observed, X1 and X2, which differed by 5 to 6 bands. Furthermore, outbreak isolates X3 and X4 were closely related to X1, differing by four and three DNA fragments, respectively. Similar results were obtained after digestion with a second restriction endonuclease, *Spe*I (5'-ACTAGT-3'; pattern designation S). Although fewer bands were seen compared to PFGE, ribotyping of these isolates using *Spe*I-digested genomic DNA largely confirmed the PFGE results in that the sporadic isolates gave unique profiles and only three closely related ribotype profiles were detected among the outbreak isolates. Two Malaysian isolates of *S. paratyphi* A included for comparison gave patterns very different from the Indian isolates by both PFGE (F = 0.44-0.65) and ribotyping. Also, it was determined that isolates A-117 (X1/S1) and A-123 (X2/S2) belonged to the index cases and that, as the outbreak progressed, other patterns (X3/S3 and X4/S4), which differed from the original patterns by one to four bands, appeared during weeks 2 to 3 of the outbreak. Notably, patterns X1 and X2 reappeared at the end of the outbreak.

Although molecular analysis of *S. typhi* and *S. paratyphi* B by ribotyping (2,4) and PFGE (3) has been reported, to the best of our knowledge the present study is the first performed with *S. paratyphi* A. The data obtained agree with those observed for *S. typhi* (3) in that outbreak isolates are more clonal and limited in diversity, whereas sporadic isolates are more diverse genetically and belong to unrelated clones. According to the criteria of Tenover et al. (5), it seems likely that the present outbreak was associated with two distinct clones/strains of *S. paratyphi* A (X1/S1 and X2/S2) that are related (5) but have distinct PFGE profiles. This observation is perhaps not surprising given the fact that both clones are phage type 1 and that contaminated potable water was incriminated in the outbreak (1). The PFGE results were largely confirmed by ribotyping, although this technique appears to be slightly less sensitive and discriminating in that fewer bands were seen and the differences between outbreak isolates were much less obvious.

We thus conclude that the outbreak in New Delhi, India, was caused by two related but distinct clones of *S. paratyphi* A. There also appears to be substantial genetic diversity among *S. paratyphi* A strains as the Malaysian isolates were very different from those from India. The data also suggested minor genetic changes among the *S. paratyphi* A isolates during the 2-month outbreak. This observation agrees with the high mutation rates noted among pathogenic *Salmonella* spp. (6) and the plasticity of the genome of salmonellae associated with enteric fever (7). How these changes affected the biologic behavior of these isolates will be the subject of further study. Our study reaffirms the usefulness of PFGE and ribotyping in the molecular typing and discrimination of individual *Salmonella* isolates for epidemiologic investigations.

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References

1. Kapil A, Sood S, Reddaiah VP, Das B, Seth P. Paratyphoid fever due to *Salmonella enterica* serotype paratyphi A. Emerg Infect Dis 1997;3:407.
2. Pang T, Altwegg M, Martinetti G, Koh CL, Puthucheary SD. Genetic variation among Malaysian isolates of *Salmonella typhi* as detected by ribosomal RNA gene restriction patterns. Microbiol Immunol 1992;36:539-43.
3. Thong KL, Cheong YM, Puthucheary S, Koh CL, Pang T. Epidemiologic analysis of sporadic and outbreak *Salmonella typhi* isolates by pulsed field gel electrophoresis. J Clin Microbiol 1994;32:1135-41.
4. Ezquerra E, Burnens A, Jones C, Stanley J. Genotypic typing and phylogenetic analysis of *Salmonella paratyphi* B and *S. java* with IS200. J Gen Microbiol 1993;139:2409-14.
5. Tenover FC, Arbeit RD, Goering RV, Mickelson PA, Murray BE, Persing DH, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol 1995;33:2233-9.
6. Leclerc JE, Li B, Payne WL, Cebula TA. High mutation frequencies among *Escherichia coli* and *Salmonella* pathogens. Science 1996;274:1208-11.
7. Liu SL, Sanderson KE. Highly plastic chromosomal organization in *Salmonella typhi*. Proc Natl Acad Sci U S A 1996;93;10303-8.

Unrecognized Ebola Hemorrhagic Fever at Mosango Hospital during the 1995 Epidemic in Kikwit, Democratic Republic of the Congo

To the Editor: We report here the clinical description of a hemorrhagic syndrome observed

in Mosango General Hospital that, retrospectively, was one of the first cases of the Ebola hemorrhagic fever outbreak in the Bandundu province of former Zaire in the spring of 1995 (1).

