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Changing Patterns in Enteric Fever Incidence and Increasing Antibiotic Resistance of Enteric Fever Isolates in the United States, 2008–2012

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Abstract

Background—Enteric fever in the United States has been primarily associated with travel and with worrisome changes in global patterns of antimicrobial resistance. We present the first comprehensive report of National Typhoid and Paratyphoid Fever Surveillance System (NTPFS) data for a 5-year period (2008–2012).

Methods—We reviewed data on laboratory-confirmed cases reported to NTPFS, and related antimicrobial susceptibility results of *Salmonella* Typhi and Paratyphi A isolates sent for testing by participating public health laboratories to the Centers for Disease Control and Prevention's National Antimicrobial Resistance Monitoring System laboratory.

Results—During 2008–2012, 2341 enteric fever cases were reported, 80% typhoid and 20% paratyphoid A. The proportion caused by paratyphoid A increased from 16% (2008) to 22% (2012). Foreign travel within 30 days preceding illness onset was reported by 1961 (86%) patients (86% typhoid and 92% paratyphoid A). Travel to southern Asia was common (82% for typhoid, 97% for paratyphoid A). Among 1091 (58%) typhoid and 262 (56%) paratyphoid A isolates tested for antimicrobial susceptibility, the proportion resistant to nalidixic acid (NAL-R) increased from 2008 to 2012 (Typhi, 60% to 68%; Paratyphi A, 91% to 94%). Almost all NAL-R isolates were resistant or showed decreased susceptibility to ciprofloxacin. Resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (multidrug resistant [MDR]) was limited to Typhi isolates, primarily acquired in southern Asia (13%). Most MDR isolates were also NAL-R.

Conclusions—Enteric fever in the United States is primarily associated with travel to southern Asia, and increasing resistance is adding to treatment challenges. A bivalent typhoid and paratyphoid vaccine is needed.

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Keywords

enteric fever; typhoid and paratyphoid; surveillance; antimicrobial resistance; travelers' health

Each year, typhoid and paratyphoid fever, respectively, cause an estimated 26 million and 5 million illnesses globally [1]. Both are enteric fevers, which are acute systemic infections caused by *Salmonella enterica* serotypes Typhi and Paratyphi A and B (and rarely C) that cause an estimated 215 000 deaths annually [2]. Populations that lack access to potable water and adequate sanitation and hygiene are most affected. Incidence is highest in southern Asia and sub-Saharan Africa [3]. Paratyphi A infections have increased in Asia, with rates surpassing typhoid in some areas [4–7].

Enteric fever is transmitted via the fecal-oral route from people who are acutely infected, convalescent, or chronic carriers. It is an acute febrile illness with nonspecific symptoms. Systemic complications ranging from intestinal perforation to neurologic manifestations have been well documented [8, 9]. Typhoid and paratyphoid fever are clinically indistinguishable [10, 11], and bacterial culture remains the gold standard for diagnosis [3]. Antimicrobial therapy has reduced typhoid case-fatality rates from 15%–20% to <1% [12].

In the United States, enteric fever has been rare since the 1940s [13–16]. Travelers since 1970s, especially those returning from southern Asia, have accounted for an increasing proportion of cases [13–15]. Vaccination is recommended for US travelers to countries where typhoid is endemic [17], but no vaccine against paratyphoid fever is available. Resistance to antimicrobial agents has increased in cases diagnosed in the United States, reflecting similar changes in southern and southeastern Asia [3, 7, 18]. Multidrug-resistant (MDR) *Salmonella* Typhi, defined as resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole—agents historically used in the United States and other countries to treat enteric fever—has been reported in US patients [14, 15, 19]. Treatment recommendations include fluoroquinolones (eg, ciprofloxacin) and third-generation cephalosporins (eg, ceftriaxone), so the recent emergence of strains with decreased susceptibility to fluoroquinolone agents is concerning. Infection with these strains increases the cost and complexity of treatment [20, 21].

Typhoid fever has been nationally notifiable in the United States for many years, but paratyphoid fever is notifiable only in the general category of "salmonellosis." In 2008, however, the national typhoid surveillance program at the Centers for Disease Control and Prevention (CDC) expanded to become the National Typhoid and Paratyphoid Fever Surveillance (NTPFS) system. At the same time, the National Antibiotic Resistance Monitoring System (NARMS), which already requested *Salmonella* Typhi and some Paratyphi A and C isolates from state public health laboratories, expanded its request to include all Paratyphi A and C isolates. We reviewed data from NTPFS and NARMS during the first 5 years of expanded surveillance (2008–2012).

