

Trends and disease burden of enteric fever in Guangxi province, China, 1994–2004

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Objective To determine the burden of enteric fever through trends in morbidity and mortality, bacterial species and antimicrobial resistance in Guangxi, a southern, subtropical, coastal province of China with a disproportionately large burden of enteric fever.

Methods Data on morbidity and mortality caused by enteric fever between 1994 and 2004 were extracted from the Guangxi Center for Disease Control and Prevention. Laboratory-based surveillance and outbreak investigations were integrated with reports of notifiable infectious diseases to estimate the bacterial species-specific incidence of enteric fever. To adjust for underreporting, survey data were collected from three prefectures that represent the hyper-, moderate- and low-endemic regions of Guangxi province.

Findings In Guangxi province, enteric fever incidence rate varied over the study period, with a peak of 13.5 cases per 100 000 population in 1995 and a low of 6.5 in 2003. The disease occurred most frequently during the summer and autumn months and in the group aged 10–49 years. The incidence of enteric fever varied by region within Guangxi province. During the 11-year period covered by the study, 61 outbreaks of enteric fever were reported, and *Salmonella paratyphi* A (SPA) became the predominant causative agent in the province.

Conclusion Prospective studies may provide a better understanding of the reason for the shifting epidemiology of enteric fever in Guangxi province. Given the emergence of resistance to first- and second-line antimicrobials for the treatment of enteric fever, a bivalent vaccine against both SPA and *S. typhi* would facilitate for disease control.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Enteric fever (which includes both typhoid and paratyphoid fever) is an acute illness that can present with one or more of the following: fever, headache, abdominal pain, bradycardia, hepatomegaly and splenomegaly. The disease, which can be caused by either *Salmonella typhi* or *S. paratyphi* A (SPA), B or C,¹ is common in areas with poor sanitation and faecal contamination of food and water. In 1984 the estimated global burden of typhoid fever was 16 million cases, 600 000 of which were fatal.² However, as sanitation and water systems have improved in some regions of the world, the global incidence of typhoid fever has declined. More recent estimates suggest that about 21 million cases of typhoid fever and 210 000 deaths from the disease occurred globally during 2000.² Similarly, about 5 million episodes of paratyphoid fever are thought to have occurred globally during 2000, but the case–fatality rate is unknown.²

Enteric fever was hyper-endemic in China at one time. However, over the past two decades the country has undergone rapid economic development and substantial improvements in water supply and sanitation. Also, typhoid Vi polysaccharide vaccine has been used since 1996 in provinces with a high incidence of enteric fever. As a result, the annual incidence rate in China has declined sharply in recent years – from 6.1 per 100 000 population in 1995 to 3.9 in 2004^{3–5} – and the case–fatality rate has dropped fourfold – from 0.17% in 1995 to 0.04% in 2004.⁶ However, the decrease in incidence shows regional differences possibly related to inequalities in economic development. In 2004, 66% of all enteric fever cases reported in China came from four of the country's 33 provinces: Guangxi, Guizhou, Yunnan

and Zhejiang. Apart from Zhejiang,⁷ these provinces have a low economic development index and represent 13% of the total Chinese population.

A more complete understanding of the burden of enteric fever in China will be helpful in designing cost-effective control strategies. We therefore reviewed data on enteric fever in Guangxi province to determine trends in morbidity, mortality, distribution of bacterial species and antimicrobial resistance patterns over the period 1994–2004.

Methods

Study area

Located in southern China, Guangxi Zhuang Autonomous Region is a coastal province that borders Viet Nam and the South China Sea. The province has a short winter and long summer and annual mean temperatures of 16–23 °C. Geographically, the 14 prefectures of Guangxi can be grouped into three regions – northern, central and southern. Prefectures in the northern region, such as Guilin city, are characterized by a karst geological terrain, with carbonate rock topped by a thin soil layer.

Government statistics

China's national Notifiable Infectious Disease Reporting system (NIDR) applies to all health-care facilities at the village, township, county and city level. The *Law on the Prevention and Control of Infectious Diseases* (1989) requires health-care workers to report any of 24 infectious diseases, including enteric fever, to the provincial Centers for Disease Control and Prevention

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(CDC).⁸ After preliminary processing, the data are transferred to the national CDC, which compiles and analyses them every month. The Department of Disease Control in China's Ministry of Health issues an annual report based on these data.⁸ For this study, the Guangxi CDC provided census data, which we used to calculate disease incidence, and data on Vi polysaccharide vaccine.