Case

On April 20, 1995, a 70-year-old nun, working as a nurse in Kikwit General Hospital, was admitted to Mosango General Hospital with a 5-day history of fever, despite antimalarial treatment. The day before hospitalization she had profuse diarrhea, vomiting, high fever, and severe agitation with delirium. On arrival, quiet and apyretic, she complained of headache, loss of appetite, and severe asthenia, but she walked to her room without help. On examination, the only abnormalities recorded were severe dehydration and oral thrush-like lesions, raising a suspicion of candidiasis. Pulse rate was 80/min and blood pressure 120/80. Medical history included an amebiasis liver abscess 15 years ago and chronic coronaritis since 1990.

Electrocardiogram (ECG) abnormalities were consistent with chronic diffuse ischemia. Laboratory investigations showed the following values: few trophozoites on a thick film; erythrocyte sedimentation rate (ESR) 15 mm/h; bleeding time (BT) 7½ min; coagulation time (CT) 9 min; and white blood cells (WBC) $8.4x10^9$/L (73% neutrophils, 23% lymphocytes, 2% eosinophils, 1% basophils, 1% mastocytes). Urinalysis showed proteinuria (++), hyaline cylinders (+++), 50 white cells per field, and hematuria (+). The patient was perfused with 4L/day of glucose and 1.5 g of quinine. She was kept in a private room in the nearby nuns' convent.

Later during the day, high fever (40°C) and severe diarrhea with melena developed; the pulse rate was normal (80/min). Typhoid fever was suspected despite the lack of hepatosplenomegaly; Widal test was not available for confirmation. Treatment was started with intravenous (i.v.) amoxicillin (1g/6h during the first 24 h and then 1g/4h) and i.v. chloramphenicol (2g/24h). Subsequently, coagulation abnormalities developed in addition to the melena; vitamin K and epsilon amino caproic acid were added to i.v. therapy. Watery vomits remained frequent and abundant, and the patient's condition was unresponsive to treatment.

On hospitalization day 2, the clinical picture remained the same, with severe asthenia, anorexia, abundant blackish diarrhea, and watery vomits. An intractable hiccup developed. The fever remained in plateau around 40°C with spikes. Obnubilation occurred during episodes of high fever. Pulse and blood pressure remained stable. ECG showed no modifications. Cutaneous examination detected for the first time a maculopapular rash and petechiae on flanks and limbs, and the patient complained of gastric pain for which the neurologic examination was normal. Urine was abundant and clear.

On hospitalization day 3, high fever continued, with some defervescence during which the patient regained lucidity, although she responded only with monosyllables because of the extreme asthenia and somnolence; diarrhea persisted but without hemorrhage. The patient had less vomiting. Laboratory data showed ESR 35 mm/h; BT 10 min; CT 12 min; WBC $12.6x10^9$/L (70% neutrophils, 24% lymphocytes, 2% eosinophils, 1% basophils, 3% mastocytes). During the night, the patient maintained a high temperature, still with temperature-pulse disparity. The diagnosis of typhoid fever was questioned, and other diagnostic possibilities were reconsidered (shigellosis, mononucleosis); leukocytosis was considered against the possibility of Ebola hemorrhagic fever. Chloramphenicol was switched to rifampicin (1,200 mg/24h).

On April 23, the patient's status was unchanged with fever, asthenia, and diarrhea. Later in the day, her condition deteriorated: petechiae could be seen on the entire body, and for the first time, bruises and bleeding at injection sites were observed and precluded intramuscular injections. The patient had bleeding cracks on the lips and diffuse bleeding in the oral cavity (i.e., gums, tongue). The volume of urine was low, and antibiotic therapy was changed to cephalosporin.

On hospitalization day 5, hemorrhages increased, and fever remained high until the end of the day, when it started to normalize. Urine volume was still low (verified by vesical catheter) despite the i.v. rehydration of 4 L/day. Fresh blood transfusion (300 ml) did not slow the hemorrhaging; disseminated intravascular coagulation was suspected, and heparin treatment was started. The patient became comatose. The laboratory results showed ESR 55mm/h and WBC $30.2x10^9$/L with an unchanged formula. No coagulation was observed on BT and CT. Blood pressure fell (80/50); the clinical status remained unchanged until the patient's death on April 25 at 10:00 a.m.

