PostScript

MATTERS ARISING

Scoliosis and Trendelenburg sign in a painting by P P Rubens

In an article on Rubens' painting "The Three Graces" Dequeker suggests that hypermobility is a medical explanation of the seeming scoliosis and Trendelenburg sign in the middle figure.[1] But the posture of this middle figure should probably be interpreted as an artistic phenomenon without medical reference.

Sculptors in classical Greek and Roman periods often used the contrapposto posture. In this, by putting most weight on one leg, the other leg can be shown in a relaxed and semiflexed position. This undulating between tension and relaxation will animate the figure. A person with normal muscular function and a normal back can perfectly well pose in this way with relaxed hip abductors on the weightbearing side, a descending hip on the opposite side, and a compensating scoliotic posture. This posture is facilitated by support from the arm as in Rubens' painting. If the person tries to take a forward step, relaxation of the muscles of the weightbearing hip can no longer be maintained, and the positive Trendelenburg sign will disappear.

In the Renaissance period the use of this contrapposto posture was revived. During his stay in Rome Rubens eagerly studied the then recently excavated Laokoön sculpture with its three distorted figures.[2] He often used such distorted postures in his paintings to give the impression of vigorous muscular characters capable of performing great tasks. The best example is probably "The Debarkation at Marseilles" in the Maria de Medici cycle from 1622 to 1625 for the Luxembourg Palace in Paris.[3] Here, three young women, nereides, with curved muscular backs at the bottom of the picture nearly seem to carry the ship of Maria de Medici.

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Author's response

Dr Hansen's remarks about our recent article in the *Annals*[1] are pertinent and have to be taken as a alternative explanation for the observed functional scoliosis and positive Trendelenburg sign. I am grateful for this artistic-historical information. However, this does not exclude the possible diagnosis of benign familial hypermobility syndrome. In several other paintings by Rubens, where the three sitters (sisters) of the graces are represented, clinical signs of hypermobility can be seen. In the painting "The Judgement of Paris" (London National Gallery) a positive Trendelenburg sign and scoliosis can be seen in the two blond sisters who are now in a walking position without support. In one of them the right wrist is in 90° hyperflexion. In the painting "Sine Cerere et Baccho friget Venus" (Brussels Koninklijke Musea voor Schone Kunsten), subluxation of the left wrist is seen in the dark blond sister and hyperextension of the distal interphalangeal (DIP) joint of the fourth finger in another sister with brown hair. Hyperextension of a DIP and metacarpophalangeal finger joint and hyperflexion of a wrist joint is also seen in the brown haired sister of the painting "The Madonna and Saints" (Antwerp, Sint-Jacobskerk).

I, as well as Sven Hansen, am fully aware that errors of diagnosis are commonly made either by seeing disease where none exists or by interpreting at face value a pathological appearance that is only the expression of an artistic convention. The observations made in P P Rubens' painting, representing the sitters for "the graces" painting who are Rubens' second wife Helen Froment and her younger sisters, are very suggestive of the diagnosis of benign familial hypermobility syndrome and not a purely artistic phenomenon.

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Comparison of WOMAC with SF-36 for OA of the knee or hip

Angst *et al* compared WOMAC with the SF-36 as tools to assess the outcome of a three to four week inpatient rehabilitation programme for people with osteoarthritis of the knee or hip.[1] They concluded that both instruments capture improvement in pain levels, but functional improvement can be better detected by WOMAC. We have reservations about the use of SF-36 in this context.

We too provide residential musculoskeletal rehabilitation of usually three weeks' duration and have been searching for a suitable instrument to assess quality of life at the time of discharge from our programme. We have rejected the SF-36 for the following reasons.

A large majority of the questions in the SF-36 relate to the subject's experience over the past four weeks. The condition of most of our patients improves considerably over the three weeks of treatment. It is therefore not appropriate to ask how they have been over the previous four weeks. We note that the period of treatment in the report by Angst *et al* varies from three to four weeks.

It is not only the length of time which makes the use of the SF-36 inappropriate in this setting, many of the questions assume the subject is living an everyday life. For example, inquiry is made about "both work outside the home and housework", "other activities at home", and "normal social activities with family, friends, neighbours, or groups".

Obviously if a person is devoting time and energy to an inpatient musculoskeletal rehabilitation programme they are in no position to be truly engaged in any of these work or social activities.

Thus while the outcomes of our similar residential rehabilitation programme for people with osteoarthritis are in accordance with those of Angst *et al*, we do not feel it is appropriate to use the SF-36 to measure improvement at discharge. It is of course quite reasonable to use it before admission and at three or six months' follow up.