METHODS

Since 1975, state and local health officials have reported typhoid cases to CDC using a standard form including patient demographics, clinical information (hospitalization and outcome), typhoid vaccination status, and travel history. When paratyphoid fever was added to NTPFS in 2008, health departments began reporting cases of enteric fever in which serotypes Typhi, Paratyphi A, or Paratyphi C were isolated from a normally sterile site or from stool or urine. Paratyphi B infections are not reported to NTPFS because many public health laboratories have limited capacity to differentiate serotype Paratyphi B (which is rare and causes enteric fever) from serotype Paratyphi B variant L (+) tartrate (+) (previously called *Salmonella* Java, which is common and typically causes gastroenteritis, not enteric fever). Patients who traveled outside the United States within 30 days before symptom onset are considered to have travel-associated illness. Domestically acquired illness is defined as illness in a person without such a travel history.

Countries visited by travelers were grouped by regions based on United Nations criteria [22]. Data from the National Trade and Tourism Office (http://travel.trade.gov/outreachpages/download_data_table/2014_Outbound_Profile.pdf) on numbers of US residents traveling to different regions were used to compare the risk of typhoid and paratyphoid fever for travelers to each region from which cases were reported. Southern Asia was used as the reference, with regions with risk from 0.1 to 0.01 that of southern Asia considered as “low” risk and regions with risk from 0.009 to 0.001 that of southern Asia as “very low” risk.

The CDC NARMS laboratory uses broth microdilution (Sensititre, Trek Diagnostics, Cleveland, Ohio) to determine the minimum inhibitory concentration (MIC) for 14 antimicrobial agents. We analyzed results for 7 antimicrobial agents most relevant to enteric fever treatment: azithromycin (testing began in 2011) and ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, nalidixic acid, ciprofloxacin, and ceftriaxone (testing was conducted throughout the review period). Resistance is defined using Clinical and Laboratory Standards Institute (CLSI) MIC breakpoints, where available. NARMS methods, CLSI classes, and MIC breakpoints are detailed elsewhere [23, 24]. We defined MDR as resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole.

We calculated descriptive statistics for typhoid and paratyphoid A fever cases and compared epidemiologic characteristics, risk factors, and antimicrobial resistance patterns; paratyphoid C cases were excluded because the numbers were small. We used Pearson exact χ^2 tests for categorical variables and compared continuous variables using the Wilcoxon rank-sum test. Statistical significance was determined at a 2-tailed P value <.05. Statistical analyses were conducted using SAS software, version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

National Typhoid and Paratyphoid Fever Surveillance

During 2008–2012, a total of 2341 enteric fever cases were reported to NTPFS (1872 [80%] typhoid, and 469 [20%] paratyphoid A). The proportion caused by paratyphoid A increased

from 16% in 2008% to 22% in 2012 (Figure 1). Seasonal patterns were similar for typhoid and paratyphoid A, with about one-third of cases reported from July through September (typhoid, 35%; paratyphoid A, 34%). All 50 states reported typhoid cases, and 35 states reported paratyphoid A cases; the top states for each were California (18% of Typhi, 17% of Paratyphi A), New York (14% of Typhi, 12% of Paratyphi A), and New Jersey (8% of Typhi, 12% of Paratyphi A). Among the 10 states that reported ≥3% of typhoid cases, only Texas and Florida did not also report ≥3% of paratyphoid cases.

Patients with typhoid were slightly younger than those with paratyphoid A (median age, 23 vs 26 years; $P = .001$); 225 (16%) typhoid patients and 38 (11%) paratyphoid A patients were ≤5 years old. Among those, 52 (23%) typhoid patients and 7 (18%) paratyphoid A patients were <2 years old. Otherwise, demographic and clinical characteristics were similar for typhoid and paratyphoid A cases (Table 1). For both, slightly fewer than half the patients were female: 883 (48%) for typhoid, 228 (49%) for paratyphoid A. Although more typhoid than paratyphoid A patients were hospitalized for ≥24 hours (typhoid, 77%; paratyphoid A, 69%), this difference was not statistically significant, and the median duration of hospitalization for both was 5 days. Six typhoid patients (<1%) and 2 paratyphoid A patients (<1%) died.

Most cases were associated with foreign travel, but the percentage was slightly lower for typhoid (86%) than paratyphoid A (92%) ($P = .0006$). For the 1465 cases in which the patient traveled to a single destination (single country), southern Asia was the most common destination, accounting for 1206 (82%) typhoid cases and 370 (97%) paratyphoid A cases (Table 2). At least 10 typhoid patients each reported travel to other subregions of Asia, especially southeastern Asia (including the Philippines and Indonesia); to the western Africa subregion (especially Nigeria); and to the Caribbean (especially Haiti and the Dominican Republic) and Central America (especially Mexico and Guatemala) subregions of the Americas. Using the per-traveler risk in travelers to southern Asia as the reference, travelers to Africa and southeastern Asia were in the “low” risk category, and travelers to the Caribbean, Central America, eastern Asia, and South America were in the “very low” risk category.

