Research letters

Shigella dysenteriae serotype 1 in west Africa: intervention strategy for an outbreak in Sierra Leone

Philippe J Guerin, Christopher Brasher, Emmanuel Baron, Daniel Mic, Francine Grimont, Mike Ryan, Preben Aavitsland, Dominique Legros

In November 1999, a Médecins Sans Frontières team based in the southeastern part of Sierra Leone reported an increased number of cases of bloody diarrhoea. *Shigella dysenteriae* serotype 1 (Sd1) was isolated in the early cases. A total of 4218 cases of dysentery were reported in Kenema district from December, 1999, to March, 2000. The overall attack rate was 7·5%. The attack rate was higher among children younger than 5 years than in the rest of the population (11·2% *vs* 6·8%; relative risk=1·6; 95% CI 1·5–1·8). The case fatality was 3·1%, also higher for children younger than 5 years (6·1% *vs* 2·1%; relative risk=2·9; 95% CI 2·1–4·1]). Among 583 patients regarded at increased risk of death who were treated with ciprofloxacin in isolation centres, case fatality was 0·9%. A 5-day ciprofloxacin regimen, targeted to the most severe cases of bloody diarrhoea, was highly effective. This is the first time a large outbreak caused by Sd1 has been reported in west Africa.

Lancet 2003; **362:** 705–06

Bacillary dysentery has been a disease of poor and crowded communities throughout history, and continues to be a major cause of morbidity and mortality in the tropics, with over 140 million cases and 580 000 deaths respectively.[1] In developing countries, *Shigella dysenteriae* serotype 1 (Sd1) causes epidemics with high attack rates and high case fatality ratios (CFR) in all age groups. Since the beginning of the 1990s, large outbreaks of dysentery due to Sd1 have been reported in central, east, and southern Africa, but never in west Africa.[1] Over the past decades *Shigella* species have become resistant to most of the widely used and inexpensive antimicrobials.[1]

In November 1999, the Médecins Sans Frontières team working in the southern part of Kenema district, in the southeast of Sierra Leone (figure 1), reported an increasing number of consultations for bloody diarrhoea. In December, 1999, the Institut Pasteur in Paris identified Sd1 in stool specimens from those patients.

A case management strategy was based on risk stratification of affected patients: Patients at a higher risk of death[2]—ie, bloody diarrhoea in persons younger than 5 years or older than 50 years of age, in malnourished people, or in those with severe illness (patients presenting with dehydration, temperature over 38·5°C, convulsions, or coma)—were admitted to temporary isolation centres and received a 5-day course of ciprofloxacin (500 mg orally every 12 h for adults and 15 mg/kg every 12 h for children). They remained hospitalised for the entire duration of the treatment. Health-care workers directly observed the drug intake. Each patient received a food ration equivalent to 2300 kcal per day.

Patients who did not meet these criteria when seen by health workers received oral rehydration salts, hygiene advice, and information about where to get treatment if their condition deteriorated.

Between Nov 22, 1999, and Feb 27, 2000, 4218 cases of bloody diarrhoea were reported from the area (figure 2). The overall attack rate was 7·5% (estimated population of 55 875). The male/female sex ratio was 1·02. The attack rate in the

Figure 1: **Outbreak of Sd1 in a country at war**
Entrance of Kenema hospital, Sierra Leone.