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Reference

1 **Angst F**, Aeschlimann A, Steiner W, Stucki G. Responsiveness of the WOMAC osteoarthritis index as compared with the SF-36 in patients with osteoarthritis of the legs undergoing a comprehensive rehabilitation intervention. Ann Rheum Dis 2001;60:834–40.

Authors' response

In their letter commenting on our article,[1] Jones and Leighton deal with two major problems which might arise in the application of the SF-36 to inpatients. We would like to stimulate discussion about this issue by our following response.

The first problem concerns the fact that many of the SF-36 items ask about subjective health status over the past four weeks at the time of administration of the questionnaire. Jones and Leighton suggest, therefore, that the results at the end of an inpatient rehabilitation (three or four weeks) reflect some kind of an average of the health status during that rehabilitation period in which most of the patients have improved considerably. We agree that this assessment is unlikely to show the maximum of improvement that may be expected at the day of discharge from the clinic or shortly thereafter. However, one can assume that the result overestimates the health status for the time periods close to the day of administration of the questionnaire (for example, at the day of discharge) owing to the fact that the response is based on the patient's memory. The same problem, but in the opposite direction, would arise if we administered the SF-36 two or four weeks after the day of discharge. Thus we possibly miss the maximal effect, which may last only a few days, but we do obtain an assessment of a certain time period, which is likely to be more valid and more clinically important than that of a single day. To take account of this point, we also reported results

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of the three month follow up (that is, two months after discharge) in our study[1] in order to reflect the course of the effects and whether the different responsiveness of the SF-36 compared with the WOMAC remained consistent. In addition, we will publish further results of three monthly assessments up to the two year follow up of our patients during the next year.

The second issue deals with the fact that some items ask about activities of daily living and social participation which are not demanded or hardly possible to perform during a stay in the clinic. These are mainly the items contained in questions four (4a–4d) and five (5a–5c) comprising the role physical and role emotional scales. For this reason, we reported these two scales as part of the SF-36 for the sake of completeness, but we did not include them in the analysis of the comparison of WOMAC and the SF-36. Nevertheless, item 8, which is the bodily pain scale, is also affected by this problem. Müller *et al* dealt with this issue recently.[2] The authors created a modified SF-36m, which was adapted in items 4, 5, and 8 to the situation of a clinic stay. They concluded that bodily pain and role emotional did not show significantly different effects from those obtained by the original SF-36, but that the role physical scale was slightly more responsive in the SF-36m.

We used the SF-36 for three reasons. Firstly, the SF-36 assesses health status comprehensively—that is, not only pain and disease-specific scales as physical function, etc but also psychometric dimensions and dimensions of social participation. As a result, it gives an overall assessment of the patient's health status which is compatible with the WHO's new ICIDH or the future ICF concept defining health.[3 4] Secondly, the SF-36 can also be administered to "healthy" people and to patients with different diseases, which allows a comparison of the results with those for other patient groups and the general population. Thirdly, the SF-36 is one of the best tested, best known, and most widely used health measure all over the world.

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LETTERS

Is pamidronate effective for acute rheumatic pain?

Parenteral pamidronate is licensed in the United Kingdom for the management of Paget's disease, tumour related hypercalcaemia, and metastatic bone pain, where it can rapidly relieve symptoms.[1] It is also widely used for the prevention and treatment of osteoporosis, although this represents unlicensed use of the drug, and there is some evidence that it can be rapidly effective for pain relief in patients with osteoporotic vertebral fractures.[2 3] It has been used with some effect for the management of ankylosing spondylitis,[4] but the full extent of any analgesic properties of the drug has not been fully explored. These properties became apparent to us quite by chance in the three cases described here.

Case reports

Patient A

A 25 year old female nurse with known ankylosing spondylitis was admitted to hospital with worsening back and right buttock pain uncontrolled by regular opiate analgesia and a variety of potent non-steroidal anti-inflammatory drugs. Parenteral methylprednisolone was prescribed, followed by pamidronate 30 mg for "bone protection". In the event, pamidronate was given but not methylprednisolone, deferred owing to unexplained pyrexia. Shortly after receiving her pamidronate, her intractable pain was so greatly improved that methylprednisolone was declined and she was discharged three days later. The improvement seen has been sustained for over six months. The unexpected analgesic effect of pamidronate in this case led to its use in two subsequent cases.

Patient B

A 38 year old housewife with chronic low back pain was admitted with a short history of acute back pain and a modestly raised C reactive protein (14 mg/l). Isotope bone scan showed increased uptake in the fifth lumbar intervertebral disc. Magnetic resonance imaging identified abnormal signal from this disc suggestive of discitis. An infective cause was felt to be unlikely: antibiotics were not prescribed, but in view of her persistent symptoms, pamidronate 30 mg was given by intravenous infusion, with sufficient sustained improvement in her acute back pain to allow discharge two days later.

