Informing the public health management of Typhoid and Paratyphoid: the Australian context

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Abstract

Objective

To examine outcomes of public health (PH) management of notified enteric fever cases in south-east Queensland (SEQ) over the last five years to inform future PH management strategies.

Methods

Notification records of typhoid and paratyphoid infection in SEQ 2008-2012 (inclusive) were reviewed to determine likelihood of cases and contacts adhering to present or previous recommendations for faecal clearance/screening, duration of infectiousness of cases and extent of local transmission to contacts.

Results

Sixty-nine of 85 cases and 218 of 265 contacts submitted at least one faecal specimen. Cases were 2.7 (95%CI 1.2-6.0) and contacts were 4.4 (95%CI 3.0-6.4) times more likely to complete recommended faecal clearance/screening under previous compared to present guidelines (requiring more specimens). In ten cases with positive post-treatment specimens, last recorded infectiousness was 19 days to six months after notification. The documented rate of local transmission of infection was 18/1000 contacts submitting at least one faecal specimen (95%CI 6-48/1000).

Conclusions

Local transmission risk of enteric fever in SEQ is low; though small numbers of cases may have prolonged bacilli excretion post-treatment. More complex clearance/screening regimens are associated with decreased compliance.

Implications

Pursuing extensive faecal clearance/screening regimens is unlikely to be effective in terms of PH management of enteric fever in SEQ. We suggest a unified national approach focussing on cases/contacts at high risk of disease transmission.

The bacterial pathogens *Salmonella enterica* subspecies *enterica* serovars Typhi (S. Typhi - typhoid) and Paratyphi (S. Paratyphi - paratyphoid) both cause the systemic illness enteric fever. They are important public health pathogens due to both severity of the illness and potential to cause outbreaks in the community and among close contacts.

Transmission of S. Typhi and S. Paratyphi is by the faecal-oral route and humans are the only known reservoir (1, 2). Some cases may become chronic carriers (ongoing shedding of the bacilli for more than 12 months (3)) with a distinct risk of transmission to others, particularly when the carrier is a food handler (4, 5). While around 10 percent of untreated cases may excrete bacilli for up to 3 months and 2 to 5 percent of untreated cases may become chronic carriers (1), estimates of long-term carriage among those treated with appropriate antibiotics are less clear and rates are likely to be very low (6).

Enteric fever is uncommon in Australia. In Queensland, cases of S. Typhi and S. Paratyphi are notifiable, meaning laboratories are required to report confirmed cases to Queensland Health. Between 2008 and 2012 (inclusive) the average annual number of notifications for typhoid and paratyphoid was 18 and 7 respectively (7). Most cases were reported in the more urbanised south east of Queensland.

The goal of public health management is to identify undiagnosed cases and identify cases with ongoing excretion so measures to prevent the spread of the infection to others can be implemented. In Queensland, this involves rigorous schedules of sequential stool specimens for cases and contacts, as well as restriction of cases and contacts from 'high risk duties' such as food handling or provision of health care until demonstration of consecutive negative specimens (8).

Here, as elsewhere, the requirement to complete an extensive schedule of clearance and screening stool specimens is resource intensive for Public Health Units and is often intrusive for cases, contacts and their families. Others have questioned the effectiveness and efficiency of broad screening regimens (5, 9). Thomas and colleagues highlighted the difficulty in ensuring case and contact adherence to lengthy sampling regimens and went on to estimate a cost of £3463 to detect one person with a positive stool sample. These authors suggest a focus on high-risk groups may be a more efficient approach. An earlier Australian review of national and international typhoid public health management guidelines (6) recommended screening all close contacts of typhoid cases, although these authors also state that there is a lack of evidence for any single approach.

The United Kingdom has recently amended national public health guidelines for the management of notified typhoid and paratyphoid cases (10). Based on a literature review, enhanced surveillance data, international guidelines, and expert consensus, the new guidelines recommend considerable reduction in clearance schedules from previous versions, focussing on risk groups and non-travel related cases, and decreasing the breadth of screening, focussing on co-travellers and identifying the source of infection if the index case is not travel-related. These current UK guidelines are similar to those of British Columbia, Canada (11). Other Canadian states have a similar focus on high risk cases, but also screen high risk contacts (12, 13).

