MAJOR ARTICLE

A Large Outbreak of Typhoid Fever Associated With a High Rate of Intestinal Perforation in Kasese District, Uganda, 2008–2009

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(See the Major Article by Lutterloh et al, on pages 1100–6 and the Editorial Commentary by Crump, on pages 1107–9.)

Background. *Salmonella enterica* serovar Typhi (*Salmonella* Typhi) causes an estimated 22 million typhoid fever cases and 216 000 deaths annually worldwide. In Africa, the lack of laboratory diagnostic capacity limits the ability to recognize endemic typhoid fever and to detect outbreaks. We report a large laboratory-confirmed outbreak of typhoid fever in Uganda with a high proportion of intestinal perforations (IPs).

Methods. A suspected case of typhoid fever was defined as fever and abdominal pain in a person with either vomiting, diarrhea, constipation, headache, weakness, arthralgia, poor response to antimalarial medications, or IP. From March 4, 2009 to April 17, 2009, specimens for blood and stool cultures and serology were collected from suspected cases. Antimicrobial susceptibility testing and pulsed-field gel electrophoresis (PFGE) were performed on *Salmonella* Typhi isolates. Surgical specimens from patients with IP were examined. A community survey was conducted to characterize the extent of the outbreak.

Results. From December 27, 2007 to July 30, 2009, 577 cases, 289 hospitalizations, 249 IPs, and 47 deaths from typhoid fever occurred; *Salmonella* Typhi was isolated from 27 (33%) of 81 patients. Isolates demonstrated multiple PFGE patterns and uniform susceptibility to ciprofloxacin. Surgical specimens from 30 patients were consistent with typhoid fever. Estimated typhoid fever incidence in the community survey was 8092 cases per 100 000 persons.

Conclusions. This typhoid fever outbreak was detected because of an elevated number of IPs. Underreporting of milder illnesses and delayed and inadequate antimicrobial treatment contributed to the high perforation rate. Enhancing laboratory capacity for detection is critical to improving typhoid fever control.

Salmonella enterica serovar Typhi (*Salmonella* Typhi) causes an estimated 22 million cases of typhoid fever and 216 000 deaths annually worldwide [1]. Infection occurs by fecal-oral transmission, predominantly in developing countries without safe water or sanitation. Typhoid fever is a systemic illness characterized by fever, malaise, headache, abdominal pain, and other gastrointestinal symptoms. Case-fatality rate is approximately 1% with prompt, appropriate antimicrobial therapy but approaches 30%–40% after intestinal perforation (IP) [2, 3], which occurs in 1%–3% of hospitalized patients [2–5].

The burden of typhoid fever in Africa is not well characterized [6]. Annual typhoid fever incidence in

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population-based studies from Africa ranges from 13 to 845 cases per 100 000 population [1, 7–9]. Typhoid fever is confirmed by isolation of *Salmonella* Typhi from bone marrow, blood, or another site in a patient with compatible illness [10]; however, the sensitivity of blood culture can be as low as 40% [11]. Most areas in Africa lack laboratory capacity [12]. As of 2004, no routine surveillance system in Africa required blood culture for confirmation [1]. Typhoid fever clinically resembles other febrile illnesses (eg, malaria) and is easily misdiagnosed without laboratory confirmation, likely resulting in unrecognized outbreaks and underestimation of incidence.

We report a large outbreak of typhoid fever in Uganda, which was initially detected because of a high number of patients with IPs, and confirmed through laboratory-enhanced surveillance. Kasese (population approximately 670 000) is a rural district in western Uganda and borders the Democratic Republic of Congo (DRC) [13]. It is served by health centers of varying capacities [14]: only 1 of 3 hospitals had any microbiological culture capacity. In August 2008, Kasese District hospitals encountered many patients with IP and an undiagnosed febrile illness. From initial investigations and clinical impressions, the Uganda Ministry of Health suspected typhoid fever as the etiology. Although *Salmonella* Typhi was isolated from 3 of 12 stool cultures, none of the 17 blood cultures yielded the organism. Outbreak control measures, including promotion of household water treatment, were undertaken, but cases of IP continued. From February 2009 to April 2009, we implemented laboratory-enhanced surveillance and conducted a community survey to determine etiology and scope of the outbreak.