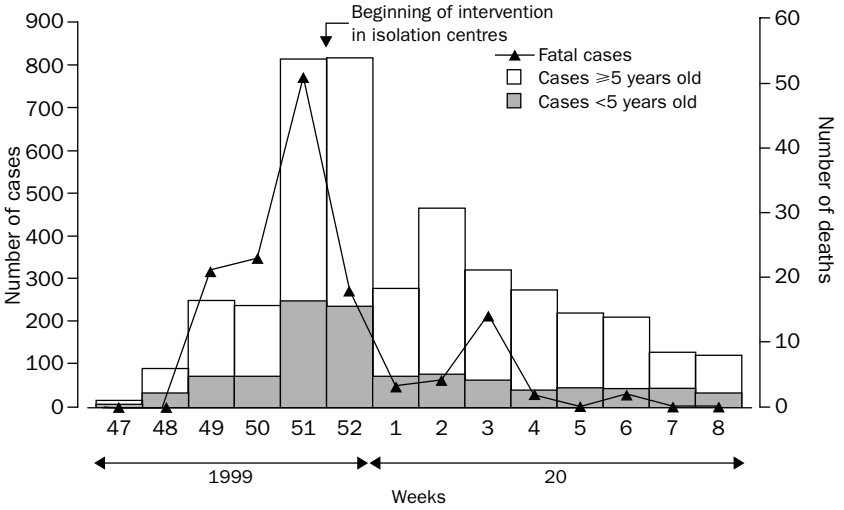

Figure 2: **Cases of bloody diarrhoea reported per week**

population under 5 years old was 11·2%, which was higher than the 6·8% rate for those aged over 5 years (relative risk 1·6, 95% CI 1·5–1·8). 131 deaths due to bloody diarrhoea were recorded during the outbreak period, giving an overall case fatality rate of 3·1%, which was higher for children younger than 5 years old (6·1% *vs* 2·1%; relative risk 2·9, 95% CI 2·1–4·1). A total of 583 patients were treated in the isolation centres from Jan 1, 2000, to Feb 27, 2000. Of these, 581 completed their treatment (compliance 99·7%); two defaulted on day 3. The overall case fatality rate in isolation centres was 0·9% (five of 583).When comparing the number of deaths to the number of cases, we see a clear reduction in the number of cases after introduction of the full-scale intervention, in which the most severe cases were treated in isolation centres (figure 2). The case fatality rate was 5·1% (113 of 2214) in the period before Jan 1, and 1·2% (25 of 2004) in the period after this date (relative risk 4·1, 95% CI 2·6–6·5).

On December 23, 1999, the Institut Pasteur isolated Sd1 in six stool specimens out of 19 specimens from Kenema district. Later, 20 strains of Sd1 were isolated in different laboratories from 69 samples. All were resistant to amoxicillin, amoxicillin plus clavulanic acid, tetracycline, trimethoprim-sulfamethoxazole, and chloramphenicol. They were sensitive to gentamicin, nalidixic acid, ciprofloxacin, ofloxacin, cefixime, and ceftriaxone.

This outbreak is the first large epidemic caused by Sd1 reported in west Africa. In 4 months, 4218 cases of dysentery were reported in Kenema district, with an overall attack rate of 7·5% and a case fatality rate of 3·1%.

We believe that the reduction of the case fatality rate noted after implementation of the risk stratification strategy can be attributed to effective antibiotic therapy for the most severe cases. For cases without severity criteria, oral rehydration together with health and sanitation education was also effective. Together, these measures constitute a strategy to reduce the number of deaths in complex emergencies, such as that in Sierra Leone.

The choice of treatment regimen was between nalidixic acid and ciprofloxacin. For bacillary dysentery, recommendations for nalidixic acid state that this treatment should be given four times a day for 5 days. As experienced in central Africa, poor compliance to this regimen facilitates rapid emergence of resistance to nalidixic acid, which is the first step in the acquisition of resistance to ciprofloxacin.[3,4] Costs of fluoroquinolones, especially of ciprofloxacin, should no longer be a limitation in resource-poor contexts in the future, since patent rights are expiring in most countries and ciprofloxacin treatment is therefore becoming cheaper. Although not yet approved for paediatric use, fluoroquinolones have proved safe and effective for use in childhood shigellosis.[5]

Population movements and concentrations are common in western Africa, and favour the emergence of outbreaks. Public health authorities of west African countries should be aware of and well prepared for potential new outbreaks of Sd1. The current treatment recommended by WHO in case of Sd1 outbreaks in west Africa is nalidixic acid. In the light of our results and other published data, this choice should be carefully reconsidered.