Around Australia, the public health management of enteric fever varies across jurisdictions (6) and to these international guidelines. Published state guidelines indicate a requirement for stool specimens from all cases in New South Wales (14), Queensland (7) and Victoria (15), but only from high risk cases in Western Australia (16). Queensland and New South Wales require screening of all contacts. The state of Victoria screens co-travellers, but exercises discretion in screening other contacts

(15), whereas, Western Australia screens high risk contacts (health care, residential and child care workers; food handlers; children in child care; people with faecal incontinence) with similar exposure to the case.

This study seeks to add to the literature on the public health management of typhoid and paratyphoid from the Australian context; answering questions about how long cases are likely to be infectious, whether there is any evidence of local transmission from cases to contacts within our study area, and how likely cases and contacts are to follow past and present recommendations for faecal clearance and screening respectively. Given these, the evidence base, and comparison to international guidelines, we make recommendations regarding future public health management of enteric fever in Australia.

Methods:

We interrogated existing electronic and paper records of the public health management and follow up of all notifications of typhoid and paratyphoid infection in south-east Queensland from 2008 -2012 inclusive. The study area (Figure 1) included the following local government areas: Brisbane City, Ipswich City, Lockyer Valley, Logan City, Moreton Bay Region, Redland City, and Somerset Region. Between 2008 and 2012, this area was responsible for 74% of all Queensland notifications of typhoid and paratyphoid.

Cases were followed up in accordance with Queensland Health guidelines for public health management of enteric fever (8, 17). Guidelines were updated in 2010 and consequently clearance and screening schedules (for cases and contacts respectively) changed during the study period (Box 1). The main schedule changes related to the inclusion of additional clearance and screening stool specimens.

We entered data relating to cases and contacts into a purpose built Excel workbook. Fields collected included: public health unit, date of notification, age at onset in years, gender, ethnicity, date of symptom onset, whether the person was considered at 'high risk' of transmitting the disease, the dates and results of all faecal specimens and treatment received. For cases only, we recorded dates and locations of travel during the exposure period. For contacts only, we recorded the nature of the contact (eg household, travel companion).

Analysis was undertaken in SPSS version 21; with confidence intervals calculated using EpiInfo6. In SPSS, proportions were compared using the chi-squared test, and medians were compared using the median test.

We examined the following outcomes: proportion of positive contacts, rate of local transmission to contacts, the proportion of cases and contacts who completed recommended faecal clearance and screening respectively, the length of time from notification to completion of faecal clearance / screening or completion of public health follow up where recommended clearance / screening was not followed, the rate of intermittent shedding and chronic carriage among cases, and the length of time from onset of symptoms to last positive specimen.

Contacts with one or more positive faecal specimens were deemed to have acquired disease locally when this was indicated by the timing of symptom onset in relation to the index case, travel history, and the nature of contact with the index case. We calculated the rate of local transmission to contacts by dividing the number of such contacts by the total number of known contacts and calculated a 95% confidence interval. As failure to submit faecal specimens may bias this result, we also calculated the rate of local transmission using the number of contacts who submitted

at least one faecal specimen as the denominator and calculated a 95% confidence interval.

We calculated the proportion of cases and the proportion of known contacts who completed recommended faecal clearance / screening. As Queensland guidelines changed during the study period (Box 1), we considered the recommendations active at the time of follow up to make this determination. We also calculated the median and range of time to completion of recommended clearance / screening for cases and contacts, and where this was not completed, we calculated the median and range of time to cessation of public health follow up. We examined the effect of age and gender on these results in univariate analyses using the median test. Missing data precluded examining the effect of ethnicity, whether the person was considered 'at high risk' of disease transmission and treatment on these results.

Intermittent shedding was defined as one or more negative results followed by at least one positive result among post treatment faecal samples. Chronic carriage was defined as one or more positive faecal samples more than 12 months after notification. The rate of intermittent shedding and chronic carriage was calculated using all notified cases as a denominator and also using cases who submitted at least one post-treatment faecal sample as a denominator. Ninety-five percent confidence intervals were calculated.