No special nursing precautions were taken either during the hospitalization or after the death, and the body was transferred to Kikwit to be buried. On April 30, another nun who took care of the index patient during the night of April 23 became ill with fever, headache, and myalgia. Over the next few days, the second patient had a clinical picture identical to that of the index patient, including high fever, severe asthenia, vomiting, hiccups, and diarrhea. On May 5, epistaxis and coagulation abnormalities developed, followed by other clinical signs of the hemorrhagic syndrome. The second patient was transferred to Kikwit General Hospital, where she died 6 days later. A laboratory confirmation of Ebola hemorrhagic fever was made on a blood specimen collected on May 5 and sent to Special Pathogens Branch (Centers for Disease Control and Prevention, Atlanta, GA).

These cases of unrecognized Ebola hemorrhagic fever were part of the hospital outbreak that precipitated and mobilized international community efforts (2). Retrospectively, the clinical symptoms observed were typical of Ebola hemorrhagic fever (3,4) and were described again in subsequent patients during this outbreak (5). In tropical Africa, the presence of hemorrhagic symptoms in the course of a febrile illness should raise the possibility of one of the viral hemorrhagic fever diseases. In viral hemorrhagic fevers, maculopapular rash is constantly observed only in filovirus disease. Typically, the clinical laboratory findings include an early lymphopenia and marked thrombocytopenia. Containment and barrier nursing procedures should be initiated until the diagnosis of viral hemorrhagic fever can be ruled out. The index patient described here was the third patient transferred from Kikwit General Hospital in less than 1 month to die of a hemorrhagic illness after a few days of an unexplained febrile syndrome. Two patients were health-care workers in Kikwit General Hospital. This cluster of hemorrhagic illness and possible human-to-human transmission, particularly among hospital staff, was (and should always be) sufficient to suspect a viral hemorrhagic fever. The laboratory confirmation of this presumptive diagnosis was the clenching factor in the multinational effort in Kikwit.

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References

1. Muyembe T, Kipasa M, the International Scientific and Technical Committee, WHO Collaborating Centre for Haemorrhagic Fevers. Ebola haemorrhagic fever in Kikwit, Zaire. Lancet 1995;345:1448.
2. Khan AS, Kweteminga TF, Heymann DL, LeGuenno B, Nabeth P, Kerstiens B, et al. The reemergence of Ebola hemorrhagic fever, Zaire, 1995. J Infect Dis. In press 1998.
3. Piot P, Sureau P, Breman JG, Heymann D, Kintoki V, Masamba M, et al. Clinical aspects of Ebola virus infection in Yambuku area, Zaire, 1976. In: Pattyn SR, editor. Ebola virus haemorrhagic fever. Amsterdam: Elsevier/North-Holland Biomedical Press; 1977. p. 7-14.
4. Sureau PH. Firsthand clinical observations of hemorrhagic manifestations in Ebola hemorrhagic fever in Kitwit, Democratic Republic of the Congo (former Zaire): clinical observations in 103 patients. Review of Infectious Diseases 1989;11:S790-3.
5. Bwaka MA, Bonnet M-J, Calain P, Colebunders R, De Roo A, Guimard Y, et al. Ebola hemorrhagic fever in Kikwit, Democratic Republic of the Congo (former Zaire): clinical observations in 103 patients. J Infect Dis. In press 1998.

Classification of Reactive Arthritides

To the Editor: We read with interest J.A. Lindsay's article on sequelae of foodborne disease (1). However, we believe that there are errors in the classification of the reactive arthritides. Lindsay states that ankylosing spondylitis (AS) is a "rheumatoid inflammation of synovial joints and entheses within and distal to the spine." Although not the primary focus of the article, the classification and etiopathogeneses of rheumatoid arthritis (RA) and the seronegative spondyloarthropathies, including AS, should be clarified. The term spondylitis, from the Greek *spondylos*, for vertebra, means inflammation of the vertebrae. The term rheumatoid is generally taken to apply to rheumatoid arthritis, while rheumatic is a more general term applying to all connective tissue diseases.

AS is a chronic, systemic, inflammatory disorder primarily affecting the axial skeleton, with sacroiliac joint involvement as its hallmark. Back pain is the first clinical manifestation in approximately 75% of the patients (2). The backache is usually insidious in onset, dull, and difficult to localize. After several months, it generally becomes bilateral and persistent. The ache is often worse in the morning or after periods of inactivity and improves with move-