Underreporting

To detect and correct for underreporting in the NIDR system, the Ministry of Health has developed standardized surveys, both community- and health-care facility-based,⁹ that aim to explore the potential underreporting of treated and untreated cases. A multistage stratified cluster sampling method with probability proportional to size is applied, in accordance with World Health Organization (WHO) guidelines.¹⁰ For community-based surveys, the city or county is stratified into north, south, west, east and central areas. The district or township is the primary sampling unit, and the sub-district or village is the secondary one. Health-care history and information on undiagnosed illnesses are collected from all members of selected households and compared with the records in the NIDR system. For health-care facility-based surveys, the health-care facilities in a city or county are stratified to township hospital, county or city hospital, and provincial hospital. Several hospitals are randomly selected from each stratum. Logbooks from outpatient, inpatient and emergency departments are reviewed, together with discharge cards, which contain the final diagnosis; the logbooks are then compared with the records in the NIDR system. The community-based and health-care facility-based underreporting rate is calculated as the number of underreported cases (N_u) divided by the sum of reported and unreported cases ($N_r + N_u$):

$$N_u / (N_u + N_r).$$

Both community-based and health-care facility-based surveys are carried out routinely by the local CDC to complement and adjust data from the NIDR system. Most patients with fever for more than 7 days will present to a health-care facility. Thus, enteric fever is usually not included in the community-based survey.⁹

To adjust for underreporting, we obtained results from the surveys con-

ducted between 1998 and 2004 in Guilin, Beihai and Yulin, which represent hyper-, moderate- and low-endemic regions, respectively. To adjust for the incidence of enteric fever derived from NIDR data, we applied the means of the underreporting rates.

Laboratory-based surveillance

As in other provinces in China, the health-care system in Guangxi province consists of township, county, prefecture (city) and provincial hospitals. The laboratory-based surveillance system covers all clinical laboratories (except for township hospitals, where bacterial cultures are not routinely performed). *Salmonella* spp. isolates obtained from sporadic enteric fever patients at each clinical laboratory in the system are sent to the provincial CDC for confirmation.¹¹ For isolates confirmed as *Salmonella*, antimicrobial resistance is measured by the disc diffusion method, in compliance with Clinical and Laboratory Standards Institute guidelines¹² for the antibiotics ampicillin, cefotaxime, chloramphenicol, ciprofloxacin, cotrimoxazole, nalidixic acid and norfloxacin. *Escherichia coli* American Type Culture Collection strain 25922 is used for quality control. Data on the annual proportion of cases of enteric fever caused by *S. typhi* and other *Salmonella* spp., as well as on antimicrobial resistance patterns from 1994 to 2004, were obtained from the Guangxi CDC.

Outbreak investigation

According to Ministry of Health guidelines, during an outbreak all clinically suspected enteric fever cases and their close contacts must be individually investigated by the local CDC. A standardized case report form must be completed, and a blood sample is required from each case. Isolates from blood culture are identified, and antimicrobial resistance is then tested using the disc diffusion method. Seven days after the end of an outbreak, the local CDC must submit to the provincial CDC a technical report describing the outbreak, the index case, the epidemiological characteristics, the cause of the outbreak, relevant laboratory information, the control measures implemented, and the effectiveness of those measures. An outbreak is defined as five or more cases of enteric fever associated in time (within a 2-week period) and place (in the same community or institution).¹¹

A case of enteric fever is defined as a person with prolonged fever ($\geq 40^\circ\text{C}$ for 7 days or more) plus any of the following: typhoid facies (a thin, flushed face with a staring, apathetic expression), relative bradycardia, splenomegaly, hepatomegaly or rose spots. The clinical diagnosis of enteric fever is supported by leukopenia or granulocytopenia (or both), or by characteristic findings in bone marrow specimens.

The definitive, laboratory-confirmed diagnosis of enteric fever is made by isolation of *S. typhi* or another *Salmonella* spp. from blood, bone marrow or urine, or by a positive Widal test.¹³ A Widal test is positive when the titre of *S. typhi* or another *Salmonella* spp. O antigen is $\geq 1:80$, and the titre of *S. typhi* or another *Salmonella* spp. H antigen is $\geq 1:160$.¹³

Incidence estimate

Both clinical and definitive diagnoses of enteric fever have to be reported to the NIDR, according to the *Law of the People's Republic of China on the Prevention and Control of Infectious Diseases* (1989).

