Epidemiol. Infect. (1995), **114**, 41–50

Typhoid fever from water desalinized using reverse osmosis

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(*Accepted 26 July 1994*)

SUMMARY

In May 1992, 81 bacteriologically confirmed cases of typhoid fever (TF) were identified in all districts of Tabuk City in northwestern Saudi Arabia. Attack rates (AR) in residential districts ranged from 0·9–10·3 per 10000. Confirmed cases included 9 workers in the city's referral hospital, King Khalid Hospital (AR 140/10000), 2 in families of medical staff, 57 in the community (AR 4·4/10000) and 13 in a local military cantonment (AR 0·8/10000). The outbreak began with the onset of TF in the three areas within 5 days, continued for 7 weeks, and ended 2 weeks after chlorination began. Among water sources, the odds ratio (OR) was highest (2·6; 95% confidence interval [CI] 1·25–5·39) for water purchased from reverse osmosis (RO) plants, especially RO plants supplied by one well (ASUW) (OR = 7·05; 95% CI 2.51–20·7). The aquifer for ASUW lay partially beneath a depression where city sewage collected. Unchlorinated water samples from ASUW 1 month after the outbreak ended yielded coliforms. ASUW probably became contaminated with *Salmonella typhi* when KKH demand overtaxed the aquifer and drew in surface water. Membranes in RO plants using this unchlorinated well water could then become fouled with *S. typhi*. RO plants, which are common throughout Saudi Arabia, need close monitoring. Water for RO must be prechlorinated to prevent microbiologic fouling of the membranes.

INTRODUCTION

Typhoid fever (TF) persists at a high incidence in countries where there is neither a safe water supply nor adequate sewage disposal and spreads through faecal contamination of food or water [1, 2]. The disease is endemic throughout the Middle East, where while occurring infrequently in native populations it is relatively common in expatriate workers, especially those from the Indian subcontinent, who constitute about 24% of the total population [3]. Most of the

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sporadic outbreaks could be traced to index cases among expatriates (e.g. cooks who were carriers), but the potential for large outbreaks exists [3]. However, although in the last two decades Saudi Arabia has witnessed a substantial improvement in living conditions, occasional outbreaks of TF are reported in different parts of the Kingdom.

In Tabuk City, 12–24 cases of TF are usually reported every year. In May 1992, officials in Tabuk City became concerned about increasing reports of TF. The early reported cases included several staff of the city's referral hospital (King Khalid Hospital (KKH)). Besides involvement in containment of the outbreak, we carried out investigations to identify the source of the outbreak, the routes of transmission, and related risk factors.

MATERIAL AND METHODS

Background

Tabuk City (population 130000) lies in northwestern Saudi Arabia adjacent to Tabuk Military City (TMC). Tabuk City has 3 public hospitals, 2 military hospitals and 13 primary health care centres (PHCCs). Ten municipality wells and 5 private wells supply Tabuk City with water. Water from the municipality wells is either piped (intermittently pumped) or hauled by trucks (capacity 6000 l) to the houses and stored in tanks. There are 20 private reverse osmosis (RO) desalination (Tahleyah) stations. These stations sell drinking water by the gallon, either at the station itself or distributed to houses in 3000-l trucks. Each Tahleyah station gets its raw water from specific private or municipal wells. Bottled drinking water imported from other cities is available. Water from municipal and private wells was not chlorinated and Tahleyah stations did not chlorinate their water.

Tabuk has no sewerage system. Accordingly, each house has a sewage holding tank designed to be permeable. TMC used to have an open sewage drainage canal (not piped) that passes about 1 km from the Abu-Sabaa underground well (ASUW). The city (altitude of about 750 m above sea level) lies in a depression between two mountain ranges from the west and east; the depression is 140 km long and 80 km wide, and is further trapped from the north and south by two other sets of mountains, with no drainage into the Red Sea. The soil is damp in many areas, and in some areas underground water surfaces. The surface water is removed through a pipeline to a remote area along Dhuba road (Fig. 1). To escape the cost of emptying their frequently refilling sewage-holding tanks, some residents in some quarters (Al-Muntazah and Al-Khaldeyah) illegally connected their sewage holding tanks to this pipeline.