METHODS

Case Definition

A suspected case of typhoid fever was defined as illness with onset between December 27, 2007 and July 30, 2009 in a person with fever, abdominal pain, and ≥1 of the following symptoms: gastrointestinal complaints (ie, vomiting, diarrhea, or constipation), general body weakness, joint pain, headache, no response to antimalarial medications, or IP.

Case Finding

We reviewed line lists of patients diagnosed with IP at 2 hospitals and cases of typhoid fever reported to public health officials to retrospectively identify suspected cases. Beginning on February 25, 2009, suspected cases were identified prospectively through patient interviews and implementation of an enhanced surveillance system, as described below.

Enhanced Surveillance

Enhanced surveillance was conducted from March 4, 2009 to July 30, 2009. We provided case surveillance forms, training, and management recommendations to 79 health centers in Kasese District. Health centers were asked to complete a surveillance form on patients meeting the case definition. The form elicited information about patient demographics, clinical history, and possible risk factors. Eleven health centers, including 2 hospitals, with specimen collection capacity were instructed to collect blood, serum, and stool specimens from the first 3 outpatients meeting the case definition each day and from all patients hospitalized with suspected IP.

Laboratory Testing

From March 4, 2009 to April 17, 2009, blood, serum, and stool specimens were collected from patients who met the suspected case definition (case patient). The US Centers for Disease Control and Prevention (CDC) provided supplies for specimen collection and testing and trained technicians at 2 hospital laboratories to isolate and identify *Salmonella* Typhi from blood and stool cultures and perform rapid serologic testing for antibodies to *Salmonella* Typhi as per the product insert (TUBEX TF; IDL Biotech).

Blood specimens (adult, 7 mL; children, <13 kg: 1–3 mL) were inoculated into BBL SEPTI-CHEK bottles (adult, 70 mL SEPTI-CHEK TSB with resins; pediatric, 20 mL SEPTI-CHEK TSB) and transported to reference laboratories within 72 hours. Blood and stool cultures were performed per standard protocols for isolation of *Salmonella* Typhi. Isolates that are biochemically typical of *Salmonella* Typhi were forwarded to the CDC for serotyping and broth microdilution antimicrobial susceptibility testing (Sensititre; Trek Diagnostics, Westlake, OH), and pulsed-field gel electrophoresis (PFGE) was performed per standard protocols [15–17].

Pathology

Available formalin-fixed surgical specimens from patients who underwent laparotomy for IP were sent to CDC for gross and microscopic examination. Specimens were tested by using an indirect immunoalkaline phosphatase protocol described elsewhere [18]. The 2 monoclonal antibodies used were raised against the O:9 antigen and the virulence factor (Vi) of *Salmonella* Typhi, respectively.

Community Household Survey

From March 14, 2009 to March 18, 2009, we conducted a community survey to assess the typhoid fever burden in 4 subcounties (Bugoye, Kitswamba, Kyabarungira, and Maliba) within the most severely affected health subdistrict (Busongora North) in Kasese. We randomly selected 10 villages per subcounty and 8 households per village. A questionnaire was administered to heads of household to obtain household demographics, clinical and healthcare-seeking information for all household members meeting the case definition

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during the prior year, and to assess the acceptability of typhoid vaccination.

Data Analysis

Data were entered into electronic databases and analyzed using SAS 9.1 (SAS Institute). Statistical testing was done using Wilcoxon rank-sum test for continuous data and the χ^2 test for categorical data. P values <0.05 were considered significant.

RESULTS

Case Finding

Five hundred seventy-seven suspected cases of typhoid fever with illness onset dates from December 27, 2007 to July 8, 2009 were identified (Figure 1), 323 cases retrospectively and 254 prospectively. The median age of case patients was 16 years (range, <1–75 years) (Table 1). Fifty-two percent of illnesses occurred in persons 5–19 years old (Figure 2*a*). Overall, 59% of case patients were male; males predominated in most age groups (Figure 2*b*).