US citizens (ie, not visitors or noncitizen US residents) accounted for a lower percentage of travel-associated typhoid cases (552/838 [66%]) than paratyphoid A cases (183/231 [79%]) ($P = .0001$). Among those reporting the travel purpose (>1 purpose could be reported), visiting friends or relatives was the most common, reported in 966 (85%) of typhoid and 246 (88%) of paratyphoid A cases. Tourism (typhoid, 95 [11%]; paratyphoid A, 36 [17%]) and business travel (typhoid, 79 [9%]; paratyphoid A, 23 [11%]) were also reported. Travelers immigrating to the United States during the 30 days before their diagnosis accounted for 113 (13%) of travel-associated typhoid cases and 1 (6%) of travel-associated paratyphoid A cases.

Among travel-associated cases with known typhoid vaccination status, significantly fewer typhoid patients than paratyphoid A patients had been vaccinated within 5 years (6% [56/983] vs 23% [45/199]; $P < .0001$).

Enteric fever was acquired domestically in 524 (14%) typhoid cases and 36 (8%) paratyphoid A cases. Of these, 29 (6%) typhoid cases and 1 (3%) paratyphoid A case were related to outbreaks (≥2 epidemiologically related cases). An asymptomatic carrier thought to have been the source was identified for 32 (15%) domestically acquired typhoid cases and 1 (3%) domestically acquired paratyphoid A case.

Antimicrobial Resistance

Antimicrobial susceptibility testing was available for isolates from 1091 (58%) typhoid cases and 262 (56%) paratyphoid A cases. Of these, 786 were tested during 2008–2010, when the panel did not include azithromycin, and 567 were tested during 2011–2012, when azithromycin was included. Specimen sources for Typhi isolates included blood (867 [79%]), stool (158 [15%]), urine (15 [1%]), and other/unknown sites (51 [5%]). Most Paratyphi A isolates were also obtained from blood (226 [86%]); other sources included stool (29 [11%]), urine (1 [<1%]), and other/unknown sites (6 [2%]).

Antimicrobial resistance was common. Among Typhi isolates, 314 (29%) were susceptible to all clinically relevant antimicrobial agents, 750 (69%) were resistant to nalidixic acid (NAL-R) or had decreased susceptibility to ciprofloxacin (NAL-R/DSC), 127 (12%) were MDR, and 108 (10%) were both NAL-R/DSC and MDR (Table 3). Among NAL-R Typhi isolates, 99% were either resistant or displayed decreased susceptibility to ciprofloxacin. One Typhi isolate from a traveler to India had intermediate susceptibility to ceftriaxone, but none were resistant. All Typhi isolates tested were susceptibleto azithromycin. NAL-R/DSC and MDR were more frequent in Typhi isolates from travel-associated cases. NAL-R/DSC was particularly common in isolates from travelers to India (91%) and Bangladesh (93%), and NAL-R/DSC with MDR was seen in 53% of isolates from travelers to Pakistan. Overall, the percentage of NAL-R/DSC Typhi increased somewhat from 2008 through 2012 (range, 60%–74%), whereas the proportion of MDR Typhi isolates remained stable (range, 10%–13%). Susceptibility to all clinically relevant agents was most frequent in isolates from travelers to destinations in the Americas.

Susceptibility to all agents was less common for Paratyphi A isolates (n = 13 [5%]) than for Typhi. NAL-R/DSC was common in Paratyphi A isolates (246 [94%]; $P < .0001$), but no isolates were MDR. All isolates were susceptible to ceftriax-one, and all tested with azithromycin were susceptible. The proportion of NAL-R/DSC Paratyphi A remained generally stable from 2008 through 2012 (range, 88%–94%).

Rates and duration of hospitalization were similar regardless of antimicrobial resistance pattern. Specifically, for typhoid, hospitalization was reported for 81% (584, median of 5 days) of patients with NAL-R/DSC infections, 80% (102, median of 6 days) of those with MDR infections, and 77% (239, median of 5 days) of those with infections susceptible to all clinically relevant agents. Similarly, for paratyphoid A, hospitalization was reported for 72% (167, median of 5 days) of patients with NAL-R/ DSC infections and 77% (10, median of 4 days) of those whose infections were susceptible to all clinically relevant agents.

Paratyphoid C Cases

Two cases of paratyphoid C were reported (2008 and 2011). The patients were 2 and 6 years old, both boys. Neither reported travel outside the United States. One isolate submitted to NARMS was susceptible to all agents tested.

DISCUSSION

This review of enteric fever cases diagnosed in the United States from 2008 through 2012 reveals recent developments that are important for treatment and prevention. The decrease in domestically acquired enteric fever observed over recent decades [11, 14] continues, with about 90% of cases acquired abroad. Paratyphoid fever, primarily caused by Paratyphi A acquired in southern Asia, accounts for a substantial and steadily increasing proportion of cases. High rates of antimicrobial resistance, especially in infections acquired in southern Asia, pose a continued challenge to effective treatment and highlight the importance of prevention.