ASUW is 17 years old and 400 m deep, and has 120 m of casing. It is the only underground well that lies in a tangible depression in the lowest part of the city. It lies 800 m away from one of the pumps that remove surface water. Water is pumped from ASUW on demand. The flow of water is estimated as 144000 gallons per hour. This well supplied only two Tahleyah stations: STS and NTS.

King Khalid Hospital (KKH), a 264-bed referral hospital, has its own well and RO unit, but without chlorination. Processed water was piped to the hospital and to all staff housing in the hospital compound. Doctors and nurses on duty at KKH

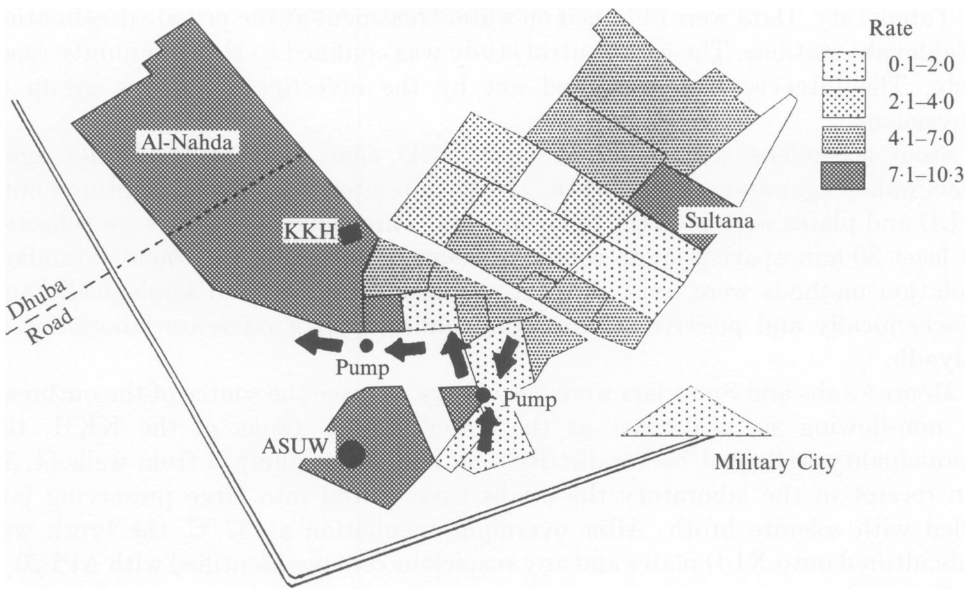

Fig. 1. Map of Tabuk City: A map of Tabuk City shows the attack rates of TF per 10000 by PHCC catchment areas during the outbreak. All the quarters of the city were affected. The highest attack rates of TF were observed in Al-Royaiat quarter, where Abu-Sabaa underground well (ASUW) lies, and in Sultana and Al-Nahda quarters, where the Tahleyah stations get their untreated water from ASUW. ASUW lies in a depression, surrounded by sewerage (doubled line) of Tabuk Military City (represented by a triangle) and pumps that remove surfacing water.

and in-patients are served with free meals, including bottled water. Other workers are housed in six rented buildings in different parts of Tabuk City; one compound is attached to the hospital. A week before the outbreak, the pump of KKH underground well broke and remained out of action for 1 month due to technical failure. ASUW provided KKH with its water needs 50000 l per day in addition to its regular truck customers and two Tahleyah stations.

The TMC has its own water treatment plant, where chlorination of water is carefully monitored. However, some of the residents of the TMC did not like the smell or taste of chlorine in water and bought their drinking water from a nearby Tahleyah station (STS).

Methods

We reviewed admission and laboratory logbooks of all Tabuk hospitals. A suspected case of TF was defined as any patient during the outbreak period (April–June 1992) for whom the differential diagnosis included TF and for which no other confirmed diagnosis was established. A confirmed case was defined as a suspect case of TF with *Salmonella typhi* isolated from blood, stool, urine or other clinical specimen. We actively sought the reporting of suspected cases. KKH records of water use were reviewed and hospital workers and non-typhoid inpatients interviewed about their source of drinking water. The houses of all patients were visited and household food and water sources of each TF patient were compared with those of 199 control houses selected at random from all houses at Tabuk City. Data were obtained on water treatment at the private desalination (Tahleyah) stations. The case-control study was confined to the community cases only. The interviews were carried out by the investigators and a group of physicians.

