LETTERS

Typhoid Fever among Children, Ghana

To the Editor: Typhoid fever (TF) remains a problem of concern in many low-income countries. Salmonella enterica serovar Typhi causes $\approx 22,000,000$ symptomatic infections and 220,000 fatalities worldwide annually (1). However, the effect and incidence of TF in many parts of sub-Saharan Africa are largely unknown because diagnostic laboratories are lacking and fatal TF is frequently attributed to malaria (2,3). In Ghana, TF ranks among the leading 20 causes of outpatient illness, accounting for 0.92% of hospital admissions (4).

We conducted our study at the rural Agogo Presbyterian Hospital in the Ashanti Region of Ghana. The percentage of residents of 99 villages and household clusters of buildings (population size 18-13,559 persons, median 277 persons) with access to the study hospital was assessed in a healthcare utilization survey. A proportional-to-size number of children were randomly selected in each village, and a standardized interview was conducted. TF incidences were calculated for September 2007-November 2008 (Table). A bacteriology laboratory with BACTEC 9050 automated blood culture system (Becton Dickinson, Sparks, MD, USA) was established in the study hospital and run to assess the number of admissions with TF, the incidence of TF in the adjoining community and S. en*terica* ser. Typhi resistance to a panel of antimicrobial drugs.

The study included 1,456 children <15 years of age who were admitted to the pediatric ward of Agogo Presbyterian Hospital over the 23-month study period. Overall, 52.1% were male; mean age of children was 32.2 months (SD \pm 36.0 months; median 19 months, range 0–174 months). Blood was cultured by using a BACTEC 9050 blood

culture system (Becton Dickinson), and positive samples were examined by standard methods. Antimicrobial drug susceptibility testing was performed on all serovar Typhi isolates by using the Kirby-Bauer disk-diffusion method for ampicillin, chloramphenicol, tetracycline, trimethoprim/sulfamethoxazole, amoxicillin/clavulanicacid, gentamicin, ciprofloxacin, and ceftriaxone.

Children <2 years of age had the highest proportion of positive blood cultures (164/1,456, 21.3%; online Appendix Figure, www.cdc.gov/EID/ content/16/11/1796-appF.htm). Of 298 blood cultures yielding positive growth for bacterial pathogens or for Candida spp., 37 (12.4%) isolates (2.5% of the 1,456 hospitalized children) were positive for S. enterica ser. Typhi. The frequency of TF was low among children <2 years of age (7/1,018, 0.7%), increased among those 2 to <11 years of age (29/417, 7.0%), and decreased among children \geq 11 years of age (1/22, 4.6%) (online Appendix Figure). One (2.7%) child with TF died. Malaria parasites were detected in 2 children with S. enterica ser. Typhi. Pathogens other than S. enterica ser. Typhi were identified among 21.3% and 11.8% of children 0 to <2 years and 5 to <8 years of age, respectively. These pathogens included nontyphoidal salmonellae, Staphylococcus aureus, and Streptococcus pneumoniae. S. enterica ser. Typhi isolates were resistant to chloramphenicol (73%), trimethoprim/sulfamethoxazole (71%), ampicillin/amoxicillin (70%), tetracycline (64%), gentamicin (46%), and amoxicillin/clavulanic acid (24%) but susceptible to ciprofloxacin and ceftriaxone.

TF incidence in children <5 years of age was ≈190 cases/100,000 population and highest in children 2-5 years of age (290/100,000 per year)and 5-8 years of age (200/100,000 per year) (Table). In children older than 8, incidence decreased continuously, and the number of cases was too low to enable precise age-stratified incidence calculations. The incidences in the study area point to a higher impact of TF than expected (4)and may reflect an underestimation of TF in other West African regions as well. Our high incidence figure may still underestimate the incidence because of a low sensitivity of standard microbiologic methods (up to 50%), which are prone to underdiagnose moderate bacteremia in Salmonella infections (5,6).

Compared with Asia, only limited data are available from Africa on S. enterica ser. Typhi drug resistance. A study from Nigeria showed that, among serovar Typhi strains isolated from hospitalized patients in Lagos during 1997-2004, resistance rates reached 87% for ampicillin and were 0.7% for ciprofloxacin, compared with 70% and 0%, respectively, in the present study. Resistance to trimethoprim/ sulfamethoxazole was 59% in Nigeria, compared with 71% in Ghana. In Togo, proportions of serovar Typhi strains resistant to chloramphenicol and trimethoprim/sulfamethoxazole

30 (-20 to 80)

Table. Estimates of Salmonella enterica serovar Typhi incidence in children, Ghana,			
Age group, v	No. S. enterica ser. Typhi isolates*	Coverage	Incidence‡ (95% confidence interval)
0–15	16	14,933	120 (70 to 170)
<2	1	2,133	50 (-30 to 140)
2-<5	8	3,200	290 (120 to 450)
5-<8	5	2,880	200 (50 to 340)
8–<11	1	2,880	40 (-30 to 110)

*Observation period 15 mo (period of complete and uninterrupted assessment of blood culture data). †No. residents of each community with access to Agogo Presbyterian Hospital. ‡Per 100,000 persons per year.