The last positive specimen was chosen in preference to other measures (eg first negative specimen or completion of recommended follow up) as a proxy for duration of infectivity as it is the least susceptible to bias as a result of lack of compliance with follow up. The median and range of time from notification to last positive specimen among those with at least one positive post treatment specimen were calculated.

Because of the small number of cases that had one or more positive post treatment specimens the effect of other variables on intermittent carriage and duration of infectivity could not be examined.

The study was approved by the Queensland Health Central Human Research Ethics Committee (HREC/12/QHC/48).

Results:

Cases

Eighty-five cases were notified during 2008-2012 in the study area. Twenty-six cases (31%) were infected with *S. Paratyphi* and 59 cases (69%) were infected with *S. Typhi*. Cases ranged in age from 2 years to 80 years, with an average of 29 years. Thirty-seven cases were female (43.5%). Eighty cases acquired infection overseas, most commonly in India (37 cases). Five cases were believed to have acquired infection in Australia. These Australian-acquired cases were all household contacts of another notified or presumed case, although three were also travel companions (see '*Contacts*' results below).

Of the 85 cases, 69 submitted at least one clearance faecal sample (81%) (Figure 1). However, only 27 cases (32%) completed the recommended faecal clearance. Ten cases submitted no samples (12%), forty-two cases (49%) commenced but did not complete recommended clearance, four returned to their home country and were not followed up in Australia (5%), and the records were incomplete for two (2%). Of those completing clearance, the median time from notification to final negative sample was 35 days (range 12 – 170 days). Of those not completing clearance, the median time to cessation of public health follow up was 63 days (range 34 – 465 days), and the median time to collection of last faecal specimen (where the cessation of public health follow up was not recorded) was 42 days (range 3 – 396 days). Age

and gender did not impact on these results (all p values >0.05). However, cases were 2.7 times (95%CI 1.2 – 6.0) more likely to complete recommended faecal clearance prior to the change in guideline than after it (p = 0.006).

Two cases met our definition for intermittent shedding, and though eight more had at least one positive post-treatment faecal specimen, none met the definition for chronic carriage. The overall positive yield from cases with at least one clearance specimen was 14% (10/69). The rate of intermittent shedding was 24 per 1000 notified cases (95%CI 4 – 76 per 1000) and 29 per 1000 notified cases who submitted at least one post treatment faecal sample (95%CI 2 – 106 per 1000). The two cases deemed 'intermittent shedders' had two and three post treatment specimens that were negative before having a positive specimen. The case with three negative specimens was retested rather than cleared at that point because the last specimen was submitted too close to the previous one according to the guideline in place at the time. There was no significant difference in the proportion of 'intermittent shedders' detected after the change in guideline (1/27) compared to before it (1/42) (p=0.749). The longest time between notification and last positive faecal specimen was 189 days (median 37 days; range 19-189 days). Three of the ten with at least one positive post-treatment specimen completed recommended clearance.

Contacts

Three hundred and seven contacts were recorded during 2008-2012 (Figure 2); an average of 3.6 contacts for each case. Where recorded (n=230), contacts ranged in age from newborn to 81 years, with an average age of 28 years. Gender was recorded for 235 contacts. One hundred and six contacts were female (35%) and 129 were male (42%). Gender was not recorded for the remainder. Forty-two of the 307 contacts were travel companions (13.5%), 214 were household contacts (70%), and 51 (16.5%) were both household contacts and travel companions. Thirty-three

(11%) travel companions and nine (3%) household members were not contactable for active follow up, usually because they were not residing in Australia. Faecal screening was recommended and active follow up pursued for the remaining 265.

