Reactive arthritis and the investigation of novel organisms

The clinical study of Sert et al.[1] provides limited strength of evidence[2,3] to support a diagnostic decision to discount toxoplasmosis as a cause of reactive arthritis in seropositive patients in their clinical setting. This unlikely diagnosis should not be pursued without strong suspicion beyond serology since an etiological relationship has not been demonstrated.

The negative finding of this paper is welcome. Having committed time to the investigation of a topic, authors may be inclined to invest too much significance in a vaguely positive finding and so to introduce bias to the corpus on the subject. This tendency may serve up red herrings that waste the time of other investigators, but may also deliver benefits through providing ideas that lead to the generation of new hypotheses. Reactive arthritis commonly arises after Chlamydia trachomatis or Gram-negative gastrointestinal infection and is often linked to HLA-B27. Systematic examination with particular attention to sexual and food histories along with laboratory testing and knowledge of local epidemiology are important for diagnosis. In certain cases antibiotics may be required. Otherwise treatment is symptomatic using anti-inflammatories, analgesics and immunosuppressants.

Toxoplasma gondii is a common protozoon parasite that infects mammals and birds worldwide. Serological testing can exclude acute toxoplasmosis in the immunocompetent and did so in these patients who also lacked historical and serological evidence of other infections. Failure to discount Toxoplasma as a cause could lead to more likely infections, such as Chlamydia, not being treated. Recent and current infections other than toxoplasmosis should be investigated and treated as necessary.

Chronic asymptomatic toxoplasmosis is estimated to exist in up to 65% of the world’s population and it would be surprising if a general relationship with reactive arthritis had not been identified sooner. Published evidence that toxoplasma reactive arthritis may exist is minimal, but suspicions of causation may continue to arise where established microbial agents are absent. T. gondii is one of a number of microorganisms that has been associated with adult-onset Still’s disease,[4] a rare adult form of juvenile rheumatoid arthritis with a double quotidain fever and variable clinical course that may also have serious musculoskeletal sequelae. False-positive Toxoplasma titres due to rheumatoid factor have been reported. PubMed lists 26 papers when searched using the terms “toxoplasma arthritis.” One publication mentions reactive arthritis[5] and it may perhaps be a more likely cause in certain age groups or HLA-B27 subtypes which vary with ethnicity and geography. In the context of pediatric cases, Kowalewski et al commented: “The most uncommon cases, hardly ever described in the literature concern arthritis caused by protozoon Toxoplasma gondii. The
immune mechanism is still unknown (we believe in the occurrence of immune complexes). On the other hand, the persistence of high titre despite the treatment (3 out of 4 patients) is the evidence for a long-lasting presence of T. gondii antigens in organism.[6]

Toxoplasma’s involvement with reactive arthritis is worthy of continued consideration but is not a priority for the large international studies that would be required to detect a rare cause of illness. Any future studies need to be multicenter, much larger to achieve the necessary power, should choose appropriate Toxoplasma epitopes for recognition,[8] investigate the HLA-B27 subtypes and nonHLA genes involved and consider the advice on strategic test selection in the Health Protection Agency QSOP 59 Investigation of Toxoplasma infection in pregnancy (URL: http://www.hpa-standardmethods. org.uk).

Clinicians should not pursue toxoplasma reactive arthritis in seropositive adults since this condition has not been clearly identified in the literature and its diagnosis would not alter the symptomatic treatment in immunocompetent cases. As understanding develops, investigators must maintain vigilance for new modes of pathogen activity and immune dysfunction, but while doing so maintain conservative diagnostic investigation that makes provident use of clinical and laboratory resources.

References