There is no record in CDC statistics of whether a diagnosis is based on clinical signs or laboratory tests. To track the methods used to diagnose cases of enteric fever reported to the NIDR system in Guangxi, an investigation was conducted in 2002. It indicated that 40% of the sporadic cases reported were based on a clinical diagnosis only, 40% on Widal test results and 20% on confirmatory blood culture results.¹⁴ In contrast, all enteric fever cases reported during outbreaks must be confirmed by laboratory tests. The annual enteric fever cases reported through the NIDR are grouped into sporadic cases from routine clinical practice or cases from outbreak investigations. To calculate the *Salmonella* species-specific incidence, we multiplied all CDC-reported cases by the percentage of enteric fever cases caused by each *Salmonella* spp., as derived from routine laboratory-based surveillance.

Regional variation

Guangxi province consists of 14 administrative prefectures that include 21 cities and 68 counties. To categorize the enteric fever endemicity of prefectures, we calculated each prefecture's median incidence rate between 1994 and 2004. Prefectures were grouped into hyper-, moderate- and low-endemic regions in accordance with their median annual incidence rates (per

Table 1. Annual incidence, mortality and case-fatality rates for enteric fever in Guangxi province, China, 1994–2004^a

Year	Cases	Deaths	Case fatality (per 1000)	Incidence (per 100 000)	Mortality (per 100 000)
1994	5307	3	0.6	11.9	0.007
1995	6090	6	1.0	13.5	0.013
1996	3690	5	1.4	8.1	0.011
1997	3021	2	0.7	6.6	0.004
1998	3701	6	1.6	8.0	0.013
1999	4900	6	1.2	10.5	0.013
2000	6231	5	0.8	13.2	0.011
2001	5538	0	0.0	11.6	0.000
2002	4221	2	0.5	8.8	0.004
2003	3140	2	0.6	6.5	0.004
2004	4950	0	0.0	10.1	0.000

^a Data from China's Notifiable Infectious Disease Reporting system, clinical diagnosis applied, Guangxi Centers for Disease Control and Prevention, Guangxi, China.

100 000 population): > 10, 1 to ≤ 10, and ≤ 1, respectively.

Results

Incidence and mortality rates

There were 50 789 clinically diagnosed cases of enteric fever in Guangxi province between 1994 and 2004 (annual average: 4617). Overall, enteric fever incidence rates did not decline appreciably during the study period. They fluctuated from year to year and peaked in 1995 and 2000 (Table 1).

Seasonality and age

During the study period, the incidence of enteric fever was highest in the group

aged 10–49 years in Guangxi province, and the age distribution did not appear to change (data not shown, available from corresponding author). Most episodes of enteric fever were detected during the summer and autumn (between June and October) (Fig. 1).

Regional variation

The highest median annual incidence of enteric fever (54.6 cases per 100 000 population) was found in the administrative prefecture of Guilin, followed by Hechi (12.5) and Baise (11.3). These three prefectures are located in the hyper-endemic north of Guangxi province. The lowest median annual incidence rate of enteric fever (≤ 1 per 100 000 popula-

tion) was found in the prefectures of Fangchenggang, Guigang, Qinzhou and Yulin, which are located in the south of Guangxi province. The prefectures located in the central region, including Beihai, are considered moderate-endemic regions (data not shown, available from corresponding author).

Underreporting

A review of underreporting rates was conducted in Beihai, Guilin and Yulin prefectures. Overall, 2000 treated cases of enteric fever were investigated in the three prefectures between 1998 and 2004. Of such cases, 70 (3.5%; standard deviation, SD: 0.4) were missed by the NIDR system. The highest underreporting rate, 7.0% (SD: 3.4), was found in Beihai, and the next highest, 3.4% (SD: 0.4), in Guilin. No missed cases were reported in Yulin. After adjusting for an average underreporting rate of 3.5%, the annual incidence rate of enteric fever in 2004 in Guangxi province was 10.5 per 100 000.