Stool specimens were cultured onto XLD agar, *Salmonella-Shigella* agar, MacConkey agar and selenite broth. The selenite broth was also subcultured onto XLD and plates were read the following day. Three blood cultures were collected at least 30 min apart prior to commencement of antibiotic treatment. Standard isolation methods were used. Suspect colonies were identified serologically and biochemically and positive strains were confirmed at a reference laboratory in Riyadh.

Moore swabs and Spira jars were used to try to trace the source of the outbreak in non-flowing surface water at the water storage tanks of the KKH, the municipality wells just before distribution, and water pumped from wells [4, 5]. On receipt in the laboratory the swabs were placed into large preserving jars filled with selenite broth. After overnight incubation at 37 °C, the broth was subcultured onto XLD plates and any suspicious colonies identified with API 20 E as for stools.

Control measures included the chlorination of all local water sources, which began on 22 May. Working groups were created to monitor control measures, define the needs for laboratory tests, standardize regimens of treatment and monitor daily reporting.

Data were entered and analysed using Epi Info software (version 5·01 b) [6]. The odds ratios (OR) and the exact 95% confidence intervals (95% CI) were calculated. The *t*-test was used when indicated.

RESULTS

During the outbreak period (21 April–26 June 1992), there were 81 (43·8%) bacteriologically confirmed cases (CC), and 104 (56·2%) suspected cases (SC) of TF diagnosed on clinical grounds alone. *Salmonella typhi* were identified, and all had the same API code: 440450. The antibiogram for all isolates was identical.

There were 11 CC in KKH (9 staff members and 2 in family of the staff; attack rate [AR] = 140/10000), 13 CC in the TMC (AR = 0·8/10000) and 57 community cases (AR = 4·4/10000). The first five cases of TF occurred within a 5-day period in unrelated people who lived in the three different quarters of the city. They included a hospital dietician, a child from TMC, and two young adults (a man and a woman) living at Abu Sabaa (Fig. 1). The number of CC rose steadily throughout May (Fig. 2). There was a sharp decline in the number of cases of TF after water chlorination was begun. Cases stopped in KKH about a week earlier than in the TMC and the community. Despite the sharp drop in the number of cases of TF after initiation of chlorination, CC of TF continued to appear in the community for about 5 weeks, mostly as sporadic new cases in the last 2 weeks of the outbreak.

Among CC in the community, the male–female ratio of the confirmed cases was 2:1 (Table 1). All age groups were affected, except for children under 1 year of age. CCs were highest among 15–44 year old males (Table 2). The mean age ± S.D. was 22 ± 10·3 years for CC and 23·4 ± 14·9 years for SC; the difference was