IP, most commonly in the ileum, was reported in 249 patients (43%). Males accounted for 67% of patients with IP, compared with 52% of those without ($P < .01$) (Table 1). The median ages of patients with perforation (17 years) and without IP (16 years) were similar; however, 55% of patients with IP were 10–24 years old, compared with only 42% of patients without IP. Overall, 289 (57%) patients were hospitalized, and 47 died (case-fatality rate 9%) (Table 1). Patients with known IP accounted for 80% of hospitalizations and 94% of fatalities.

Patients from Kasese District lived in 21 subcounties and 284 villages; 255 (48%) of 530 patients who reported subcounty information were from the 5 subcounties comprising the Busongora North health subdistrict, home to only 26% of the Kasese District population (2002 census). Five patients resided in neighboring Districts (Kabarole [4] and Bushenyi [1]), whereas 15 people resided in DRC.

Enhanced Surveillance

Case surveillance forms for 241 case patients were collected from March 4, 2009 to July 30, 2009. In addition to fever and abdominal pain, both required by the case definition, the most frequently reported symptoms were general body weakness (98%) and headache (94%) (Table 2). Seventy-seven (32%) of 241 patients were hospitalized (median duration, 3 days; range, 1–60 days), and at least 13 (5%) reported IP.

Among 210 patients reporting information, 153 (73%) sought healthcare before presentation to the health facility where the form was completed. Of these, 81 (53%) went to a pharmacy or drug shop, 70 (46%) went to a health clinic or hospital, and 5 (3%) went to a traditional healer; 18 (12%) sought care from >1 source. The median reported time between onset of symptoms and presentation to the reporting health center was 14 days (range, 2–180 days) for patients with IP and 7 days (range, 1–150 days) for those without IP ($P = .02$).

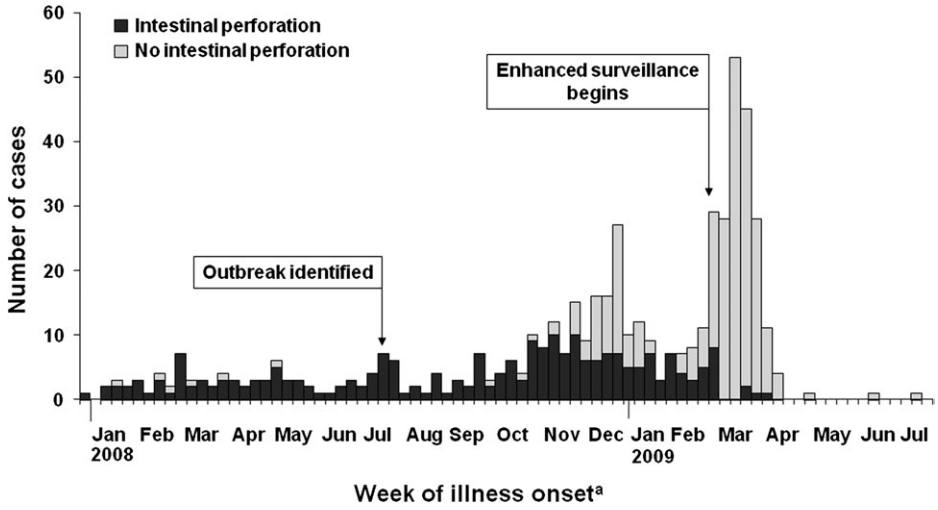

Figure 1. Cases of typhoid fever in Kasese District, Uganda, by week of illness onset, and intestinal perforation status, December 27, 2007–July 30, 2009 (n = 514). Illness onset dates were estimated for case patients without reported onset dates but with known admission dates by determining the median lag between admission date and illness onset date for patients for whom both dates were known, then subtracting that from the patient's admission date. Excludes 63 patients for whom an onset date could not be estimated.