For years, the proportion of enteric fever cases acquired during international travel has increased in the United States [11, 13–15] and in other industrialized countries [20, 25–27]. In our 5-year study, 86% of typhoid cases were travel-associated, compared with 79% during 1999–2006 [14]; the travel-associated percentage was even higher (91%) for paratyphoid fever. Careful attention to food and water safety while traveling reduces the risk of typhoid and paratyphoid fever [28]. Although we do not have data on whether the patients reported here received information on food and water precautions before traveling, it is likely that few did. Most patients reported visiting family and friends as the primary reason for travel. Surveys of international travelers indicate that most travelers to high-risk regions do not seek travel health advice beforehand [29–31] and that those visiting family and friends are even less likely than other travelers to do so [32]. In these surveys, respondents who sought advice reported that the Internet and primary care physicians were their main information sources. Traveler health outreach and education programs, especially programs tailored for people visiting family and friends, are needed. Prevention messages available through multiple sources including websites, social media, primary health practitioners, and small businesses serving immigrant communities may have impact.

Paratyphoid A continues to spread, becoming more common in areas where it is already established [6, 33] and emerging in new areas, primarily in Asia [34, 35]. US surveillance data reflect both trends—the percentage of cases associated with travel was even higher for paratyphoid A than typhoid, as was the percentage of cases linked to travel in Asia. Notably, among cases of domestically acquired enteric fever, fewer paratyphoid A than typhoid cases were linked to a domestic outbreak. Also, a chronic carrier was less commonly identified in investigations of paratyphoid A (3%) than typhoid (15%). These patterns suggest that there are fewer carriers of paratyphoid A than typhoid in the United States, which may be due to immigration patterns and recent emergence of Paratyphi A. Our data showed similar rates and duration of hospitalization and case-fatality rates for paratyphoid A and typhoid. These findings are consistent with other recent studies [10, 11].

We observed concerning increases in antimicrobial resistance [11, 14], particularly in resistance to nalidixic acid, a marker of decreased susceptibility or resistance to fluoroquinolones such as ciprofloxacin. Although hospitalization rates and durations were similar in our data, resistant infections can be associated with greater likelihood of treatment failure and pose higher treatment costs [21, 36]. Our review shows patterns of antimicrobial resistance linked to specific destinations and consistent with reports from affected countries, with NAL-R strains of Typhi and Paratyphi originating mainly in southern Asia [3, 5, 6, 37–39], and MDR cases originating in southern Asia and Africa [40–42]. Fluoroquinolones are recommended for empiric treatment of enteric fever in adults [9], but rates of quinolone resistance exceeding 80% in typhoid and paratyphoid A among travelers to southern and southeastern Asia suggest that treatment failures will occur. Resistance to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (multidrug resistance), agents that were widely used for treatment of enteric fever before resistance in Typhi became widespread, was seen only in Typhi in our review, not in Paratyphi. Furthermore, our review demonstrated that multidrug resistance was relatively stable, probably because these agents are now less often used to treat enteric fever. Decreasing multidrug resistance concurrent with increasing fluoroquinolone resistance has been reported previously for Typhi [43]. We documented no resistance to ceftriaxone or, since testing began in 2011, to azithromycin. Both agents are recommended alternatives to fluoroquinolones. Because ceftriaxone and azithromycin resistance have been reported from other parts of the world, continued surveillance will be important [44].

Despite the availability of 2 licensed typhoid vaccines in the United States and recommendations for typhoid immunization before international travel [45], <25% of the enteric fever patients had been immunized against typhoid. Improved strategies for educating travelers about the availability of typhoid vaccines and the need for pretravel vaccination might be helpful. In a 2009–2011 survey, <50% of international travelers visiting family and friends had been vaccinated for typhoid [30]. These travelers were also more likely than those traveling for other reasons to refuse typhoid vaccine when offered [31]. Though effective, available typhoid vaccines have limitations. The protection is moderate—about 80% for US travelers [46]. Typhoid vaccines provide no protection against Paratyphi A infections, cannot be given to children <2 years old, and provide protection for only 2–5 years. Typhoid conjugate vaccines that induce higher levels of immunity, offer longer duration of protection, and are included in routine childhood vaccination, as well as bivalent vaccines that protect against paratyphoid A, could greatly reduce the burden of enteric fever—not only in travelers, but also in residents of countries where typhoid and paratyphoid fever are endemic [47–49].