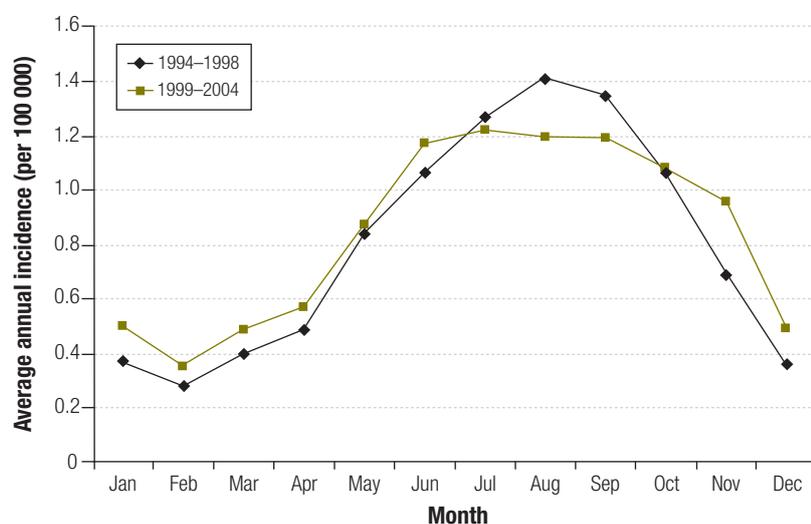
Enteric fever outbreaks

A total of 61 enteric fever outbreaks occurred in Guangxi between 1994 and 2004, resulting in 7455 culture-confirmed cases, equivalent to 15% of all reported cases in that 11-year period. Of the 61 outbreaks, 49 (80%) were caused by SPA, 12 (20%) by *S. typhi*, and 2 by both SPA and *S. typhi*. In terms of location, 72% of the outbreaks (44/61) occurred in hyper-endemic regions (Baise, Guilin and Hechi), 23% (14/61) in intermediate-endemic regions (Hezhou, Laibin, Liuzhou and Nanning) and 5% (3/61) in low-endemic regions (Guigang and Yulin). No outbreaks were reported from Beihai, Chongzou, Fangchenggang, Qinzhou and Wuzhou. Schools – including elementary schools, middle schools and colleges – accounted for 62% (38/61) of all outbreaks, 77% (47/61) of which were associated with an unsafe water supply. Of the 7455 *Salmonella* isolates, 4481 (60%) were identified as SPA (data not shown, available from corresponding author). No outbreaks caused by *S. paratyphi* B or C were reported during the study period.

Salmonella paratyphi A

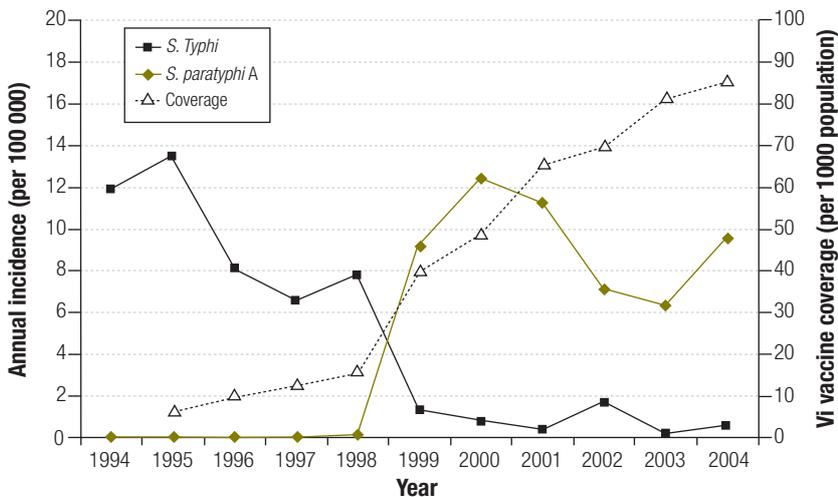
Until 1999, *S. typhi* was the only *Salmonella* spp. isolated from sporadic cases of enteric fever in Guangxi province. Data from laboratory-based surveillance showed that SPA was first isolated in

Fig. 1. The seasonality of enteric fever throughout Guangxi province, China, 1994–2004



Data from China's Notifiable Infectious Disease Reporting system, Guangxi Centers for Disease Control and Prevention, Guangxi, China.

Fig. 2. Estimated *Salmonella typhi* and *Salmonella paratyphi* A incidence with cumulative Vi polysaccharide immunization coverage in Guangxi province, China, 1994–2004



Data from China's Notifiable Infectious Disease Reporting system, laboratory surveillance and outbreak investigation, Guangxi Centers for Disease Control and Prevention, Guangxi, China.