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Table 1. Characteristics of Patients Reported With Suspected Typhoid Fever, by Intestinal Perforation Status, Kasese District, December 27, 2007–July 30, 2009

Characteristic	Perforation (n = 249) Number (%)[a]	No Perforation (n = 328) Number (%)[a]	All Cases (n = 577) Number (%)[a]	*P* Value[b]
Median age (range), in years	17 (2–70)	16 (<1–75)	16 (<1–75)	.039
Age group	(n = 247)	(n = 309)	(n = 556)	
<1 year	0 (0)	9 (3)	9 (2)	
1–4 years	8 (3)	33 (11)	41 (7)	
5–9 years	37 (15)	52 (17)	89 (16)	
10–14 years	48 (19)	48 (16)	96 (17)	
15–19 years	55 (22)	51 (17)	106 (19)	
20–24 years	32 (13)	30 (10)	62 (11)	
25–29 years	19 (8)	27 (9)	46 (8)	
30–34 years	13 (5)	15 (5)	28 (5)	
35–39 years	8 (3)	11 (4)	19 (3)	
40–44 years	9 (4)	14 (5)	23 (4)	
45–49 years	3 (1)	4 (1)	7 (1)	
50–54 years	5 (2)	6 (2)	11 (2)	
55–59 years	5 (2)	2 (1)	7 (1)	
60–64 years	3 (1)	5 (2)	8 (1)	
≥65 years	2 (1)	2 (1)	4 (1)	
Gender	(n = 249)	(n = 308)	(n = 557)	
Male	168 (67)	160 (52)	328 (59)	<.001
Female	81 (33)	148 (48)	229 (41)	
Hospitalized	(n = 245)	(n = 261)	(n = 506)	
Hospitalized	232 (95)	57 (22)	289 (57)	<.001
Died	(n = 244)	(n = 261)	(n = 505)	
Died	44 (18)	3 (1)	47 (9)	<.001

[a] Percentages may not sum to 100% due to rounding.

[b] *P* value for statistical testing between case patients with and without intestinal perforation. χ^2 test used for categorical variables, and Wilcoxon rank-sum test used for continuous variables.

Antimalarial medications were taken by 134 (64%) of 211 patients. Seventy-six (35%) of 220 patients reported prior antimicrobial use for a median of 5 days (range, 1–180 days) before presentation to the reporting clinic. Twenty-two (29%) patients reported using cotrimoxazole, 12 (16%) patients reported using ciprofloxacin, 7 (9%) patients reported using chloramphenicol, and 18 (24%) patients reported using an unknown antimicrobial; metronidazole, tetracycline, penicillin, ampicillin, and gentamicin were also reported. Compared to patients without IP, those with IP were significantly more likely to report having taken antimicrobial (80% vs. 43%, $P = .04$) and antimalarial medications (85% vs. 52%, $P = .03$).

Among 219 case patients reporting a single major source of household drinking water during the month before illness, 141 (64%) used untreated tap water, 29 (13%) used rivers, 16 (7%) used bore holes, 12 (5%) used streams, 9 (4%) used wells, and 12 (5%) reported a different source. Forty-nine (22%) of 221 patients reported treating household drinking water during the month before illness: 40 (82%) boiled the water, whereas 9 (18%) used a chlorination product. Only 24 (49%) of the 49 patients (11% of all 221 patients) reported always treating their drinking water.

Laboratory Investigation

Specimens for culture were collected from 102 case patients, but results were available for only 81, of whom 27 (33%) were laboratory confirmed as *Salmonella* Typhi infection. Overall, 19 (35%) of 54 blood cultures, 10 (16%) of 61 stool cultures, and 6 (67%) of 9 cultures from an unlabeled source (ie, either blood or stool) were positive.

Salmonella Typhi isolates from 21 of the 27 laboratory-confirmed cases underwent antimicrobial susceptibility testing. Isolates from 16 (76%) patients were resistant to ampicillin, streptomycin, sulfisoxazole, tetracycline, and cotrimoxazole, but were susceptible to chloramphenicol. An isolate from 1