Our data have several limitations besides those already mentioned. Cases of enteric fever not reported to state health departments are not reported to NTPFS. Among reported cases, epidemiologic and clinical data are largely self-reported by patients during state health department case investigations. Some data were missing, and others, such as travel histories, may have been inaccurate. Isolates are submitted by state and local public health laboratories to NARMS independent of reporting to NTPFS. Due to limitations in identifying information submitted with isolates and NTPFS case report forms, we were able to match NARMS data to only 58% of typhoid and 56% of paratyphoid A cases. Because of

limitations in the data on the number of US travelers, their destinations, and the duration of their trips, we provided only comparisons between regions, not specific rates. Finally, paratyphoid B was not included.

Although enteric fever in the United States is acquired primarily through travel to endemic countries, the few cases in our review that were acquired domestically highlight the small but persistent risk of transmission within the United States. Transmission can occur from chronic carriers, from acute or convalescent patients, or from eating contaminated foods imported from countries in which enteric fever is endemic [16, 45, 50]. Ultimately, because enteric fever in the United States is so strongly linked to international travel, elimination will only be achieved through efforts to reduce transmission in endemic countries. An integrated approach to controlling enteric fever via safe water, improved sanitation, adequate food hygiene, and vaccination is needed to achieve this.

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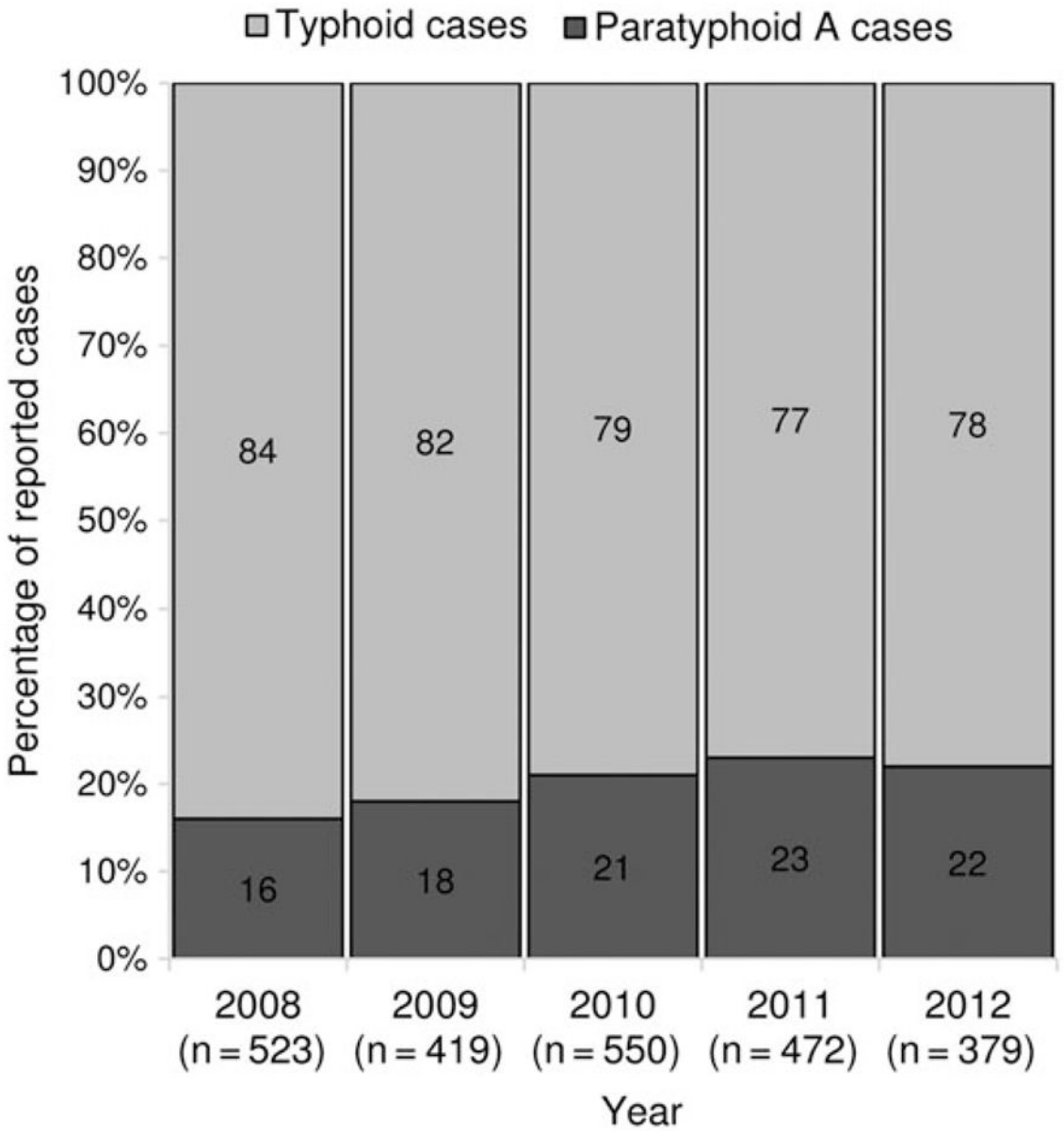

Figure 1.