Guangxi province in 1999, when it accounted for 86% of all culture-confirmed enteric fever cases. The proportion of enteric fever episodes associated with SPA increased to 94% in 2000 and peaked at 96% in 2001 and 2003 (data not shown, available from corresponding author). On average, SPA accounted for 80% of culture-confirmed enteric fever cases between 1994 and 2004 in Guangxi province. *S. paratyphi* B and C were not detected by the laboratory-based surveillance system during that period.

Species-specific incidence

The enteric fever cases reported for each year by the NIDR system were classified as caused by either *S. typhi* or SPA (Fig. 2). The classification was based on the annual number of outbreak-related cases caused by *S. typhi* and SPA from outbreak investigations, and the annual proportions caused by *S. typhi* and SPA from laboratory-based surveillance. The incidence rate of *S. typhi* in the province declined from 11.9 per 100 000 in 1996 to 0.6 per 100 000 in 2004. No similar decline in cases caused by SPA was observed since SPA was first detected in the province in 1998.

Antimicrobial resistance

A high proportion of *S. typhi* isolates are now resistant to cotrimoxazole, whereas most SPA isolates are still susceptible (Table 2). In contrast, most SPA isolates are now resistant to nalidixic acid, whereas most *S. typhi* isolates are still susceptible.

Most isolates of both *Salmonella* spp. remain susceptible to chloramphenicol, but some isolates of *S. typhi* are now resistant to norfloxacin, while resistance has yet to emerge in SPA isolates. *S. typhi* and SPA isolates remain susceptible to ciprofloxacin. We found similar antimicrobial susceptibility patterns for isolates of the two species obtained during enteric fever outbreaks and in sporadic cases (Table 2).

For *S. typhi* isolates, the most common cross-resistance was found between cotrimoxazole and nalidixic acid (12%, 4/33), cotrimoxazole and norfloxacin (7%, 9/122), cotrimoxazole and nalidixic acid (11%, 19/177), and cotrimoxazole and ampicillin (5%, 11/232).

Discussion

Although the incidence of enteric fever is decreasing in China as a whole, fluctuations in disease incidence were observed in Guangxi province, where annual incidence rates ranged from 6.5 to 13.5 per 100 000. Enteric fever seemed to peak in a cyclical fashion in Guangxi province, and sporadic cases and cases related to outbreaks caused considerable morbidity but little mortality.

In Guangxi province, enteric fever occurred most frequently in young people during the summer and autumn, with no change in pattern over the study period. Within the province the annual incidence of enteric fever varied considerably by region and was highest in its northern parts, where the province's karst terrain is distributed. For example, Guilin city

had a substantially higher incidence of enteric fever than the central and southern prefectures; 54% of all reported enteric fever cases in Guangxi province over the study period were in Guilin city, more than likely as a result of an unsafe drinking water supply. In rural areas and boarding schools, the cool groundwater collected from wells is widely used for drinking without being boiled. Shallow aquifers are more vulnerable to groundwater contamination in karst areas than in other geologic terrains. Dye traces have shown that septic tank effluent can travel through the thin soil layer into an aquifer and then to a spring within a few hours.¹⁵ Surveys of drinking water in Guangxi province indicated that only 18% of wells in rural areas and 27% of wells in boarding schools produced safe drinking water, and that bacteria were the main microbial contaminants.^{16,17} Correspondingly, outbreaks of waterborne disease occurred more frequently in Guangxi province than in China overall.¹⁸ In Guilin city, 91% of outbreaks were attributed to contaminated drinking water.¹⁹

No outbreaks due to SPA were reported until 1998, three years after Vi polysaccharide typhoid fever vaccine was introduced in the province.^{6,20,21} Since 1998, more than 80% of enteric fever outbreaks have been caused by SPA. The largest one (495 episodes), which occurred in 2004 in Luocheng county, was caused by a contaminated water supply system. Results from laboratory-based surveillance also indicate that the ratio of SPA to *S. typhi* cases has increased and that SPA has been the predominant cause of enteric fever in Guangxi since 1999.^{6,20,21} A significant decline in typhoid fever incidence was observed between 1998 and 1999, a period during which the cumulative coverage of Vi polysaccharide vaccination increased from 38% to 76% in the hyper-endemic regions of Guangxi.²¹ The routinely collected data used for this review suggests that the use of Vi polysaccharide vaccine resulted in a marked decline in typhoid fever, which coincided with a subtle increase in fever episodes caused by SPA. This could be a chance coincidence, since the emergence of SPA was also reported in south Asian countries (e.g. India, Nepal and Pakistan) where typhoid fever vaccine had not yet been introduced or coverage was low.^{22–24} Data collected in other endemic areas will be helpful in investigating the emergence of SPA following the successful control of typhoid fever through immunization.

