club members. To determine the magnitude of the outbreak, the source of infection and to prevent further transmission, an outbreak investigation was performed.

Methods

The three patients underwent intensive questioning regarding activities at the pony club, leisure activities, eating habits, and restaurant visits during the 60 days prior to symptom onset (twice the maximum incubation period [1]). At the time of the outbreak investigation, incubation periods of between three and 30 days were cited in the 17th edition of the Control of Communicable Diseases Manual [1]. In the 18th edition however, the incubation period is given as 'from three to over 60 days' [2]. We believed that extending the period of inquiry further backwards to include another two months of possible food item exposures would not have given two insight into possible vehicles of infection. Other relevant exposures like travel to endemic regions and contacts to persons returning from such regions or food items brought from these regions were inquired about from 1 January 2004 to date of interview.

The other 12 members of the pony club and other individuals connected to the pony farm or one of the patients were contacted and tested for *S. Typhi*. Active case finding was performed among the population of Leipzig and surrounding counties. All hospitals, general practitioners, and paediatricians were contacted. The media were also involved. A suspected case was defined as a person with unexplained fever of at least 38.5°C for three or more days since 1 May 2004 (corresponding to date of symptom onset of index cases minus twice the maximum incubation period of 30 days [1] and an additional two weeks as a safety margin) and up to 31 July 2004. Additional positive serological reactions (Widal test and/or specific ELISA) defined a probable case and isolation of *S. Typhi* from blood or stool cultures defined a confirmed case. Presuming a common source outbreak, the probable period of infection was calculated assuming that the case with the earliest symptom onset had the shortest (3 days) and the case with the latest symptom onset had the longest (30 days) incubation period.

A retrospective cohort study was performed with all 15 club members. Demographical and clinical data, data on travel, food consumption, activities on the farm and contact with persons returning from endemic regions were collected using a standardised questionnaire. Data entry and analysis was performed using Epi Info version 3.3 (CDC Atlanta, 2004).

A site visit to the pony farm and to a snack bar regularly visited by the members was conducted. The farm's water supply was examined for *S. Typhi* at different collection points. At the snack bar, selected food items were examined and all employees interviewed and tested. All club members, contacts, snack bar workers, and suspected cases underwent blood and stool examination. At least three stool samples from each person were collected at two day intervals and examined. During a similar outbreak in a Paris bistro in 2003 [3], an asymptomatic chronic carrier responsible for salad preparation was not found positive for *S. Typhi* until the fourth stool sample had been tested. Thus, at least eight stool samples, daily or in two day intervals, were requested from all workers at the snack bar.

Phage typing and PFGE typing were performed for all isolates at the National Reference Centre (NRC) for *Salmonella* and other enteric pathogens, where approximately 50 *S. Typhi* isolates from patients as well as carrier strains are collected and phage typed yearly for comparison investigations.

A Widal test was performed on all serum samples and titres above 1:100 were considered positive for *S. Typhi* infection. At the NRC, serum samples of all club members underwent specific in-house agglutination and ELISA tests developed according to Veling [4]. Phage types of chronic carriers in the Leipzig area known to the local health department were compared to verify if they were possibly the source of infection. Since gallstones may favour the persistence of *S. Typhi* in the bile ducts and therefore predispose to chronic carrier status [5], sonographical examination of the upper abdomen was performed on all outbreak patients to exclude gall bladder or bile duct stones.

Results

In addition to the three known cases, three further cases were identified among club members. Despite intensive investigation, no further cases were found among their contacts, snack bar workers, or the population of Leipzig and surrounding areas. The most common symptoms were fatigue, fever, myalgia, and headache (100%) and cough (80%).

Among the six cases, *S. Typhi* was isolated from blood and/or stool in four (confirmed cases), one had positive Widal and specific agglutination tests and ELISA reaction (probable case) and one remained a suspected case, as *S. Typhi* specific antibodies could not be demonstrated. The probable period of infection was calculated to be between 15 May and 5 June 2004 [Figure 1]. During this period, all cases had been on the farm on 25 and 26 May 2004, leading to the hypothesis that some local factor common to all cases on these days was the source of infection in this outbreak. On 25 May 2004, one of the ponies had fallen seriously ill. While the veterinarian was treating the pony, some members bought sandwiches with herb dressing from a nearby snack bar, which were consumed at the farm. The next day, sandwiches with herb dressing from the same snack bar were again consumed on the farm. Except for these sandwiches, no other food items were prepared or consumed at the farm during this period. All six cases had consumed either meat or cheese sandwiches, all with the same herb dressing on either 25 or 26 May 2004, (RR= , P=0.007, Fisher's exact test). Of these, five consumed sandwiches with herb dressing on 25 May (RR=5.7; 95%CI 0.9-37.9) [Table]. Thus, members who had consumed sandwiches with herb dressing on these days were at least six times more likely to become a case than those who had not. By excluding the suspected case from risk analysis, the relative risk for consumption of sandwiches with herb dressing on 25 May 2004 was 4.6 (95%CI 0.7-31.9), remaining unchanged for consuming