Percentage of reported cases of enteric fever due to *Salmonella* Typhi and Paratyphi A, National Typhoid and Paratyphoid Fever Surveillance—United States, 2008–2012.

Table 1

Demographic and Clinical Characteristics of Patients With Typhoid Fever and Paratyphoid A Fever Reported to National Typhoid and Paratyphoid Fever Surveillance, by State—United States, 2008–2012

Characteristic	Typhoid	Paratyphoid A
Total reported cases, No.	1872	469
Median age, y (range)	23 (0–93)	26 (1–83)
Female	883/1853 (48)	228/467 (49)
US citizen	701/1036 (68)	203/261 (78)
Vaccinated[a]	61/1176 (5)	47/216 (22)
Travel status		
Travel-associated	1546/1799 (86)	415/451 (92)
Domestically acquired	253 (14)	36 (8)
Site of isolation		
Blood	1383/1801 (85)	409/457 (87)
Stool	211/1801 (12)	40/457 (9)
Other	2 (<1)	0/457 (0)
Multiple sites	205/1801 (11)	25/457 (5)
Hospitalized	1420/1833 (77)	311/454 (69)
Died	6/1693 (<1)	2/422 (<1)

Data are presented as no./No. (%) unless otherwise specified. Note that typhoid vaccination does not protect against paratyphoid fever.

[a]Received typhoid vaccination within 5 years before onset of illness.

Table 2

Destinations of Patients With Travel-Associated Typhoid and Paratyphoid A Fever Who Reported Travel to a Single Country or United Nations Region or Subregion, National Typhoid and Paratyphoid Fever Surveillance —United States, 2008–2012

Destination[a]	Typhoid (n = 1465)	Paratyphoid A (n = 382)
Asia	1259 (86)	376 (98)
Southern Asia	1206 (82)	370 (97)
India	894 (61)	280 (73)
Bangladesh	172 (12)	44 (12)
Pakistan	124 (8)	30 (8)
Nepal	13 (<1)	14 (4)
Other[b]	3 (<1)	2 (<1)
Southeastern Asia	41 (3)	4 (<1)
Philippines	19 (1)	2 (<1)
Indonesia	11 (<1)	1 (<1)
Other[c]	10 (<1)	1 (<1)
Other Asian subregions[d]	12 (<1)	2 (<1)
Africa	50 (3)	2 (<1)
Western Africa	37 (3)	2 (<1)
Nigeria	19 (1)	0 (0)
Other[e]	18 (1)	2 (<1)
Other African subregions[f]	13 (<1)	0 (0)
Americas	121 (8)	2 (<1)
Caribbean	41 (3)	0 (0)
Haiti	34 (2)	0 (0)
Other[g]	7 (<1)	0 (0)
Central America	68 (5)	0 (0)
Mexico	46 (3)	0 (0)
Guatemala	12 (<1)	0 (0)
Other[h]	10 (<1)	0 (0)
Other American subregions[i]	12 (<1)	2 (<1)
Oceania[j]	9 (<1)	0 (0)
Other regions[k]	4 (<1)	2 (<1)

Data are presented as No. (%) of patients.

[a] For each region, subregion, and country, totals include travelers who reported travel only to that destination. Destinations to which ≥10 patients with either typhoid, paratyphoid A, or both reported travel are included. Because travelers can report travel to >1 country in a single region or subregion, numbers at the country level will usually be lower than at the region or subregion levels. Similarly, numbers at the subregion level may usually be lower than the regional totals.

[b] For typhoid, includes Afghanistan (2) and Sri Lanka (1). For paratyphoid A, includes Sri Lanka (2).

[c]For typhoid, includes Myanmar (3), Vietnam (3), Laos (2), Cambodia (1), Malaysia (1), and Singapore (1). For paratyphoid A, includes Myanmar (1).

[d]For typhoid, includes Lebanon (8), Iraq (3), and China (1). For paratyphoid A, includes China (2).

[e]For typhoid, includes Ghana (7), Guinea (3), Liberia (2), Senegal (2), Mali (1), Niger (1), Sierra Leone (1), and Togo (1). For paratyphoid A, includes Ghana (1) and Sierra Leone (1).

[f]For typhoid, includes Egypt (3), Tanzania (3), Burundi (2), Cameroon (1), Central African Republic (1), Kenya (1), Uganda (1), and Zimbabwe (1).

[g]For typhoid, includes Dominican Republic (7).

[h]For typhoid, includes El Salvador (9) and Panama (1).