Of these, 218 contacts (82%) submitted at least one faecal sample, but 160 (60%) submitted the requested number of samples. Of those completing screening, the median time taken between case notification and final negative contact sample was 9 days with a range 1 to 162 days. Of those not completing screening, the median time to cessation of public health follow up was 65 days (range 8 – 415 days), and the median time to collection of last faecal specimen (where the cessation of public health follow up was not recorded) was 15 days (range 1 – 86 days). Age and gender did not impact on these results (all p values >0.05). However, contacts were 4.4 times (95%CI 3.0 - 6.4) more likely to complete screening if the case was notified prior to the change in guideline than after it ($p<0.001$).

Five of 218 contacts (2.3%) submitting at least one faecal specimen had a positive result. All were positive on the first specimen. There was no significant difference in the proportion of contacts with a positive specimen after the change in guideline (2/76) compared to before it (3/142) ($p=0.807$).

Three of the five contacts with a positive result were symptomatic. Both asymptomatic contacts with a positive result were identified in the period after the change in guideline. There was no significant difference in the proportion of asymptomatic contacts with a positive specimen after the change in guideline (2/76) compared to before it (0/139) ($p=0.055$).

Four of the five contacts with a positive result were most likely to have acquired disease via household contact within Australia (Figure 2). The rate of documented

local transmission of infection was thus 15 per 1000 known contacts (95%CI 5 – 40 per 1000) and 18 per 1000 contacts submitting at least one faecal sample (95%CI 6 – 48 per 1000). In addition, one index case gave a history of household contact with a sick relative in Australia for whom no other details were available. This case had no history of travel to an endemic area, and was deemed to have acquired disease within Australia.

Conclusions and Implications:

In this retrospective review of public health records in south east Queensland, Australia, both cases and contacts were significantly more likely to complete requested public health follow up prior to a change in guidelines, that is, when fewer faecal specimens were required of them. Others have also noted the difficulties in obtaining compliance with clearance and screening regimens (5, 9, 10).

Our estimate of the duration of infectivity of cases is limited by the fact that only one third of cases completed the recommended faecal clearance. With this limitation in mind, the ten cases who had at least one positive specimen post-treatment were last recorded infectious between 19 days and six months after notification. While not treated comparably to today's cases, a cohort study of hospital patients between 1920 and 1947 reported 153 of 1387 patients (11%) temporarily excreted bacilli in either faeces, urine or both, while a further 32 (2.3%) became chronic carriers (18). All but one of those who ceased excreting bacilli spontaneously did so within the first three months of convalescence. This proportion seems similar to our study where the overall positive yield was 14% of the cases submitting at least one specimen.

In eight of the ten cases with a positive post-treatment specimen in our study, the first post treatment specimen was positive, and hence, ongoing follow up was

predicated. Others have also found the first clearance specimen provides the highest yield and that subsequent samples are much less likely to be positive (9, 19).

Ninety-four percent of the cases in our study acquired the infection overseas. This is consistent with findings from other Australian and international studies. In a 2000 study from south-eastern Sydney, 33 of 39 cases with known travel histories acquired their illness overseas (20), while a later study from western Sydney found all 20 cases where travel history was known had acquired their illnesses in typhoid endemic countries (21). Fifty of 54 cases in a 2001 study from Victoria were overseas-acquired (6). Ninety-three percent of cases in a recent UK study were acquired in endemic areas (9).

The incidence of local transmission to screened contacts in our series was very low at between 15 and 18 per 1000 contacts. Thomas and colleagues reported similar results in 2006, with three of 251 (1%) contacts having positive screening samples (5). Our results are also very similar to those of a recent study in the United Kingdom, where 1.6% (10/645) of contacts yielded positive results on screening samples (9). In the UK study, all ten contacts with positive results had travelled to endemic areas with the original case. The authors concluded these contacts were more likely to have been exposed to the same source rather than secondary cases. In our series, three of the four contacts concluded to be secondary cases were travel companions of the related index cases. However, each gave a history of illness onset in Australia an incubation period after their case's illness onset. The remaining contact deemed a secondary case was not a travel companion of their index case.

The low return on screening samples is further emphasised by the fact that three of the five contacts in our study with positive faecal specimens sought medical care for symptoms at the time of specimen collection and thus would likely have been

identified in the absence of a screening regimen. True screening then detected just two asymptomatic cases (positive yield of 0.9% of those with at least one specimen). Again, this is very similar to the results of other studies (5, 9, 19).