Source: Robert Koch-Institut and Health Department of Leipzig

TABLE

Attack rates among exposed and non-exposed pony club members, according to potential risk factors for *Salmonella Typhi* infection in Leipzig, Germany, June 2004

Exposure	Exposed			Not exposed			RR (95% CI)
	Cases	Total	AR%	Cases	Total	AR%	
Contact with ill pony on 25 May 2004	5	9	55.6	1	6	16.7	3.3 (0.5-21.9)
Sandwich with herb dressing on 25 May 2004 only	5	7	71.4	1	8	12.5	5.7 (0.9-37.9)
Sandwich with herb dressing on 25 and/or 26 May 2004	6	8	75.0	0	7	0.0	undefined

FIGURE 2

PFGE tests of the *Salmonella Typhi* isolates, typhoid fever outbreak in Leipzig, Germany, June 2004

sandwiches on either day. No other activities during the probable period of infection showed any association with *S. Typhi* infection [Figure 2]. All isolates belonged to phage type C1 and had identical PFGE patterns. Known chronic carriers residing in the area all had phage types other than C1 and could be excluded as source of infection.

Officially, there were three people working at the snack bar during the probable time of infection. During site inspection however, an additional employee, an asylum seeker not registered with the health authorities, was identified. According to the owner, he was employed as a cleaner. However, during site inspection, he was observed preparing foods and serving customers. All blood and stool samples from the snack bar workers, including the unregistered worker, tested negative. The herb dressing was prepared every second day with fresh herbs and commercially manufactured mayonnaise by the owner. All food specimens collected from the snack bar at the time of the investigation tested negative – samples from the probable time of infection were not available. Environmental samples collected at the farm were also negative. The remains of the sick pony, which had subsequently died, had been incinerated and could not be examined.

The confirmed and probable cases underwent monthly stool, urine and blood examinations during the following six months to rule out chronic carriage state. All samples tested negative for *S. Typhi*. Sonographical examination of the upper abdomen showed no pathological alterations of gall bladder and bile ducts.

Discussion

The epidemiological investigation suggests that sandwiches with herb dressing were the probable vehicle of infection in this outbreak. Five of the six cases consumed sandwiches with herb dressing on 25 May 2004. Potential study limitations have to be considered. Given the small sample size, the likelihood of detecting statistically significant differences is low and confidence intervals wide and inaccurate. However, in our study, the association between infection and consumption of sandwiches from the snack bar is such that despite small numbers and low study power, the 2-sided Fisher's exact test is significant at the $P=0.007$ level. Although we cannot rule out an incidental association, we believe epidemiological evidence should be taken into account, given that 100% of the cases were exposed to sandwiches with herb dressing.

Food items have often been established as vehicles of *S. Typhi* infection in other outbreaks [3, 6-8]. Contamination of the dressing, which was prepared every second day, would explain why the sixth case, who consumed a sandwich with herb dressing on 26 May 2004, also became ill. Although all food specimens and workers tested negative, the possibility that additional unregistered snack bar workers may have acted as a source of food contamination cannot be excluded. If herb dressing served at a busy snack bar was the vehicle of infection, the question remains of why no further cases could be identified among the population of Leipzig despite intensive case-finding activities. One reason could be that relatively mild symptoms, like those experienced by the cases, had gone unnoticed and thus remained undiagnosed. It remains puzzling that cases were found among club members only. However, intense environmental investigation and enquiry was not able to implicate any other food consumed at the farm nor any other activity or environmental factor as source or vehicle of infection.

A similar typhoid fever outbreak in Paris in November 2003 described by de Valk et al was linked to salads served in a bistro [3]. The worker responsible for salad preparation had last been to an

endemic country in 2002, where he probably became infected. As described above *S. Typhi* was only identified in the fourth of six stool samples he submitted for investigation. The French health authorities were expecting many more cases at the time, but similar to the outbreak described here, only seven cases, six confirmed and one probable, could be identified. The investigators tentatively explained this finding with either an intermittent shedding of *Salmonella* or a temporary change in the personal hygienic habits of the bistro worker and thus a limited time span where the bacteria could have contaminated food items and infected the bistro guests. This could be another reason why no more cases were detected in Leipzig.

Immediate reporting of *S. Typhi* infection by physicians and laboratories is important in order to identify the source of infection and prevent further transmission as soon as possible. In this outbreak, phage typing of the isolated strains was an important tool to exclude chronic carriers of the Leipzig area as sources of infection. Although the source of infection in this cluster could not be confirmed by microbiological methods, there is strong epidemiological evidence implicating contamination of a food item by an unidentified person, thus emphasising the importance of strict compliance to proper hygiene practices for food handlers. When managing patients with fever of undefined origin, physicians should be aware that in addition to travel to endemic countries, contact with infected individuals returning from these countries or bringing contaminated food items from endemic regions, and chronic carriers handling food items can act as a source of *S. Typhi* infection in developed countries.

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