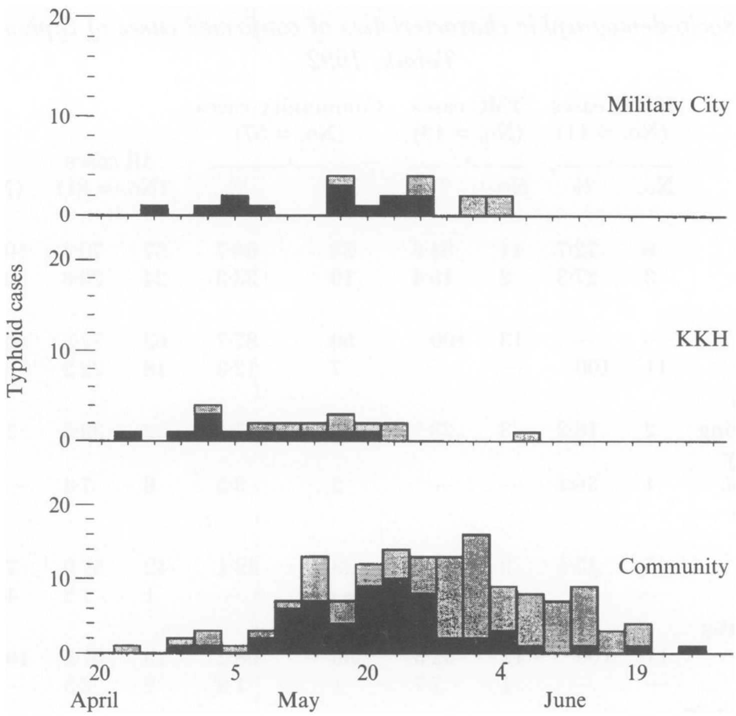

Fig. 2. The epidemic curve stratified by locality (Military City, KKH and community) by date of onset of symptoms (3-day intervals). Solid black indicates CCs and grey indicates SC. Chlorination of water started on 22 May. The onset of symptoms of the first case of typhoid fever in the outbreak was on 21 April 1992. The last SC was reported on 26 June, before the occurrence of the last CC of TF. CC of TF continued to appear in the community for 15 days after chlorination, followed by some new sporadic cases in the subsequent 2 weeks. It was easier to control the epidemic in KKH and the Military City as they were closed communities.

statistically significant (*t*-test for two means, $P = 0{\cdot}05$). Age distribution for KKH and TMC was not available. However, the ARs for KKH staff by sex were 127/10000 for males and 135/10000 for females.

KKH and five other housing compounds, located in different parts of the city, used KKH Tahleyah water for drinking. All CC lived in these six housing compounds. Except for the cleaners compound (AR 154/10000), which used a mixture of different sources for drinking water, AR ranged from 210/10000 to 330/10000. The AR did not differ among the different job classification of hospital workers at KKH (AR per 10000 was 200 for doctors, 180 for nurses, 219 for cleaners and 277 for technicians). During the outbreak period, 2036 patients were hospitalized at KKH. None of these patients developed TF during or after his or her admission.

All quarters of Tabuk City were affected. The attack rate of TF in the different quarters ranged from 0·9–10·3 per 10000. Sultana and Al-Nahda quarters were most affected. The detailed questionnaire used in the study pointed neither to a common dining place (e.g. a certain restaurant) nor to a specific food item.

The odds ratios and the 95% CI for using municipality (piped) water and water distributed by Tahleyah trucks were below 1 (OR = 0·29, 95% CI: 0·12–0·65 piped

Table 1. *Socio-demographic characteristics of confirmed cases of typhoid fever. Tabuk, 1992*

Variable	KKH cases (No. = 11) No.	%	TMC cases (No. = 13) No.	%	Community cases (No. = 57) No.	%	All cases (No. = 81)		Control (No. = 199)	
Sex										
Male	8	72·7	11	84·6	38	66·7	57	70·4	100	50·3
Female	3	27·3	2	15·4	19	33·3	24	29·6	99	49·7
Nationality										
Saudi	—	—	13	100	50	87·7	63	77·8	168	84·4
Non-Saudi	11	100	—	—	7	12·3	18	22·2	31	15·6
Marital status										
Married: living with family	2	18·2	3	23·1	27	47·4	32	39·5	76	38·2
Married: not living with family	4	36·4	—	—	2	3·5	6	7·4	—	—
Single	5	45·4	9	69·2	28	49·1	42	51·9	77	38·7
Child	—	—	1	7·7	—	—	1	1·2	46	23·1
Residency status										
Resident	11	100	12	92·3	56	98·2	79	97·5	199	100·0
Visitor	—	—	1	7·7	1	1·8	2	2·5	—	—
Education level of household head										
College	7	63·6	1	7·7	2	3·5	10	12·4	12	14·8
Secondary	—	—	1	7·7	6	10·5	7	8·6	6	7·4
Intermediate	1	9·1	2	15·4	8	14·0	11	13·6	9	11·1
Primary	—	—	8	61·5	38	66·7	46	56·8	48	59·3
Uneducated	3	27·3	1	7·7	3	5·3	7	8·6	6	7·4

