diabetes mellitus and hypertension, inactive lifestyle at a nursing home with chronic osteoarthritis and minimal persistent left pleural disease of over one year's duration and of uncertain cause. The patient had also been treated for herpes zoster infection about one year before the development of nocardial arthritis. Possibly, therefore, he might have had a subnormal immune defence mechanism against opportunistic infections. The patient's chest radiograph showed marked improvement in pleural disease after treatment of the arthritis with trimethoprim-sulphamethoxazole/amoxycillin-clavulanate. This suggests that the portal of entry was the respiratory tract, and the patient might have had chronic pleural disease with culture negative nocardial infection.

Successful treatment of nocardial septic arthritis seem to require prolonged antibiotic treatment for three to six months or longer.[5] From among all the antibiotics tested in vivo and in vitro, the use of trimethoprim-sulphamethoxazole in the treatment of human nocardiosis has been well established.[5 6] There is some evidence to suggest that amoxycillin-clavulanate may be useful in the treatment of nocardial infections.[7]

In summary, septic arthritis due to *Nocardia caviae* occurred in an elderly patient with multiple underlying diseases and was successfully treated with trimethoprim-sulphamethoxazole/amoxycillin-clavulanate combination antibiotic regimen. To our knowledge, *N caviae* arthritis has not been previously reported. Nocardial infection must be considered when undiagnosed, longstanding pleuropulmonary disease persists in an immunocompromised patient who later develops septic arthritis. Finally, although it requires the long term use of antibiotics, septic arthritis due to *N caviae* can be treated successfully.

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Sex ratios in HLA related autoimmune disease

Sir: With respect to the interesting article by James[1] we would like to describe data which support the hypothesis that sex ratios are disturbed in the families of probands with HLA related autoimmune disease.

Primary Sjögren's syndrome is a heterogeneous disease with a strong female preponderance.[2] A large family study of the disease has been completed in north east England and confirmed the association between HLA-DR3 and primary Sjögren's syndrome.[3] The families were ascertained from 40 white probands who all satisfied Fox's criteria for definite primary Sjögren's syndrome.[4] Two hundred and seven relatives from a potential pool of 224 were included. The table shows the female:male sex ratio among the family members.

Female:male sex ratio among family members of patients with primary Sjögren's syndrome

	Women	*Men*	χ^2 *or Fisher's test*	*p Value*
Index cases (n)	38	2	20·3	<0·001
Total relatives* (n)	150	74	13·3	<0·001
Relatives in study† (n)	142	65	95·4	<0·001
Siblings in study (n)	49	27	3·25	<0·1
Offspring of probands (n)	19	22	0·11	<0·1

*Refers to the potential pool of relatives.
†Refers to the relatives actually seen.

There was a trend for a female excess in siblings, though this did not reach statistical significance. A significant female preponderance, however, was seen in index cases and for the relatives as a whole. The availability of all the family pedigrees shows this to be a true phenomenon and not merely attributable to those consenting to the study.

We have reported definite/probable primary Sjögren's syndrome occurring exclusively in the female relatives with a strong association with HLA-DR3 (5/8 (63%)).[3] In addition, a cohort of young relatives (under 45 years) who expressed some features consistent with primary Sjögren's syndrome were also identified. Twenty eight of these 45 subjects were female (female:male ratio 1·65:1, $\chi^2=1·365$, NS). For these women there was a strong association with HLA-DR3 (18/28 (64%)) compared with the association for the men (5/17 (29%), $\chi^2=3·85$, $p<0·05$). We suggested that these women may be at risk of developing definite primary Sjögren's syndrome in the future, and a prospective study will help to support or refute this hypothesis.

This suggests that the inheritance of HLA-DR3 may influence the sex ratio of the offspring as well as the susceptibility to primary Sjögren's syndrome.