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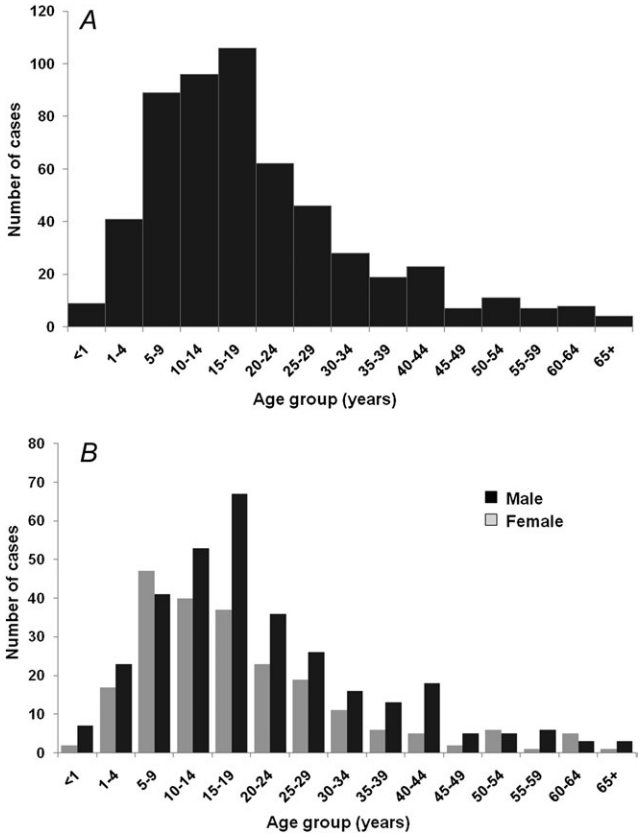

Figure 2. Cases of typhoid fever in Kasese District, Uganda, by (*A*) age group (n = 556), and (*B*) age group and sex (n = 544), December 27, 2007–July 30, 2009.

patient (5%) was additionally resistant to chloramphenicol. Isolates from 4 (19%) patients were susceptible to all antimicrobials tested. No resistance to nalidixic acid or ciprofloxacin was detected.

Table 2. Clinical Features, Besides Fever and Abdominal Pain,[a] Reported on Case Surveillance Forms for Patients Meeting the Typhoid Fever Suspected Case Definition (n = 241), March 4, 2009–July 30, 2009

Clinical Feature	Number/n (%)
Generalized body weakness	208/213 (98)
Headache	191/203 (94)
Joint pain	153/190 (81)
No response to antimalarials	82/122 (67)
Diarrhea	125/210 (60)
Vomiting	107/194 (55)
Constipation	72/143 (50)
Intestinal perforation	13/77 (17)[b]
Hospitalized for illness	77/241 (32)

[a] The case definition specified that both fever and abdominal pain must be present.

[b] Or 5% of all 241 patients reported through the enhanced surveillance system.

Thirty-three *Salmonella* Typhi isolates from 22 patients were examined by PFGE. Thirteen XbaI/BlnI enzyme pattern combinations were identified. Individual isolates from 4 of 10 patients with multiple isolates had different PFGE patterns. The predominant PFGE pattern combination was seen in 9 (41%) of patients and in 15 (45%) of isolates; it was indistinguishable from those of 2 isolates collected before 2008 from patients in the Kampala area and 2 stool isolates obtained during an initial investigation of this outbreak in August 2008.

TUBEX TF results were known for 76 patients; 26 (34%) were positive, 4 (5%) were equivocal, and 46 (61%) were negative. Among the 49 patients who had either a positive (17) or a negative (32) microbiological culture result and a TUBEX TF result from serum collected ≥4 days after the illness onset, sensitivity of the TUBEX TF test was 88% and specificity was 84%.

Pathology

Twenty-seven small intestinal specimens and 3 lymph nodes from 30 patients were examined. On gross examination, 22 (81%) of 27 small intestinal specimens revealed perforation; 5 (19%) had no appreciable perforation. Under microscopic examination, all 27 intestinal specimens showed fibrinopurulent exudates and inflammation on the serosal surface. Abundant mixed bacterial organisms were seen on serosal and mucosal surfaces and within the intestinal lumen. Various degrees of hemorrhage, edema, necrosis, and mixed inflammation with neutrophils, lymphocytes, plasma cells, and macrophages in mucosa, submucosa, and muscularis propria were also identified (Figure 3). All lymph node-only specimens and 19 (70%) intestinal specimens containing regional lymph nodes revealed necrotizing lymphadenitis. Gross and microbiologic findings were compatible with severe gastrointestinal infection and enteric perforation due to *Salmonella* Typhi, *Yersinia*, tuberculosis, *Campylobacter*, or other invasive bacteria. Among the 30 cases, specimens from 16 people were positive for *Salmonella* Typhi by the O:9 monoclonal antibody; 14 of those were also stained by the Vi monoclonal antibody.

