Conclusion

Concluding remarks

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A number of speakers have suggested that Reiters syndrome (RS) is a misnomer. Alternatives such as 'sexually acquired reactive arthritis' or the much maligned 'B27-associated disease' have been put forward. But they have obvious drawbacks—the first in assuming that all urethritis is sexually acquired (something that, to my mind, is questionable dogma) and the second because over 20% of these cases are B27-negative. The problem was stated by Dr. J. T. Scott, who concluded: 'we all know what we're talking about but can't define it'.

The important observations on incomplete forms of RS have opened up—as they do in almost all rheumatological syndromes—the shady areas of overlap, where dogma is especially out of place. Certainly, from the historic viewpoint, RS is wrongly named. Although the syndrome probably dates from prechristian times the best early description is by Benjamin Brodie. In his first edition of Diseases of the Joints, published in 1834, Brodie long precedes Reiter's report with a description that is still striking in its clarity.

One recurrent theme at this meeting has been that reactive arthritis may be troublesome and chronic, with a 40% late disability rate in Dr. G. W. Csonka's 410 patients, for example, and a similar rate in Dr. A. Calin's series. While the mortality is low the morbidity may be higher than previous reports have stated, one troublesome feature being heel pain. The problem of patient selection and of long-term follow-up in this often transient disease of transients makes for difficulties in interpreting these figures.

This meeting has also shown that the reported incidence of the clinical features of RS depends on the index of suspicion with which the various manifestations such as balanitis, eye changes, or sacroiliitis are pursued. The radiological pitfalls of interpreting sacroiliitis in children and teenagers have been emphasised by Professor W. Martel. For this reason we may hope that sacroiliac scanning, which has the advantages of sensitivity and computer-assisted rather than visual analysis, will be an advance. As we have heard from Professor A. S. Russell, this is certainly the case. Though their interpretation is in its infancy, the high incidence of B27-positive and B27-negative patients with a clinical diagnosis of degenerative low back pain reported in our studies is worrying. A workshop such as this might be devoted to this technique in the future. It must be stated that, on present evidence, an increased uptake in a scan of the sacroiliac region does not necessarily indicate sacroiliitis. This is reviewed in the general discussion after Professor Russell's paper.

Professor T. Bitter has worked on a very similar line and has resuscitated Short and Bauer's 'atyypical rheumatoid arthritis' under the more descriptive label of 'persistent yet reversible asymmetric pauciarticular arthritis (PRAP), a discreet and apparently highly homogeneous cluster of young patients with seronegative arthritis in whom the asymmetry—and a B27 association in 40%—heralds the benign course and good prognosis. This group may overlap considerably some of the patients with pauciarticular arthritis described by Professor C. Fink and Dr. P. Stastny.

The pieces of evidence as they have been marshalled at this meeting are somewhat diverse in terms of aetiology. A significant number of patients in whom the disease is associated with non-specific urethritis are associated with positive cultures for chlamydia or mycoplasma, though this area has clearly been a scientific mine field. As we heard from Professor J. Storz, the clear demonstration of direct, widespread infection in the animal disease argues, at least in that example, against the concept of reactive arthritis or possibly against any immunological mechanism in this disease.

Perhaps more easily recognised and more open to
study is gut-associated disease. A number of lessons have been learnt from the saga of the good ship Little Rock. As history recalls, it steamed out of Trieste harbour in 1962, whereupon 600 or so men on board went down with shigella dysentery. Ten subsequently developed acute reactive arthritis. The 13-year follow-up by Drs Calin and Fries underlined the chronicity and severity of the disease in a small minority of B27-positive patients. While this study suggested that B27 might endow a more severe disease on the patients, a finding we have also heard made in respect of yersinia, other data presented by a number of speakers yesterday and today indicate that this may not be so. It was of considerable interest in relation to the shigella-associated arthritis to hear of the identification of an association of RS with Shigella flexneri 2A, raising the distinct possibility that arthritogenic strains exist.

Another well-studied antigen is Yersinia, which again underscores the strong association between B27 and a known antigen. Some 90% of patients with reactive arthritis have B27.

I have selected these two samples because they have the obvious advantage for further study of being defined antigens. In most papers reporting immune complexes in various diseases the antigen has not been demonstrated. In only a few, such as some cases of polyarteritis nodosa, bacterial endocarditis, and malaria, where the antigens are known, has direct evidence of a pathogenic mechanism been shown. In reactive arthritis we have a partially genetically determined disease in which at least some of the antigens are known.

An interesting model for gut-associated reactive arthritis has come from the operation of jejunal colic bypass for obesity, which is sometimes followed by a severe arthritis. In this situation antigens have been demonstrated in circulating cryoprecipitins, which may well play a role. Professor C. M. Pearson has pointed out that other antigens that might be searched for in blood or tissue might include bacterial cell wall antigens. An even more interesting accident of nature was reported by Rose and his colleagues, who observed that in two B27-positive patients who underwent this operation the pattern of disease was a severe spondylitis. Here, supporting some of the comments made by Professor D. K. Ford, was evidence that antibiotic treatment in the acute phase modified the disease.

Finally, we have heard provocative views on the role of genetic make-up. I think Dr. J. C. Woodrow coined the phrase ‘seeing the genes through the fog’. The association with the major histocompatibility gene B27 (on chromosome 6) has, as Dr. D. A. Brewerton pointed out, raised far more questions than answers in this particular field. A number of speakers cautioned against ascribing all so-called complications of RS to the gene.

I would like to end by mentioning a case which I think emphasises some of the difficulties in analysing a disease such as this.

A 31-year-old man developed acute and severe polyarthritis and spondylitis. His spine was so painful and rigid that he had to be lifted out of bed, though two weeks before he had been an active squash player. He also had acute pericarditis with myocarditis, both well recognised associations with RS. In view of the pericarditis, Coxsackie antibodies were measured and B4 titres were high and rising. Over the next two months his heart and joint lesions settled. He was B27-positive, his sacroiliac joints were abnormal, and, in retrospect, he had previously complained for several years of occasional low back pain after games of squash.

We have since seen a second B27-positive patient with acute reactive arthritis, pericarditis, and high titres of Coxsackie B antibodies. This perhaps supports the view that pericarditis, well recognised as an occasional complication of reactive arthritis, may at least in some cases be associated with a completely different aetiology. Conversely, it might just conceivably be argued that in a B27-positive individual viral agents as well as the bacterial and other infections which we have been hearing about may trigger the disease. Indeed, evidence that responses to virus infection may be partially genetically determined is rapidly accumulating.

I wish the ARA subcommittee success in its difficult task of drawing up classification criteria. In the difficult situation where partial forms or overlaps occur we must, as has been repeatedly emphasised in this symposium, keep an open mind. This has been one of the most enjoyable and productive workshops I have attended. It has been a privilege to have been able to hear from colleagues whose experience is not only of hundreds of patients with RS but also goes back over a medical lifetime. On behalf of all of us I thank Professor Tom Bitter and his wife for arranging a memorable meeting.