LETTERS TO THE EDITOR

Familial Salmonella-Triggered reactive arthritis

Sir—Familial Salmonella-triggered reactive arthritis (ReA) has been exceptionally reported [1]. We describe two family members (a father and his son) who developed ReA after Salmonella infection in an outbreak at home. Both patients had a history of polyarticular and monarticular peripheral arthritis at the age of 45 and 10 yr, respectively. Another family member (the mother) who suffered diarrhoea remained asymptomatic.

Case 1, a 65-yr-old male, had a history of polyarthritis affecting his shoulders, wrists, MCP joints, PIP joints and bilateral heel pain. During 7 yr, he remained with exacerbation and remission of his affected joints. There were no genitourinary or gastrointestinal symptoms, and no conjunctivitis or other mucocutaneous lesions. He remained asymptomatic until 64 yr old, when he noted acute onset of fever, chills and diarrhoea with 2–3 watery stools per day. Three weeks later, he developed marked pain, swelling and tenderness in his ankles, both knees, wrist, first and second right MTFJs, and several MCJFs. Physical examination showed a temperature of 38°C and polyarthritis of affected joints. Laboratory studies revealed ESR of 55 mm/h and CRP of 30 mg/l (normal values <5.0 mg/l). Tests for RF and ANA were negative. Antibodies to Salmonella O antigen by indirect haemagglutination were negative. Three months later, he remained symptom free with anti-inflammmatory analgesic therapy and the Widal test was negative.

Case 2, the 31-yr-old son of the above patient, had a history of arthritis of the right knee of 1 year duration, 20 yr before our evaluation. The effusion in the right knee recurred during the time of his military service. He remained asymptomatic until 3 weeks before admission, time in which he presented, with profuse diarrhoea, colicky abdominal pain and high fever (38.5°C). Two weeks later, he developed pain and swelling in his left knee. Physical examination revealed a temperature of 37.7°C and a warm, tender, swollen left knee. No skin lesions were present. Laboratory data of significance included a WBC count of 11 800/mm, ESR of 28 mm/h and a CRP of 42 mg/l. RF, ANA and stool culture were negative. Initially, antibodies to Salmonella O antigen were negative by the Widal technique. Pelvic and knee radiographs were normal. A bone scan showed an increased uptake of isotope in the left knee and left temporomandibular joints. SF obtained from the knee was inflammatory. Gram stain and culture were negative. No crystals were seen under polarized light microscopy. HLA-27 antigen was positive.

Six weeks later, the Widal agglutination test was positive at 1/40. Therapy with indomethacin was started and the arthritis improved. Ten months later, the joint had returned to normal. The Widal agglutination test was negative.

Case 3, the 62-yr-old mother of the family, presented with a profuse diarrhoea lasting 2 days, but she had no joint symptoms. Physical examination and laboratory tests were normal. HLA-B27 antigen was negative. Serological evidence of recent Salmonella infection was equally detected by the Widal technique which was positive at 1/160.

Cases of familial Salmonella-triggered ReA have been exceptionally reported in spite of its genetic predisposition linked to the HLA-B27 antigen. Jones et al. [1] described two HLA-B27-positive brothers who developed ReA after Salmonella infection in a similar report. Familial aggregation in ankylosing spondylitis (AS) is higher than in Reiter’s syndrome; relatives of a patient with AS are more likely to develop AS than Reiter’s syndrome [2], probably because the environmental factors contributing to AS are more ubiquitous, while those triggering Reiter’s syndrome are more restricted or less frequently encountered [3]. The pattern of joint involvement in a previous report of familial Salmonella-triggered ReA [1] and the cases reported here with peripheral arthritis alone without AS or sacroiliitis showed the apparent exclusivity of the disease pattern within these families. These entities often ‘breed true’ within families [3].