Community Household Survey

Among 2138 persons living in 320 study households, 173 persons met the case definition for suspected typhoid fever during the prior year, an overall annual incidence of 8092 suspected cases per 100 000 persons in the study population. Among the 4 subcounties in the study, estimated annual incidence rates ranged from 5609 to 10 906 suspected cases per 100 000 persons (Table 3).

The median age of suspected cases was 18 years (range, <1–92), compared with 14 years (range, <1–110) for well household members. Fifty-nine (34%) of 172 patients reported hospitalization. IP was reported for 11 (8%) of 139

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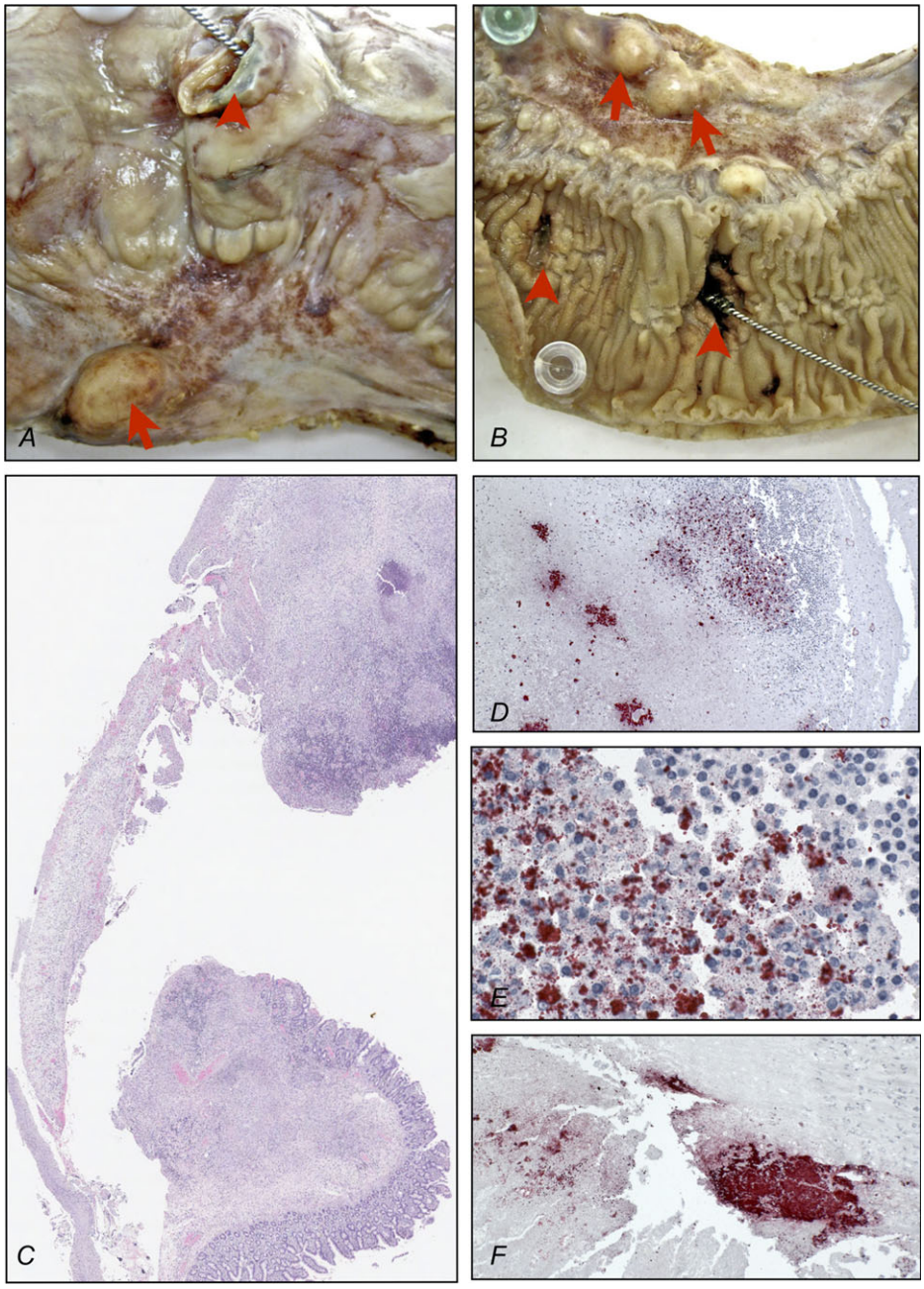