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Nanocolloid scintigraphy for rheumatic diseases of the hands

Sir: The importance of early diagnosis of inflammatory rheumatic diseases has been emphasised recently. Nevertheless, the medical history and the physical examination of patients are difficult to assess, and laboratory and radiological modifications are often delayed. For several years scintigraphy has been proposed as a helpful device for diagnosis of initial or atypical bone and joint diseases. Most studies were performed with technetium-99m (^{99m}Tc) bisphosphonates, but other isotopes are now available.[1] Among these, ^{99m}Tc labelled nanocolloid, which spreads to the extravascular space at sites of inflammation with increased vascular permeability[2] is under study. As its clinical usefulness is still a matter for debate we compared joint pain, joint swelling, radiographs, and a palmar view scintigraphy (45 minutes after intravenous injection of 925 MBq of ^{99m}Tc nanocolloid; 200 000 counts or 15 minutes) of the hands of 27 subjects (seven controls, five patients with nodular osteoarthrosis, and 15 with classical or definite rheumatoid arthritis (RA)) who were examined in our department. The wrist, the metacarpal joints, the interphalangeal joint of the thumb, and the second to fifth proximal interphalangeal joints of each hand were included in the study, giving a total of 594 joints.

Joint pain and swelling, radiographic abnormalities, and nanocolloid scintigraphy were estimated on a four point scale: 0 representing a normal and 3 a very painful or swollen joint, a severe radiological change, or a marked increase of the isotopic uptake. The clinical assessment was made just after radiography and scintigraphy by an observer who was unaware of the results of the previous investigations. Six patients with RA also underwent ^{99m}Tc diphosphonopropanedicarboxylic acid scintigraphy on adjoining days.

Joint isotopic uptake was usually easily discernible, but interpretation was difficult in several subjects owing to diffuse longitudinal uptake (fig 1) attributed to tenosynovial accumulation in three of seven controls, three of five patients with nodular osteoarthrosis (without tenosynovitis), and four of 15 patients

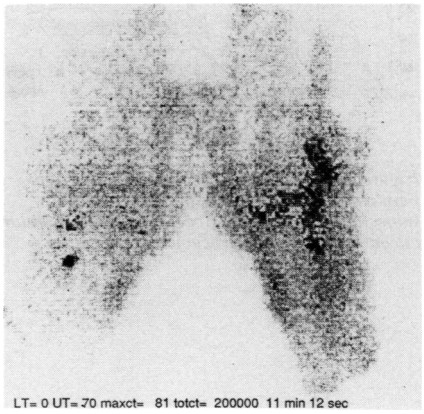

Figure 1 Technetium-99m labelled nanocolloid scintigram. Accumulation in the joints and along the tenosynovial sheath of the fourth left finger.

with RA (three with corresponding clinical tenosynovitis). On the other hand, one of seven controls and eight of 15 patients with RA with a clinical tenosynovitis did not present this special isotopic picture.

In the controls a false positive isotopic uptake was noted in 35% and a false negative in 3% of the joints when compared with joint pain.

There was only low agreement between joint pain and the radiological score in patients with nodular osteoarthrosis (42%). For patients with RA the pain and swelling scores were in total agreement in 66% of the joints. These features have been well reported.

When the nanocolloid score was plotted against the pain score the total agreement was 49% for the joints of all subjects (fig 2), 50% for those with nodular osteoarthrosis, and 41·5% for the patients with RA. When the nanocolloid score was plotted against the radiographic score the results were 39% for the joints of all subjects, 29% for those with nodular osteoarthrosis, and 31% for the patients with RA. The correlations between the nanocolloid score and the clinical and radiographic scores were always less than 0·2, which is not significant.

In the patients with RA 72% of the painful joints showed an increased isotopic uptake, but only 36 of the 56 joints (64%) which were simultaneously painful and swollen showed an enhanced nanocolloid uptake. Moreover, of the 201 neither painful nor swollen joints and of the 77 which were not painful, swollen or radiologically abnormal 99 (49%) and 32 (42%) respectively were positive on the scintigram. When the nanocolloid and diphosphonopropanedicarboxylic acid scintigrams were compared agreement was 75% (85 joints positive on both scans, 15 negative on both scans); the discordance was not specially in favour of one or other of the techniques (16 joints positive and 16 joints negative with nanocolloid scintigraphy were negative and positive respectively with diphosphonopropanedicarboxylic acid scintigraphy).