Table 2. Antimicrobial susceptibility pattern for *Salmonella typhi* and *Salmonella paratyphi A* isolates, Guangxi province, China, 1994–2004^a

Antibiotic	Susceptible						Resistant							
	Inhibition zone (mm)		Isolates from sporadic cases		Isolates from outbreak cases		Inhibition zone (mm)		Isolates from sporadic cases		Isolates from outbreak cases			
	No. tested	%	No. tested	%	No. tested	%	No. tested	%	No. tested	%	No. tested	%		
<i>Salmonella typhi</i>														
Ampicillin	≥17	122	118	96.7	217	212	97.7	≤13	122	3	2.4	217	4	1.8
Cefotaxime	≥23	35	35	100	27	27	100	≤14	35	0	0	27	0	0
Chloramphenicol	≥18	122	118	96.7	217	213	98.2	≤12	122	2	1.6	217	0	0
Ciprofloxacin	≥21	29	29	100	10	10	100	≤15	29	0	0	10	0	0
Cotrimoxazole	≥16	122	37	30.3	217	63	29.0	≤10	122	83	68.0	217	143	65.9
Nalidixic acid	≥19	33	28	84.9	13	13	100	≤13	33	5	15.1	13	0	0
Norfloxacin	≥17	122	113	92.6	217	217	100	≤12	122	9	7.4	217	0	0
<i>Salmonella paratyphi A</i>														
Ampicillin	≥17	381	343	90.0	1033	869	84.1	≤13	381	13	3.4	1033	75	7.3
Cefotaxime	≥23	425	422	99.3	745	743	99.7	≤14	425	1	0.2	745	0	0
Chloramphenicol	≥18	381	377	99.0	1033	1028	99.5	≤12	381	1	0.3	1033	4	0.4
Ciprofloxacin	≥21	387	382	98.7	587	584	99.5	≤15	387	0	0	587	0	0
Cotrimoxazole	≥16	232	188	81.0	875	612	69.9	≤10	232	34	14.7	875	218	24.9
Nalidixic acid	≥19	398	23	5.8	594	95	16.0	≤13	398	370	92.9	594	491	82.7
Norfloxacin	≥17	342	334	97.7	1033	1027	99.4	≤12	342	1	0.3	1033	1	0.1

^a Data from laboratory-based surveillance system, Guangxi Centers for Disease Control and Prevention, Guangxi, China.

In 1990, China's national health authority recommended chloramphenicol, cotrimoxazole and penicillin as first-line antibiotics for the treatment of enteric fever.²⁵ By 1996, it had switched to recommending fluoroquinolones, such as ciprofloxacin and norfloxacin, as first-line drugs.²⁶ The use of fluoroquinolone antibiotics in rural village clinics and township hospitals is more liberal than in urban centres, where strict prescription practices are now enforced. Cephalosporins, penicillins and sulfanilamide were reported as the most commonly used antibiotics in rural Guangxi province.²⁷ A large proportion of *S. typhi* isolates are no longer susceptible to cotrimoxazole, and a high percentage of SPA isolates are resistant to nalidixic acid, which is used as a marker for reduced susceptibility to fluoroquinolones.^{28–31} The susceptibility of SPA to ciprofloxacin, norfloxacin and cefotaxime, and of *S. typhi* to norfloxacin, is decreasing. The emergence of *S. typhi* and SPA strains resistant to multiple antimicrobials is worrisome because it complicates the treatment of enteric fever. Surprisingly, both *S. typhi* and SPA isolates were still susceptible to chloramphenicol, which was introduced for the treatment of typhoid fever in 1948.

Our study had several limitations. Reported data rely in part on clinical diagnosis (i.e. clinical symptoms and signs and blood cell count), and this has low sensitivity and specificity. However, some studies have suggested that in endemic areas a clinical diagnosis can have good predictive value for typhoid and paratyphoid fever.^{32–34} Also, conventional culture methods detect only about 40% of typhoid and paratyphoid fever cases.^{35–38} Common factors impairing the growth of the bacteria in culture include a low bacterial load and too small a blood specimen volume, prior use of antibiotics, and a high concentration of agglutinating antibodies against O and H antigens in the blood.³⁹ Therefore, misdiagnosis due to the poor sensitivity of conventional culture methods might result in an underestimation of the true disease burden. Furthermore, underreporting could also result in an underestimated disease burden, although the overall underreporting rate of enteric fever from surveys conducted between 1998 and 2004 was only 3.5%.