Table 2. *Age/sex-specific attack rates (AR) of community confirmed cases of typhoid fever (Tabuk, 1992)*

Age group (in years)	Males No.	AR per 10000	Females No.	AR per 10000
0–1	0	0	0	0
1–5	2	18	0	0
5–14	9	44	4	19
15–44	28	113	12	47
45–65	0	0	1	18
65+	0	0	1	85

water; OR = 0·39, 95% CI: 0·15–0·80 for Tahleyah), whereas the OR and the 95% CI for using Tahleyah water by the gallon were above 1 (OR = 2·52, 95% CI: 1·2–5·4). Among water sources the odds ratio was highest for water purchased from RO plants supplied by ASUW (OR = 7·1; 95% CI: 2·5–20). The other RO source wells had OR near or less than 1·0 (Table 3).

The Moore swabs and Spira jars (more than 40 tests) all yielded a variety of enteropathogenic bacteria but not *S. typhi*. Unchlorinated water sampled from ASUW and water from ASUW loaded in trucks for drinking purposes 1 month after the outbreak yielded coliforms.

Table 3. *Household drinking water source for the community typhoid fever cases and community controls*

Water source used for drinking	Cases (No. = 57)	Controls (No. = 199)	OR	95% CI
Source of drinking water at the house level*				
Municipality (piped	9	77	0·42	0·17–0·90
Municipality (trucked)	2	9	0·94	0·10–4·70
Private wells	2	17	0·48	0·05–2·12
Tahleyah (trucked)	9	67	0·50	0·21–1·09
Tahleyah (by gallon)	44	113	2·58	1·25–5·39
Other sources†	1	1	4·29	0·05–337·7
Source of Tahleyah water by well				
ASUW	13	8	7·05	2·51–20·71
FUW	1	3	1·17	0·02–14·85
MUW	5	16	1·10	0·30–3·34
NUW	0	6	0	0·00–2·97
Municipality	11	20	2·14	0·86–5·07
Other sources†	6	19	1·11	0·35–3·10
Unknown	21	127	0·79	0·42–1·47

* People may use more than one source of water.

† Other sources include some wells outside Tabuk City.

DISCUSSION

Laboratory results suggested that there was a common source for the outbreak. Corroborative epidemiologic evidence implicating a water source for this outbreak included the city-wide distribution of cases of TF that affected all ages except children under 1 year of age, the lack of association between the first cases, the relatively equal AR of TF among health workers at KKH regardless of socioeconomic status, the similar AR in hospital-affiliated housing compounds that get their drinking water from the hospital RO plant, and the sharp drop in the number of cases after chlorination of water. Nosocomial infection in KKH could be ruled out since there was not a single case of TF among more than 2000 patients hospitalized; they were served free bottled water as well as meals cooked inside the hospital. There was no evidence that supported a foodborne mode of transmission.

Salmonella spp. are very susceptible to chlorination [7]. The continuation of the outbreak after chlorination was most likely due to the fact that the municipality effectively chlorinated its well over a relatively longer period (more than a week), compared with KKH and the TMC, where chlorination was promptly instituted. It is also plausible that some patients were incubating TF when chlorination of water was begun, or that these cases could be ascribed to secondary infection by food handlers infected in the initial wave. However, cessation of suspected cases before the last confirmed cases could be due to inadequate reporting.

Tracing waterborne outbreaks of TF to a well-defined source is rarely cited in literature [8]. Between 1981 and 1990, contaminated or inadequately disinfected groundwater in the United States of America has consistently been responsible for more waterborne outbreaks than contaminated surface water. The investigation of most outbreaks caused by untreated groundwater was unsuccessful in identifying a cause [7]. A waterborne outbreak of TF in the Philippines underscored the risk posed by the use of booster water pumps by homeowners to increase their water supply, especially in situations where a breakdown in the water system occurs [9]. During most outbreaks, water was found to be bacteriologically contaminated, but in only a few was the etiological agent isolated from water [7]. Nishina and colleagues were able to isolate *S. typhi* from a water source using membrane filter methods [8].

How did it happen in KKH and TMC?