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11 - < 15

were 33% and 46%, respectively, before 2002 and 73% and 79% in 2003– 2004 (7) and thus similar to those in our study.

In addition, resistances to ciprofloxacin and ceftriaxone were <10%. Multidrug resistance (resistance to ampicillin, trimethoprim/sulfamethoxazole, and chloramphenicol) was observed in 63% of children in our study, compared with 7% in India, 22% in Vietnam, and 65% in Pakistan (8–10).

More effort is needed in Africa to enable reliable and standardized laboratory diagnoses of Salmonella infections and to sustain TF surveillance and drug sensitivity surveys. Moreover, introduction of a vaccination program should be discussed after more data are obtained from other areas in Ghana and West Africa. Such data currently are collected in an extensive standardized surveillance program across the continent performed by our group and others. In parallel, trials should be conducted to assess the effectiveness and cost-effectiveness of currently available and newly developed TF vaccines.

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References

- Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bull World Health Organ. 2004;82:346–53.
- Reddy EA, Shaw AV, Crump JA. Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10:417–32. DOI: 10.1016/S1473-3099(10)70072-4
- Evans JA, Adusei A, Timmann C, May J, Mack D, Agbenyega T, et al. High mortality of infant bacteraemia clinically indistinguishable from severe malaria. QJM. 2004;97:591–7. DOI: 10.1093/ qjmed/hch093
- Sory E. The health sector in Ghana. Facts and figures. Accra (Ghana): Ghana Health Service; 2009. p. 31.
- Gilman RH, Terminel M, Levine MM, Hernandez-Mendoza P, Hornick RB. Relative efficacy of blood, urine, rectal swab, bone-marrow, and rose-spot cultures for recovery of *Salmonella* typhi in typhoid fever. Lancet. 1975;1:1211–3. DOI: 10.1016/S0140-6736(75)92194-7
- Wain J, Pham VB, Ha V, Nguyen NM, To SD, Walsh AL, et al. Quantitation of bacteria in bone marrow from patients with typhoid fever: relationship between counts and clinical features. J Clin Microbiol. 2001;39:1571–6. DOI: 10.1128/ JCM.39.4.1571-1576.2001
- Dagnra AY, Akolly K, Gbadoe A, Aho K, David M. Emergence of multidrug resistant *Salmonella* strains in Lome (Togo) [in French]. Med Mal Infect. 2007;37:266–9. DOI: 10.1016/j.medmal.2007.02.002
- Chau TT, Campbell JI, Galindo CM, Van Minh Hoang N, Diep TS, Nga TT, et al. Antimicrobial drug resistance of *Salmonella enterica* serovar Typhi in Asia and molecular mechanism of reduced susceptibility to the fluoroquinolones. Antimicrob Agents Chemother. 2007;51:4315–23. DOI: 10.1128/AAC.00294-07

- Threlfall EJ, de Pinna E, Day M, Lawrence J, Jones J. Alternatives to ciprofloxacin use for enteric fever, United Kingdom. Emerg Infect Dis. 2008;14:860–1. DOI: 10.3201/ eid1405.071184
- Chuang CH, Su LH, Perera J, Carlos C, Tan BH, Kumarasinghe G, et al. Surveillance of antimicrobial resistance of *Salmonella enterica* serotype Typhi in seven Asian countries. Epidemiol Infect. 2009;137:266–9. DOI: 10.1017/ S0950268808000745

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Shigella spp. Antimicrobial Drug Resistance, Papua New Guinea, 2000-2009

To the Editor: Approximately half the Shigella spp. infections in developing countries are caused by endemic shigellae (1), which in these countries are responsible for $\approx 10\%$ of all episodes of diarrhea among children <5 years of age and up to 75% of deaths from diarrhea (2). Deaths from epidemic Shigella spp. in the community are estimated to outnumber deaths within the healthcare setting. In Papua New Guinea, diarrhea is a major cause of hospital admission and death (3); Shigella spp. are among the most common causes of enteric bacterial infection (4,5), and S. flexneri is the most common serotype (3,6). Outbreaks of bloody diarrhea are frequently reported; however, diagnosis in remote settings is challenging, partly because the storage requirements for the organism are difficult to meet.

Multidrug resistance of shigellae is not new (1); many countries have