Contributors

P J Guerin took part in protocol design, statistical analysis, and writing and editing of the manuscript. C Brasher participated in protocol design and data collection. E Baron contributed independent outcome assessment, and medical coordination of Médecins Sans Frontières in Paris. D Mic collected data. F Grimont undertook microbiology investigations. M Ryan did independent outcome assessment, and was the WHO advisor for the outbreak response team in Sierra Leone. P Aavitsland took part in statistical analysis, and writing of the report. D Legros was study coordinator and participated in writing and editing of the manuscript.

Conflict of interest statement

None declared.

Acknowledgments

We thank the Ministry of Health of Sierra Leone for their support in this investigation, the investigation team in Sierra Leone for their excellent work in a difficult context, Guy Gerbaud, Institut Pasteur Paris, for microbiological support, and Jane Moore, Merlin, for sharing medical information with us. We also thank Mathieu Nacher, John-Arne Rottingen, Alain Moren, Thomas Grein, and Francis Varaine for their valuable comments on the manuscript. This investigation was supported by Médecins Sans Frontières; C Brasher, E Baron, and D Mic were employed by this organisation.

1 Keusch GT, Bennish ML. Shigellosis. Bacterial infections of humans: epidemiology and control. New York and London: Plenum Medical Book Company, 1998: 631–56.
2 Legros D, Paquet C, Dorlencourt F, Saoult E. Risk factors for death in hospitalized dysentery patients in Rwanda. *Trop Med Int Health* 1999; **4:** 428–32.
3 Ries AA, Wells JG, Olivola D, et al. Epidemic *Shigella dysenteriae* type 1 in Burundi: panresistance and implications for prevention. *J Infect Dis* 1994; **169:** 1035–41.
4 Hooper DC. Mechanisms of action and resistance of older and newer fluoroquinolones. *Clin Infect Dis* 2000; **31** (suppl)**:** S24–28.
5 Bethell DB, Hien TT, Phi LT, et al. Effects on growth of single short courses of fluoroquinolones. *Arch Dis Child* 1996; **74:** 44–46.

Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway (P J Guerin MD, P Aavitsland MD)**; Epicentre, Paris, France** (P J Guerin, D Legros MD)**; Médecins Sans Frontières, Paris, France** (C Brasher MBBS, E Baron MD, D Mic MD)**; Centre National de Référence des *Escherichia coli* et *Shigella*, Institut Pasteur, Paris, France** (F Grimont PhD)**; Global Alert and Response Team, Department of Surveillance and Response, Communicable Diseases Cluster, WHO, Geneva, Switzerland** (M Ryan MD)**; and European Programme for Intervention Epidemiology Training** (P J Guerin)

Correspondence to: Dr Philippe J Guerin, Epicentre, Paris 75011, France
(e-mail: philippe.guerin@epicentre.msf.org)

Outcome of childhood acute lymphoblastic leukaemia in resource-poor countries

Monika L Metzger, Scott C Howard, Ligia C Fu, Armando Peña, Rene Stefan, Michael L Hancock, Zhe Zhang, Ching-Hon Pui, Judy Wilimas, Raul C Ribeiro

The causes of treatment failure in childhood acute lymphoblastic leukaemia are thought to differ between resource-rich and resource-poor countries. We assessed the records of 168 patients treated for this disease in Honduras. Abandonment of treatment (n=38), the main cause of failure, was associated with prolonged travel time to the treatment facility (2–5 h: hazard ratio 3·1, 95% CI 1·2–8·1 *vs* >5 h: 3·7, 1·3–10·9) and age younger than 4·5 years (2·6, 1·1–6·3). 35 patients died of treatment-related effects. Outcome could be substantially improved by interventions that help to prevent abandonment of therapy (such as funding for transport, satellite clinics, and support groups), and by prompt treatment of infection.

Lancet 2003; **362:** 706–08

More than 70% of children live in poor countries, where the cure rates for acute lymphoblastic leukaemia (ALL) are often less than 35%.[1] By contrast, cure rates in developed countries are about 80%.[2,3] This disparity is thought to result mainly from abandonment of treatment—a problem unique to countries where education, income, and access to tertiary medical centres are limited—and to toxicity of treatment. Abandonment of treatment can be associated with several sociocultural and economic variables. We postulated that in Honduras, where the paediatric cancer unit is distant from