[i]For typhoid, includes Peru (7), Ecuador (2), Bolivia (1), Canada (1), and Columbia (1). For paratyphoid A, includes Canada (1) and Brazil (1).

[j]For typhoid, includes Marshall Islands (6), Samoa (2), and Australia (1).

[k]For typhoid, includes Iceland (3) and Russia (1). For paratyphoid A, includes France (1) and Italy (1).

Table 3

Antimicrobial Resistance Patterns in Isolates From Patients With Travel-Associated Typhoid Fever and Paratyphoid A Fever, by Travel History—United States, 2008–2012

	NAL-R/DSC[a]				Susceptible to All Clinically Relevant Agents Tested[d]		Clinically Significant Resistance Pattern Other Than NAL-R/DSC or MDR	
Characteristic	**Typhoid**	**Paratyphoid A**	**MDR[b,c] Typhoid**	**Both NAL-R/DSC and MDR[c] Typhoid**	**Typhoid**	**Paratyphoid A**	**Typhoid**	**Paratyphoid A**
All cases[e]	750/1091 (69)	246/262 (94)	127/1091 (12)	108/1091 (10)	314/1091 (29)	13/262 (5)	8/1091 (<1)	3/262 (1)
Domestically acquired	31/147 (21)	12/14 (86)	8/147 (5)	5/147 (3)	112/147 (76)	2/14 (14)	1/147[f] (<1)	0/14 (0)
Travel-associated	689/887 (78)	220/233 (94)	116/887 (13)	100/887 (11)	175/887 (20)	10/233 (4)	7/887 (<1)	3/233 (1)
Single-travel destination[g]	664/852 (78)	210/220 (95)	110/852 (13)	94/852 (11)	165/852 (19)	8/220 (4)	7/852 (<1)	2/220 (1)
Asia	657/753 (87)	210/216 (97)	96/753 (13)	93/753 (12)	90/753 (12)	5/216 (2)	3/753 (<1)	1/216 (1)
Southern Asia	651/727 (90)	209/214 (98)	95/727 (13)	93/727 (13)	71/727 (10)	4/214 (4)	3/727 (<1)	1/214 (1)
India	476/525 (91)	153/156 (98)	26/525 (5)	25/525 (5)	45/525 (9)	2/156 (1)	3/525[h] (<1)	1/156[i] (1)
Bangladesh	112/120 (93)	30/30 (100)	28/120 (23)	28/120 (23)	8/120 (7)	0/30 (0)	0/120 (0)	0/30 (0)
Pakistan	61/75 (81)	18/19 (95)	41/75 (55)	40/75 (53)	13/75 (68)	1/19 (5)	0/75 (0)	0/19 (0)
Other	2/7[j] (29)	8/9[k] (89)	0/7 (0)	0/7 (0)	5/7[l] (71)	1/9[m] (11)	0/7 (0)	0/7 (0)
Southeastern Asia	2/20 (10)	0/1 (0)	1/20 (5)	0/20 (0)	17/20 (85)	1/1 (100)	0/20 (0)	0/1 (0)
Philippines	1/11 (9)	0/1 (0)	0/11 (0)	0/11 (0)	10/11 (91)	0/1 (0)	0/11 (0)	0/1 (0)
Other	1/9[n] (11)	0/1 (0)	1/9[o] (11)	0/9 (0)	7/9[p] (77)	1/1[q] (100)	0/9 (0)	0/1 (0)
Other Asian subregions	4/6[r] (67)	1/1[s] (100)	0/6 (0)	0/6 (0)	2/6[t] (33)	0/1 (0)	0/6 (0)	0/1 (0)
Africa	1/36 (3)	0/2 (0)	13/36 (36)	0/36 (0)	19/36 (53)	2/2 (100)	4/36 (11)	0/2 (0)