STS and NTS Tahleyah stations were located in and were serving the most affected parts of the city, Sultana and Al-Nahda respectively. ASUW had never chlorinated its water. The aquifer layer for ASUW lay partially beneath a depression where city sewage collected. ASUW probably became contaminated with *S. typhi* when KKH demand overtaxed the aquifer and drew the surface water. Membranes in RO plants using this unchlorinated well water could then become fouled with *S. typhi*. Some of the residents of the TMC used to buy their drinking water from STS to escape the chlorine smell.

S. typhi *and reverse osmosis*

Gram-negative water bacteria, including *S. typhi*, are capable not only of surviving but also of multiplying rapidly in water from different sources, even water containing relatively small amounts of organic matter. The RO process concentrates dissolved organic matter as well as salts at the in-flow side of the membrane, creating a favorable environment for growth of bacteria. These organisms can attain high levels. Bacterial inocula of 10^5–10^7 were found to be adequate to induce typhoid fever [10]. Reverse osmosis has the advantage of being able to remove bacteria and endotoxins from water [11]. Many Tahleyah stations, including NTS and STS, had not changed their filter membranes since their establishment (NTS was established in March 1990 and STS was established in December 1991).

Age-sex differences

All age groups were affected. Absence of patients under 1 year of age was expected; it could be attributed to the protected life-style of the children and may suggest a role for breast milk. Different age-specific ARs have been reported in some other studies [12–15]. Mahle and Levine (1993) reviewed published notification data from areas where TF is endemic [12]. They found that age-specific incidence of TF varied considerably from one geographical area to another. However, they noted that the incidence in children 0–4 years old of age was remarkably lower than the incidence in other school-age children or in adults over 30 years of age. The low incidence among adults was attributed to acquired immunity, but the apparent rarity of TF in children under 5 years of age was attributed to occurrence of mild clinical forms of TF.

In 1964 Ashcroft (In: Hornick, 1985 [1]) classified the status of hygiene and sanitation into four groups: appalling, poor, a mixture of primitive and modern, and excellent conditions. Tabuk City has a mixture of primitive and modern hygiene and sanitation, with rapid urbanization, and thus falls in Ashcroft's third group; outbreaks of TF that involve all age groups would be expected. However, there were more cases among adults than in children, probably because adults drink more water than children. A relatively large inoculum of bacteria is needed to cause the disease. Moreover, ingestion of 10^5 organism caused disease in about 38% of volunteers; larger inocula resulted in higher attack rates and shorter incubation periods [1]. However, the age differences in the attack rates of TF could be attributed to the fact that adults not only consume more water, but also are more likely to drink water outside their houses, in places where Tahleyah water may not be available or unaffordable (e.g. their work-places and restaurants, where untreated water from ASUW is served). Unfortunately, we were not able to measure the amount of water consumed by different age groups because cases and controls considered such a question irrelevant.

The sex difference in the AR of TF in the community cases was unusual; the male–female AR ratio of TF was 2:1. The sex ratio in some other outbreaks of TF has been 1:1 [13, 16]. Sex differentials in Saudi Arabia need further studies.

Conclusions

Private RO plants are common throughout Saudi Arabia. Water for RO must be prechlorinated to prevent microbiologic fouling of the membranes. A surveillance system to maintain the recommended residual chlorine level and the bacteriologic quality of the city's drinking water should be closely monitored, especially at the Tahleyah stations. There is need to maintain continuous positive pressure in the piped water system in Tabuk and to develop a sewerage system. The role of enforcing new health regulations remains to be seen.

A stress test, whereby the Abu-Sabaa well would experience a similar situation in which large amounts of water would be pumped daily for 4 weeks, was desirable to support the epidemiologic data in this report. However, the cost of running such an experiment was prohibitively high.

ACKNOWLEDGEMENTS

Thanks to Mr Hassan Fakhri, regional director of Health Affairs (Tabuk), all members of Department of Preventive Medicine, the directors of Tabuk civilian and military hospitals, physicians and technicians for their assistance and collaboration, especially Dr Bahgat Abdalla and Ms Cheryl M. Hill. Authors are grateful to Ms Leslie Hoffecker for her editorial assistance.

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