

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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## 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-

ment. The course is highly variable. Involvement of peripheral joints other than hips and shoulders is uncommon.

AS is strongly associated with human leukocyte antigen (HLA) B27, a major histocompatibility complex (MHC) class I allele, and may show familial aggregation. More than 90% of patients with AS have the HLA-B27 allele (3). HLA-B27 is believed to be directly involved in disease pathogenesis. Transgenic rats expressing human HLA-B27 develop a broad spectrum of disease closely resembling human disease. These rats have peripheral and axial arthritis, gastrointestinal inflammation, and diarrhea. Psoriatic-like skin changes and inflammation of the heart and male genitalia are also seen. Histologically, the joint, gut, skin, and heart lesions resemble those seen in HLA-B27-related disease in humans (4).

The inflammatory process in AS involves the synovial and cartilaginous joints, as well as the osseous attachments of tendons and ligaments (entheses). Much of the skeletal pathology of AS can be explained by the changes that take place at the entheses. After an initial inflammatory, erosive process involving the entheses, there is healing in which new bone is formed. The final outcome of this process is an irregular bony prominence with sclerosis of the adjacent cancellous bone (5). This can be contrasted with the pathology of RA, in which there is a greater tendency to affect cartilaginous joints such as the intervertebral discs and symphysis pubis. The process in RA is one of bony erosion rather than new bone formation.

The term ankylosing spondylitis, derived from the Greek for "bent spinal vertebrae," by definition requires exclusion of the other spondyloarthropathies, such as Reiter syndrome and reactive arthritides due to enteric (or urogenital) organisms. Spondylitis may occur in reactive arthritis, psoriatic arthritis, or the arthropathy associated with inflammatory bowel disease, but is less common in these diseases (approximately 50% in reactive arthritis, 20% in enteric arthritis or psoriatic arthritis). All of these diseases can be viewed as seronegative spondyloarthropathies in that, by definition, rheumatoid factor is not present.

RA is a systemic autoimmune disorder of unknown etiology. It is a chronic symmetric arthropathy of peripheral joints, associated with erosive synovitis. Enthesopathy is generally not

found. The majority of patients have elevated titers of serum rheumatoid factor, as opposed to the seronegative spondyloarthropathies. Spinal involvement in RA is seen but most often involves the cervical spine. The pathogenesis of the spinal disease is that of synovitis of the odontoid-atlas joints. The major HLA association is with HLA-DR4, an MHC class II allele.

Reactive arthritis is so named because it is felt that the arthritis and other inflammatory manifestations are an immune reaction to a distant infection. There is an association with HLA-B27 but less so than that found in AS (60% to 80%, compared with more than 90% in AS). While bacterial antigens can be found within the joint, the offending infectious process most often subsides before the onset of arthritis, and no living organisms are found in the joint (2). In many cases, no infectious trigger can be identified. Persistence of microbial antigens has been demonstrated and is likely to play a prominent role in the pathogenesis of acute and chronic inflammation. Antigens to several gastrointestinal pathogens have been isolated from the synovial fluid in patients with reactive arthritis. *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, and *Borrelia* are the most common pathogens capable of initiating reactive arthritis (2). The arthritis is generally an asymmetric oligoarthritis predominantly affecting the lower extremities and typically develops 6 to 14 days after a bout of diarrhea. However, onset can occur up to 3 months later. Diarrhea can also be absent, and there is no relationship between the severity of the arthritis and the severity of the diarrhea.

Reiter syndrome is in fact a reactive arthritis. In 1916, Hans Reiter described a triad of arthritis, urethritis, and conjunctivitis in a soldier with dysentery. However, the disease was actually first described by Sir Benjamin Brodie in the early 1800s (6). The complete triad is actually seen in only a minority of patients. Arthritis develops 1 to 3 weeks after the diarrhea or urethritis. It is generally asymmetric, involving large joints, especially in the lower extremities. The term Reiter syndrome actually refers only to the triad of arthritis, urethritis, and conjunctivitis. Reiter syndrome is both clinically and historically more accurately termed reactive arthritis. Nevertheless, the term reactive arthritis does not reflect the systemic nature of the disease.

In summary, while both reactive arthritis and ankylosing spondylitis are seronegative

spondyloarthropathies, they are separate entities. Both are distinct from rheumatoid arthritis.

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### Reply to Drs. Blumberg and Sloan

**To the Editor:** I concur with your comments. After reviewing the literature related to foodborne disease, it appears that the original classification of reactive arthritides has been in error for some time. I certainly appreciate the correction.

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### Cost of Blood Screening

**To the Editor:** In reference to G.A. Schmunis' article on the risk for transfusion-transmitted infections in Central and South America (1), I would like to comment on the cost of blood screening. In a screening program, the objective is to have safe blood units, not to assess the prevalence of different infections among potential or actual donors. Thus, while acknowledging all infections present in a given donor or potential donor is not required, detecting at least one of the infections that would make a donor noneligible is. If samples from every potential donor are subjected (by default) to all the tests, information on every infection present is provided, and the cost of screening this donor is the sum of the cost of every

test applied; in this case, both the information and the cost are greater than necessary.

Information on the prevalence of bloodborne infections among the general population or, preferably, among potential donors (particularly where professional donors are frequent) along with information on the costs of the tests to be used can form the basis of a stepwise screening scheme. Tests for infections with the highest prevalence would be applied first. For example, in many areas of Peru, using the Venereal Disease Research Laboratory (VDRL) test (for screening *Treponema pallidum* infection) first would reduce the number of samples to be subjected to other more expensive and often less available tests (e.g., HIV enzyme-linked immunosorbent assay [ELISA] or hepatitis C virus [HCV] ELISA); in others areas, a test for hepatitis B virus antigen (HB<sub>s</sub>Ag) should be used before HIV ELISA. The reduction in cost provided by stepwise screening will depend on the prevalences of the more frequent infections and the frequency of concurrent infections.

The questionnaires applied to candidate donors should be validated, and the benefit of using them should be assessed. In most settings, candidate donors are either ignorant of their status as carriers of bloodborne infection or ready to deny it; therefore, the questionnaire is of little use. In some cases candidate donors are turned down because of "hepatitis history" when in fact they have not had bloodborne hepatitis.

Finally, screening tests seem to be quite more expensive than reported in Table 4 of the Schmunis article. In Lima, at a ministry of health facility, some prices are as follows: HIV ELISA US\$12.50, VDRL US\$6.40, HB<sub>s</sub>Ag US\$13.90.

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