Figure 3. Gross and microscopic findings of intestinal perforation. (*A*) Serosal surface of a surgically resected small intestine showing perforation (arrow head) and lymphadenopathy (arrow). (*B*) Mucosal surface of the same specimen showing perforation (arrow heads) and lymphadenopathy (arrows). (*C*) Photomicrograph of the intestinal perforation from the same specimen showing disruption of mucosal surface with necrosis, hemorrhage, and inflammation. (*D–F*) Immunohistochemical assays using immunoalkaline phosphatase with 2 monoclonal anti-*Salmonella* antibodies; napthol fast red substrate and hematoxylin counterstain. The O:9 antibody reacted with *S.* Typhi, *S.* Enteritidis, and *S.* Typhimurium cultures. It did not react with cell culture controls for Paratyphi A or C, *Shigella*, *Escherichia coli*, or *Yersinia enterocolitica*. No staining was seen with either antibody against non-*Salmonella* Typhi bacterial enteritides, including *Clostridium*, anthrax, *Helicobacter pylori*, and *Klebsiella*. *Salmonella* O:9 antigens are shown in necrotic lymph node from a second specimen (lower magnification *D* and higher magnification *E*) and the necrotic intestinal wall adjacent to area of perforation from a third specimen (*F*).

suspected cases; all 11 patients with IP sought care at a health clinic or hospital, 9 were admitted for care, and 3 died. In total, 13 (8%) deaths were reported. Thirty-five (20%) suspected cases did not seek medical care; none had IP or died.

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Table 3. Incidence Rate of Suspected Typhoid Fever During the Year Preceding Interview Among Household Members Included in the Community Survey, by Subcounty, per 100 000 Persons in the Study Population

Subcounty	Cases Number	Household Members Number	Incidence Rate (Cases/100 000 Persons)
Kitswamba	59	541	10 906
Bugoye	47	556	8453
Kyabarungira	38	524	7252
Maliba	29	517	5609
Overall	173	2138	8092

When asked whether they would use a vaccine to protect the family from typhoid fever, 311 (99%) of 315 heads of household would be willing if the vaccine was offered at no cost, whereas 295 (95%) of 312 reported willingness to pay a fee for the vaccine.

DISCUSSION

This persistent outbreak of typhoid fever was detected because of an elevated number of IPs, an uncommon complication. Lack of local microbiological capacity, including lack of equipment and supplies and inadequately trained personnel, led to difficulties isolating *Salmonella* Typhi from blood culture and to a long delay in confirming the etiology. These conditions prevail in sub-Saharan Africa, where sporadic cases and outbreaks of bacteremic infections, including typhoid fever, are unable to be recognized or confirmed by available laboratory methods, which hampers an accurate estimation of typhoid fever burden. This outbreak, and a recent outbreak in the DRC [19], might have gone undetected if not for the large number of IPs noted by clinicians. In the DRC outbreak, 13 400 total cases, 615 cases of severe peritonitis (with or without IP), and 134 (10%) deaths were reported [19].

During this investigation, surveillance identified 577 suspected cases of typhoid fever, including 249 patients with IP and 47 fatalities. The true magnitude of the outbreak was probably much larger. In contrast to past studies, which report that IP occurs in 1%–3% of patients with typhoid fever [2–4], 43% of patients identified in this outbreak had IP. Preferential reporting and surveillance bias likely contributed to the high IP rate. Early in the outbreak, almost all reported cases were hospitalized with IP. In contrast, patients identified through enhanced surveillance and the community survey generally had milder illness. In March, after extending surveillance into community-based health clinics, there was a sharp rise in reported cases, most of which did not have IP. This spike reflects improved detection and reporting of patients with milder illness rather than a sudden acceleration in the outbreak. The IP rates among patients identified by enhanced surveillance and by the community survey are closer to those of past studies.