The patients suffered an undifferentiated arthropathy and developed a Salmonella-triggered ReA several years after the onset of their primary disease. The initial clinical picture of these two patients most likely represents a previously undiagnosed spondyloarthropathy, perhaps a Salmonella-triggered ReA. An episode of diarrhoea was not remembered by both patients in the initial illness. Nevertheless, the gut infection can be asymptomatic in ~10–25% of patients with enterarthritis [4]. In some way, this could be due to the silent carriage of relevant organisms [5]. Perhaps, ReA may be triggered by Salmonella reinfection several years after the onset of the initial clinical picture. In ReA after S. typhimurium infection, an HLA class I-related impairment in interleukin-2 production and in lymphocyte response was seen [6]. This impairment might lead to ineffective elimination of bacteria and could play a crucial part in Salmonella reinfection or in...
the development of ReA several years after the onset of the initial clinical picture.

Salmonellae continue to be one of the main causes of foodborne illness worldwide; in many countries, salmonellosis is the most frequently reported foodborne disease. Intestinal infections with Salmonella are becoming increasingly common in several countries. Likewise, an appreciable increase in the number of cases of ReA after Salmonella infection has recently been reported [7]. Some patients may be infected by Salmonella species on several occasions throughout their lives. These cases, on the other hand, support the notion that these individuals, despite their immunogenetic susceptibility, generally remain symptom free unless they become infected with an arthritogenic microorganism.

Enteric organisms, including Salmonella species, may aggravate another spondyloarthropathy [8]. Post-Salmonella reactive phenomena have been reported in two patients with AS [8]. Nevertheless, physical examination and the pelvic radiographs in both patients did not reveal any evidence of AS.

Lipopolysaccharide plays a crucial part in the pathogenesis of ReA [9]. Interestingly, all bacterial species associated with the development of ReA possess lipopolysaccharide which, moreover, shows cross-reactivity among species [10].

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**Dengue Arthritis**

SIR—The recent and ongoing epidemic of dengue and dengue haemorrhagic fever in Latin America has gone largely unnoticed outside The Americas. According to the World Health Organization, there have been >140 000 cases of dengue and 3600 cases of dengue haemorrhagic fever reported from at least 12 Latin American and Caribbean countries since the beginning of January 1995. These figures are probably approximate and actual figures may be higher. There is also variation within and between countries. There have been at least 38 deaths from the disease during this period. With increasing world travel and migration, rheumatologists worldwide should at least be aware of dengue.

In addition to Latin America, the disease is known to occur in South-East Asia and Africa. Dengue was found to be an important cause of acute febrile illness among US troops deployed to Somalia during Operation Restore Hope [1]. The word dengue means 'bone breaker' and the disease is caused by an arbovirus of the Group B Togavirus (flavivirus) group. There are at least six antigenic variants of the dengue virus and the vector is *Aedes aegypti*. The incubation period is <1 week.

Rheumatic manifestations are a major feature of dengue [2], although often overshadowed by other clinical features such as biphasic fever, skin rash, conjunctival suppression, pharyngitis, headache, vomiting, photophobia and orbital pain. Lymphadenopathy, leucopenia and, less commonly, hepatosplenomegaly, can occur and are also important clinical features. There may be an accompanying haemorrhagic fever presumed secondary to disseminated intravascular coagulation and complement activation, leading to vascular damage. Acute circulatory failure may follow.

Dengue involves muscles, tendons, joints and bones. A peripheral polyarthralgia is often present, but may be overshadowed by intense backache and pain in the long bones. Severe myalgia is common and the creatinine phosphokinase levels are often raised. Apart from joint and bone tenderness, there is little to find on examining the joints. Synovitis is not found. The diagnosis may be suggested by an acute viral type illness in a person from a dengue endemic area, but ultimately requires serological confirmation and, where possible, viral culture.

Blood transfusions and corticosteroids are needed where severe haemorrhagic failure occurs, otherwise treatment is symptomatic. The bone, muscle and joint pains in patients with dengue may be severe enough to warrant the use of opiates.

Normally, the immunity that follows arboviral infections protects and prevents further epidemics, but in the case of dengue, it may also predispose to a more severe disease if the person is infected with a different, but cross-reacting type. Public health measures, such as the use of bed nets and vector control, have been advocated [1] as there is currently no commercially available vaccine.