Our study is limited by its retrospective nature and thus the reliance on data previously recorded for public health management rather than research. Inherent are the problems of missing data. In particular, demographic information about contacts was frequently incomplete. However, case details and faecal specimen results were more reliable. Reassuringly, our results were very similar to available published local and international studies in non-endemic areas.

Thus, in our series, more than one post-treatment specimen detected only two additional shedding cases, and screening asymptomatic contacts detected only two additional cases. None of these cases was classified as being at high risk of disease transmission, although our series did include seven cases (8%) who were so classified. Given this; the equivalency of the former and the current Queensland guidelines in terms of the yield from both clearance and screening regimens; the limited evidence for any one approach to public health follow up suggested by the literature (6, 9, 10); and that international and some local guidelines tend to favour a high-risk approach, the Queensland guidelines for public health units were reviewed and the following amendments were endorsed: faecal specimens will now only be required for high risk cases, high risk contacts and household contacts of non-travel related cases; two rather than three negative specimens will constitute clearance for cases and a negative screen for contacts.

Looking forward, we also make the following recommendations:

1. That a unified national approach to the public health management of enteric fever be developed in Australia

2. That the development of a national guideline consider the similarities between our results and those of the UK group whose work informed that national approach (9)

Further, we suggest that prolonged attempts to gain compliance with clearance and screening regimens in Australia is not cost effective, especially for those not at 'high risk' of further transmission. Instead, in the absence of a previous positive specimen, we propose cessation of public health efforts to obtain clearance specimens after two incubation periods (60 days) and screening specimens after one incubation period (30 days). Should a positive specimen be returned by someone at high-risk of disease transmission, further efforts to ensure clearance are warranted.

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Box 1: Summary of public health management of enteric fever cases during study period		
Case / contact type	Management for period Jan 2008 to Nov 2010	Management for period Nov 2010 to Dec 2012
'High-risk' cases	Exclude from work and school until clearance proven, through two consecutive negative stool specimens taken at least one week apart. Specimens taken after completion of antibiotic therapy and resolution of diarrhoea.	Exclude from higher risk duties until clearance proven, through two consecutive stool specimens taken at least one week apart. Specimens taken at least 48 hours after completion of antibiotic therapy. Screening stool specimen one month after second clearance specimen (or earlier if symptoms recur).
Other cases	Return to work or school after illness recovery. Two clearance stool specimens taken at least one week apart. Specimens taken after completion of antibiotic therapy and resolution of diarrhoea.	Return to work or school after illness recovery. Two clearance stool specimens taken at least one week apart. Specimens taken at least 48 hours after completion of antibiotic therapy. Screening stool specimen one month after second clearance specimen (or earlier if symptoms recur).
Travel companions	Each situation assessed individually. Letter sent to	Each situation assessed individually. Letter sent to travel

	travel group.	group.
'High-risk' household contacts	Exclude from work until two negative screening stool specimens taken at least 24 hours apart.	Exclude from work until two negative screening stool specimens taken at least 24 hours apart. Third screening specimen at least 14 days after last contact with infectious case.
Other household contacts	No exclusion. Single screening stool specimen for contacts of case acquired overseas. For contacts of locally-acquired case, two screening stool specimens at least 24 hours apart.	No exclusion. Two screening stool specimens taken at least 24 hours apart, followed by third specimen 14 days after last contact with infectious case.
<p>'Contact' is defined as household contact or travel companion in both guidelines.</p> <p>'High-risk' is defined as those at high risk of transmitting enteric fever, including food handlers, carers of patients, children and elderly; those unable to maintain personal hygiene and their carers.</p>		

Figure 1. Geographic area of study

Figure 2. Public health follow up of cases of enteric fever notified to public health units in south-east Queensland 2008-2012

* Intermittent shedding was defined as one or more negative post treatment stool samples followed by at least one positive stool sample.

Figure 3. Public health follow up of contacts of cases of enteric fever notified to public health units in south-east Queensland 2008-2012

Shaded grey = felt to have acquired infection in Australia