Enteric fever occurs more frequently in the karst terrain and coastal areas of China. In karst terrain, the disease is caught primarily by drinking contami-

nated water; in the coastal region, by consuming uncooked seafood.^{6,19,40} Almost all karst terrain in China is found in the provinces of Guangxi, Guizhou and Yunnan. Enteric fever has declined dramatically in China over recent decades owing to rapid economic development, improvements in water supply and the introduction of the Vi polysaccharide vaccine. However, owing to a poorly developed economy in Guangxi, Guizhou and Yunnan, and to lifestyle changes in Zhejiang, a high burden of enteric fever could still be found in these provinces in 2004.⁷ In 77 outbreaks of enteric fever reported in China between 2004 and 2007, the average attack rate was 76 per 100 000. Of the 77 outbreaks, 53% were waterborne and 23% foodborne; 59 (77%) of them occurred in the provinces of Guangxi,

Guizhou, Yunnan and Zhejiang.¹⁸ As in Guangxi, SPA emerged in the provinces of Guizhou, Yunnan and Zhejiang at the end of the 1990s and became the predominant species in these provinces.^{6,18,41,42} Currently, there is no vaccine for SPA; therefore, improving the water supply and food sanitation is critical. A campaign to accelerate the implementation of a safe water supply started in hyper-endemic regions of Guangxi province in 2006.

Conclusion

Guangxi province continues to have a considerable enteric fever burden, especially in hyper-epidemic prefectures, such as Guilin city. Since the introduction of Vi polysaccharide vaccine, SPA has become the predominant cause of enteric

fever in the province. As antimicrobial resistance to first- and second-line drugs for the treatment of enteric fever emerges, a bivalent vaccine that protects against both SPA and *S. typhi* is desirable for controlling the burden of enteric fever in the short- and medium-term in epidemic areas. Long-term control and prevention will require improvements in water supply and sanitation systems. ■

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Competing interests: None declared.

ملخص

اتجاهات العيب المرضي للحمى المعوية في مقاطعة جوانغسي في الصين، 1994-2004

الموجودات في مقاطعة جوانغسي، تبين معدل وقوع الحمى المعوية خلال فترة الدراسة، وقد بلغت الذروة 13.5 حالة لكل 100 ألف فرد في عام 1995، وبلغ أقل معدل 6.5 في عام 2003. وكان المرض أكثر وقوعاً أثناء شهور الصيف والخريف، وفي الفئة العمرية 10-49 سنة. وتبين معدل وقوع الحمى المعوية بين المناطق الواقعة في مقاطعة جوانغسي. وخلال فترة 11 عاماً التي غطتها الدراسة، أبلغ عن وقوع 61 فاشية للحمى المعوية، وكانت السلمونية النظرية التيفية هي العامل المسبب السائد في المقاطعة. الاستنتاج يمكن للدراسات المستقبلية أن تقدم فهماً أكثر عمقاً لسبب التحول الوبائي للحمى المعوية في مقاطعة كوانغسي. ومع الأخذ في الاعتبار نشأة المقاومة لمضادات المكروبات من الصف الأول والثاني المستخدمين في معالجة الحمى المعوية، يمكن للقاح ثنائي التكافؤ المضاد للسلمونية النظرية التيفية والسلمونية التيفية أن ييسر مقاومة المرض.

الغرض تحديد عبء الحمى المعوية من خلال اتجاهات المراضة والوفيات، والإنتان البكتيري، ومقاومة مضادات المكروبات في مقاطعة جوانغسي الساحلية الجنوبية شبه المدارية والتي تعاني من عبء غير متناسب من الحمى المعوية. **الطريقة** استخلصت المعطيات الخاصة بالمراضة والوفيات الناجمة عن الحمى المعوية في الفترة من 1994 حتى 2004 من مركز جوانغسي لمكافحة وتوقي الأمراض. وأدمج التصد المختبري وتقصي الفاشيات مع التقارير الخاصة بالأمراض المعوية المبلغ عنها لتقدير معدل وقوع الحمى المعوية حسب أنواع البكتيريا. ولتصحيح نقص التبليغ، جُمعت معطيات من مسح أجري في ثلاث مناطق تمثل المناطق الوبائية المرتفعة والمتوسطة والمنخفضة في مقاطعة جوانغسي.