Other factors besides surveillance bias, including delays in treatment and treatment with antimicrobials to which the circulating strains were resistant, probably contributed to the elevated IP rate. The occurrence of inadequate antimicrobial therapy, a previously identified risk factor for IP [20, 21], was frequent. Patients sought care from traditional healers, were self-treated, or were misdiagnosed, all of which delayed appropriate antimicrobial therapy. Among the patients who reported antimicrobial use, less than one-half took ciprofloxacin or chloramphenicol, agents to which tested isolates were susceptible. IP occurs more frequently in males than in females [5, 20–22], as was observed in this outbreak, but, overall, women accounted for almost as many cases as men. Other factors, such as use of traditional medicines that could increase risk of perforation, host genetics, or a particular virulence factor in circulating strains, cannot be ruled out. If the true IP rate was the 1%–3% typically reported in the literature, between 8300 and 24 900 people may have been infected. If the true IP rate was 5%–8%, as indicated by enhanced surveillance and the community survey, then 3113–4980 people would have been infected.

IP remains a key contributor to typhoid fever morbidity and mortality. A recent publication from Ghana identified typhoid IP as the most frequent cause of abdominal surgery in children, responsible for 68% of all acute surgical abdomens in children between 1 and 15 years of age [23]. Minimizing delay in appropriate treatment is a major modifiable risk factor to decrease the risk of IP and mortality associated with typhoid fever, but it is contingent upon rapid laboratory confirmation and antimicrobial susceptibility testing. Serologic tests, which require less equipment and expertise, may help in preliminary outbreak detection in areas where culture is not readily available. However, these tests do not provide information on antimicrobial susceptibility, and they are neither sufficiently sensitive nor specific to be used in place of culture for diagnosis of typhoid fever in individual patients in endemic areas [24, 25].

We were unable to implicate a vehicle for infection; however, contaminated water was suspected. Few patients reported always treating water before drinking. Laboratory testing identified several different PFGE and antimicrobial susceptibility patterns among *Salmonella* Typhi isolates, suggesting that several strains were circulating by March 2009. This evidence and the wide geographic distribution of the outbreak suggest that, over time, multiple sources of infection may have been present. The identification of

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different PFGE patterns among *Salmonella* Typhi isolates from the same person is compatible with coinfection with multiple strains, or, as suggested by prior studies [26–28], could reflect changes that occurred in vivo during the course of the individual's infection.

Initial public health recommendations included general prevention measures such as hand washing, improved sanitation, and promotion of household water treatment. Based on reports from Asia, the World Health Organization has recommended typhoid vaccination for outbreak control, in the context of other efforts to control the disease, including health education, water quality and sanitation improvements, and training of health professionals in diagnosis and treatment [29–31]. Given the prolonged and widely dispersed nature of the outbreak, and the small proportion of cases in children <2 years old who would be ineligible to receive typhoid vaccine, a targeted vaccination campaign in affected areas might have been an effective control strategy. Data from the community survey suggest that vaccination would have been accepted by nearly all households.

Our investigation was subject to limitations. Most importantly, the case definition used in our investigation was nonspecific, medical/surveillance records were not available to identify all clinical symptoms and diagnoses in all patients, and not all cases were culture confirmed; these factors could have resulted in misclassification. Community survey data were obtained via proxy interviews with heads of household for the year preceding interview, which may have yielded inaccurate information. Because the community survey was conducted in the most severely affected subdistrict, incidence rates from the survey cannot be generalized to other parts of Kasese District.

The true burden of typhoid fever in Africa remains unclear. Lack of laboratory diagnostic capacity in many African countries limits the ability to recognize endemic typhoid fever and detect outbreaks. This typhoid fever outbreak and recent outbreaks in DRC [19], Kenya [32], and on the Malawi-Mozambique border [33] suggest that typhoid fever is widespread. Additional population-based surveillance studies with laboratory confirmation will yield more precise estimates of the incidence of typhoid fever in Africa. Meanwhile, a high index of suspicion needs to be maintained, particularly in cases of suspected or confirmed IP. Enhancing laboratory capacity for blood cultures, especially when outbreaks of typhoid fever are suspected, is critical to improving prevention and control of this deadly disease.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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