Characteristic	NAL-R/DSC[a]		MDR[b,c] Typhoid	Both NAL-R/DSC and MDR[c] Typhoid	Susceptible to All Clinically Relevant Agents Tested[d]		Clinically Significant Resistance Pattern Other Than NAL-R/DSC or MDR	
	Typhoid	Paratyphoid A			Typhoid	Paratyphoid A	Typhoid	Paratyphoid A
Western Africa	1/26 (4)	0/2 (0)	8/26 (31)	0/26 (0)	14/26 (54)	2/2 (100)	4/26 (15)	0/2 (0)
Nigeria	0/13 (0)	0/2 (0)	5/13 (38)	0/13 (0)	8/13 (62)	0/2 (0)	0/13 (0)	0/2 (0)
Other	1/13[u] (8)	0/2 (0)	3/13[v] (23)	0/2 (0)	6/13[w] (46)	2/2[x] (100)	4/13[y] (31)	0/2 (0)
Other African subregions	0/10 (0)	0/2 (0)	5/10[z] (50)	0/10 (0)	5/10[aa] (50)	0/2 (0)	0/10 (0)	0/2 (0)
Americas	5/50 (10)	0/1 (0)	1/50 (2)	1/50 (2)	45/50 (90)	0/1 (0)	0/50 (0)	1/1 (100)
Caribbean	1/18 (6)	0/1 (0)	1/18 (6)	1/18 (6)	17/18 (94)	0/1 (0)	0/18 (0)	0/1 (0)
Haiti	1/13 (8)	0/1 (0)	1/13 (8)	1/13 (8)	12/13 (92)	0/1 (0)	0/13 (0)	0/1 (0)
Dominican Republic	0/5 (0)	0/1 (0)	0/5 (0)	0/5 (0)	5/5 (100)	0/1 (0)	. . .	0/1 (0)
Central America	4/26 (15)	0/1 (0)	0/26 (0)	0/26 (0)	22/26 (85)	0/1 (0)	0/26 (0)	0/1 (0)
Mexico	2/17 (12)	0/1 (0)	0/17 (0)	0/17 (0)	15/17 (88)	0/1 (0)	0/17 (0)	0/1 (0)
Guatemala	1/6 (17)	0/1 (0)	0/6 (0)	0/6 (0)	5/6 (83)	0/1 (0)	0/6 (0)	0/1 (0)
Other	1/3[bb] (33)	0/1 (0)	0/3 (0)	0/3 (0)	2/3[cc] (67)	0/1 (0)	0/3 (0)	0/1 (0)
Other American subregions	0/7 (0)	0/1 (0)	0/6 (0)	0/6 (0)	6/6[dd] (100)	0/1 (0)	0/6 (0)	1/1[ee] (100)
Oceania	0/6 (0)	0/0 (0)	0/6 (0)	0/6 (0)	6/6[ff] (100)	0/0 (0)	0/6 (0)	0/0 (0)
Other region	1/3[gg] (33)	0/1 (0)	0/3 (0)	0/3 (0)	2/3[hh] (67)	1/1[ii] (100)	0/3 (0)	0/1 (0)

Data are presented as no./No. (%).

Abbreviations: MDR, multidrug resistant; NAL-R/DSC, resistant to nalidixic acid or had decreased susceptibility to ciprofloxacin.

[a]Resistance to at least nalidixic acid or decreased susceptibility to ciprofloxacin (resistant or intermediate). Several isolates in this category also displayed resistance to 1 or more of ampicillin, chloramphenicol, or trimethoprim-sulfamethoxazole.

[b] Multidrug resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole.

[c] No Paratyphi A isolates were MDR.

[d] Clinically relevant agents tested included nalidixic acid, ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ceftriaxone, and ciprofloxacin from 2008 through 2010. Azithromycin was included in the testing panel in 2011 and 2012.

[e] Totals for each category may exceed totals within subcategories. For example, “all cases” includes cases with unknown travel status that are not included in the “domestically acquired” and “travel-associated” subcategories.

[f] One isolate intermediate to chloramphenicol.

[g] Destinations to which ≥10 patients with either typhoid, paratyphoid A, or both reported travel are specifically included. Because travelers can report travel to >1 country in a single region or subregion, numbers at the country level will usually be lower than the totals at the region or subregion levels. Similarly, numbers at the subregion level will usually be lower than the regional totals.

[h] One isolate intermediate to ceftriaxone, 1 isolate resistant to ampicillin, 1 isolate intermediate to chloramphenicol.

[i] One isolate resistant to trimethoprim-sulfamethoxazole.

[j] Nepal (2).

[k] Nepal (6), Sri Lanka (2).

[l] Nepal (4), Sri Lanka (1).

[m] Nepal (1).

[n] Cambodia (1).

[o] Myanmar (1).

[p] Indonesia (4), Laos (2), Singapore (1).

[q] Indonesia (1).

[r] Lebanon (3), Iraq (1).

[s] China (1).

[t] Lebanon (2).

[u] Ghana (1).

[v] Ghana (1), Liberia (1), Togo (1).

[w] Ghana (3), Senegal (1), Sierra Leone (1), Niger (1).

[x] Ghana (1), Sierra Leone (1).

[y] Three isolates from travelers to Guinea and 1 from a traveler to Mali resistant to trimethoprim-sulfamethoxazole and chloramphenicol.

[z] Tanzania (3), Burundi (1), Zimbabwe (1).

[aa] Egypt (3), Central African Republic (1), Uganda (1).

[bb] El Salvador (1).

[cc] El Salvador (2).

[dd] Peru (4), Colombia (1), Ecuador (1), Canada (1).

[ee] Brazil (1). Isolate intermediate to chloramphenicol.

[ff] Marshall Islands (4), Australia (1), Samoa (1).

[gg] Iceland (1).

[hh] Iceland (1), Russia (1).

[ii] France (1).