The conclusions of this pilot study seem to be first that labelled nanocolloid can effectively accumulate in inflammatory joints and in tenosynovitis. Nevertheless, it is also retained in many normal joints (35%) from controls and in joints from patients with RA (42%) without pain, swelling, or radiographic deterioration. This might be secondary to an isotopic leakage before clinical expression, which was not investigated by a longitudinal study, but the percentage of these positive scintigrams seems too high to be explained by this hypothesis alone. Why there was no nanocolloid uptake in 28% of patients with RA with painful and swollen joints needs further investigation. Finally, in the few patients with RA for whom both scintigrams were obtained nanocolloid was no better than diphosphonopropane-dicarboxylic acid. So, despite being an inexpensive, simple, and straightforward method nanocolloid scintigraphy does not supply the rheumatologist with a detector of early inflammation. The results of our study are in agreement with those of Rüther *et al.*[3]

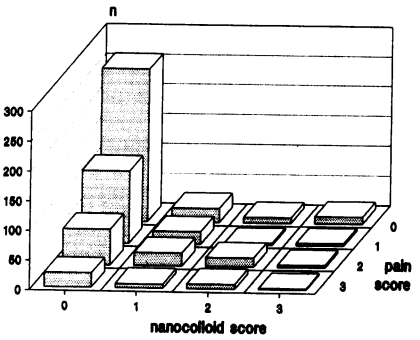

Figure 2 Comparison of the nanocolloid and pain scores of 594 joints of the hands of 27 subjects (seven controls, five patients with nodular osteoarthrosis, 15 with rheumatoid arthritis).

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Spondyloarthropathies and IgA deficiency

Sir: Herrero-Beaumont *et al* recently reported a female patient with IgA deficiency who developed ankylosing spondylitis characterised by a widespread erosive peripheral arthritis and recurrent anaemia of chronic disease.[1] They cited three additional reported cases, all with severe disease, and suggested that IgA deficiency is a marker of poor prognosis in the spondyloarthropathies, possibly warranting replacement therapy. We describe four patients with IgA deficiency and a spondyloarthropathy who had variable disease severity.

A 24 year old man presented in 1980 with a three month history of dysuria, early morning stiffness, back pain, and swelling of his knee. Examination showed balanitis and an active arthritis of the left knee. *Chlamydia trachomatis* was cultured from his urethra and he received tetracycline in addition to indomethacin. The IgA concentration was 52 IU/ml. Symptoms were well controlled with indomethacin and exercise. There was radiological evidence of sacroiliitis three years after onset and when last seen in the clinic in 1988 he remained well and active with no deformity.

In 1987 a 26 year old man developed arthritis of the left knee complicated by a ruptured Baker's cyst. This progressed over 18 months to affect his right wrist, both elbows, and lumbar spine. IgA was undetectable in both serum and synovial fluid. His HLA haplotype was A2, B5, B12 (44), DR4, DR5. Diclofenac, sulphasalazine, and repeated intra-articular steroids failed to control his arthritis satisfactorily.

The third patient, a 23 year old man, presented in 1989 with arthritis in both knees, two sausage digits, and conjunctivitis following an episode of dysuria. He was HLA-B27 positive with an IgA concentration of 47 IU/ml. Diclofenac and, later, sulphasalazine for six months failed to control persistent arthritis in his right knee.

Recently, a 24 year old man with an IgA concentration of 38 IU/ml and negative HLA-B27 was seen. He presented with a nine year history of inflammatory back pain and early morning stiffness, which responded to non-steroidal drug treatment.

In contrast with the patient reported by Herrero-Beaumont *et al*,[1] our first and last patients had mild disease, whereas the other two patients had intractable peripheral arthritis. IgA concentrations are often raised in ankylosing spondylitis,[2] and clinical improvement has been associated with falling levels.[3] These patients, however, show that IgA is not necessary in the pathogenesis of the spondyloarthropathies. IgA deficiency is common, and a true association between IgA deficiency and spondyloarthropathies has not been established. If there is an association this may be, directly, due to lack of IgA on mucosal surfaces[4 5] or, indirectly, by association with disease susceptibility genes.[6] Our patients' data do not support the suggestion that IgA deficiency is a marker of disease severity.

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