Résumé

Tendances et fardeau du choléra dans la province du Guangxi en Chine, 1994-2004

Objectif Déterminer le fardeau que représente la fièvre typhoïde au travers des tendances de morbidité et de mortalité, des espèces bactériennes et de la résistance antimicrobienne dans le Guangxi, une province subtropicale côtière du sud de la Chine présentant un fardeau anormalement important de fièvre typhoïde.

Méthodes Les données de morbidité et de mortalité causées par la fièvre typhoïde entre 1994 et 2004 ont été obtenues auprès du Centre de contrôle et de prévention des maladies du Guangxi. La surveillance en laboratoire et les enquêtes sur les résurgences ont été intégrées aux rapports des maladies infectieuses à déclaration obligatoire pour permettre d'estimer l'incidence spécifique d'espèces bactériennes de la fièvre typhoïde. Afin de compenser les sous-déclarations, les données du sondage ont été recueillies auprès de trois préfectures caractéristiques des régions hyper, modérément et faiblement endémiques de la province du Guangxi.

Résultats Dans la province du Guangxi, le taux d'incidence de la fièvre typhoïde a varié au cours de la période d'étude, avec un pic de 13,5 cas par 100 000 habitants en 1995 et un minimum de 6,5 en 2003. La maladie est fréquemment survenue pendant les mois d'été et d'automne, et dans la tranche d'âge 10-49 ans. L'incidence de la fièvre typhoïde a varié de région en région dans la province du Guangxi. Pendant la période de 11 ans couverte par l'étude, 61 résurgences de fièvre typhoïde ont été rapportées, et l'agent causatif prédominant dans la province était *Salmonella paratyphi A* (SPA).

Conclusion De futures études devraient fournir une meilleure compréhension de la raison de la variabilité épidémiologique de la fièvre typhoïde dans la province du Guangxi. Étant donné l'apparition de résistance aux première et deuxième lignes de traitements antimicrobiens de la fièvre typhoïde, un vaccin bivalent contre SPA et *S. typhi* faciliterait le contrôle de la maladie.

Resumen

Tendencias y carga de la fiebre tifoidea en la provincia de Guangxi, China, entre 1994 y 2004

Objetivos Determinar la carga de fiebre tifoidea mediante las tendencias de morbilidad y mortalidad, las especies bacterianas y la resistencia a los antibióticos en Guangxi, una provincia costera y subtropical del Sur de China, con una carga de fiebre tifoidea desproporcionalmente elevada.

Métodos Los datos sobre morbilidad y mortalidad causadas por la fiebre tifoidea entre 1994 y 2004 se recogieron en el Centro de control y prevención de enfermedades de Guangxi. Con el fin de estimar la incidencia específica de la fiebre tifoidea para cada una de las especies bacterianas se incorporaron informes de enfermedades infecciosas de declaración obligatoria a la vigilancia basada en pruebas analíticas y las investigaciones de los brotes epidémicos. Para el ajuste de los subregistros se recopilaron los datos del estudio procedentes de tres prefecturas representativas de las regiones hiperendémicas, mesoendémicas e hipoendémicas de la provincia de Guangxi.

Resultados La tasa de incidencia de la fiebre tifoidea en la provincia de Guangxi varió a lo largo del estudio, registrando un pico máximo de 13,5 casos por cada 100 000 habitantes en 1995 y un mínimo de 6,5 en 2003. La enfermedad tuvo una mayor incidencia durante los meses de verano y otoño, así como en el grupo de edad comprendido entre 10 y 49 años. La incidencia de la fiebre tifoidea varió según las regiones dentro de la misma provincia de Guangxi. Durante los 11 años que duró el estudio se declararon 61 brotes epidémicos de fiebre tifoidea, siendo la *Salmonella paratyphi A* (SPA) el agente causal predominante en la provincia.

Conclusión Los estudios prospectivos pueden ayudar a comprender mejor la causa de los datos epidemiológicos cambiantes de la fiebre tifoidea en la provincia de Guangxi. Una vacuna bivalente contra SPA y *S. typhi* facilitaría el control de la enfermedad, teniendo en cuenta la aparición de resistencias a los antibióticos de primera y segunda línea para el tratamiento de la fiebre tifoidea.

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