Patient C

A 33 year old male factory worker with a history of juvenile chronic arthritis since early childhood and spondyloarthropathy was admitted with generalised bone pain despite weekly oral methotrexate, phenylbutazone, and oral analgesia. Intercurrent diarrhoea was investigated but remained unexplained. Parenteral pamidronate 30 mg was given, leading to sustained improvement in his rheumatic pains.

Discussion

We believe these cases represent the first time that sustained analgesic efficacy has been attributed to a single dose of parenteral pamidronate in acute rheumatic pain not related to osteoporosis or neoplasia. The mechanism whereby pamidronate provides rapid onset sustained pain relief for metastatic bone disease or osteoporotic fractures is unknown. Many of the known effects of bisphosponates on bone structure and cell populations are unlikely to be rapidly analgesic.[5] However, it has been suggested that bones have complex sensory innervation, with nociception mediated by neuropeptides including substance P, prostaglandin E_2, and calcitonin gene related peptide which may be influenced by bisphosphonates.[6] There is no reason to believe that such an analgesic effect would be confined to bone affected by osteoporosis or neoplasm and might well extend to bone pain due to inflammation. In the three cases described many other factors might have led to the apparent response to parenteral pamidronate, including chance. However, the results suggest that the potential role of pamidronate in the control of acute rheumatic pain warrants further evaluation.

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Antibodies to β_2 glycoprotein I and cardiolipin in SSc

Systemic sclerosis (SSc) is a multisystem disease in which organ damage is characterised by fibrosis, microvascular occlusion, and proliferation of the vascular intima. The reported prevalence of anticardiolipin antibodies (aCL) in SSc varies from 0 to 25%,[1–7] and reports of clinical associations have been variable.[3 4 6 7] To our knowledge, only one study has examined antibodies to β_2 glycoprotein I ($a\beta_2GPI$) in SSc and shown a correlation with pulmonary hypertension and raised mean pulmonary artery pressure.[8] In our study we examined the frequency of $a\beta_2GPI$ and aCL in SSc and Raynaud's phenomenon (RP).

Twenty six patients with SSc (16 diffuse, 10 limited), 23 with RP, and 21 healthy volunteers (employees at the research facility) were included in this retrospective study. Informed consent was obtained. All 16 patients with diffuse SSc and one patient with limited SSc patients met American Rheumatism Association (ARA) preliminary criteria for scleroderma.[9] The remaining nine with limited SSc had at least three of the following: sclerodactyly, calcinosis, Raynaud's phenomenon, oesophageal dysmotility, telangiectasia, or positive anticentromere antibodies. The patients with RP had no manifestations of connective tissue disease. Clinical and laboratory assessments were recorded at the initial visit.

$a\beta_2$GPI and aCL were measured by enzyme linked immunosorbent assay (ELISA; INOVA Diagnostics, Inc, San Diego, CA and Hemagen Diagnostics, Inc Waltham, MA, respectively). Commercially obtained HEp-2 slides (Immuno Concepts, Sacramento, CA) were used for indirect immunofluorescence (IIF). Samples were tested for antibodies to topoisomerase I (Scl-70), U1 ribonucleoprotein (U1-RNP), and Sjögren's syndrome antigens A and B (SS-A/SS-B) by double immunodiffusion.

Student's *t* test (two tailed) was used for comparison of means, and Fisher's exact test (two tailed) for analysis of frequencies. Age distributions were compared with the Mann-Whitney test because healthy controls described their age in decades, not years.

Table 1 summarises the demographics and laboratory data for the study group. The patients with SSc were significantly older than both the healthy controls ($p=0.005$) and the patients with RP ($p=0.02$). All mean laboratory values were within the normal range. Figure 1 compares the values for tests among the study groups except $a\beta_2$GPI IgG, where all tests were negative. IgM $a\beta_2$GPI were found in two patients with SSc (8%), one patient with RP (4%), and none of the healthy controls ($p>0.05$). Three (12%) patients with SSc, five (22%) with RP, and one (5%) of the healthy controls had positive tests for IgG or IgM anticardiolipin ($p>0.05$). The sera positive for aCL were not the same as those positive for $a\beta_2$GPI.

The two patients with SSc positive for $a\beta_2$GPI had mean disease duration of 19 months; both had cutaneous manifestations and one had hypoxia with decreased carbon monoxide transfer factor (TLCO). The three patients with SSc and aCL had mean disease duration of 112 months. One had hypoxia (with normal TLCO and non-restrictive pulmonary function tests), one had restrictive lung disease and digital ulcers, and one had oesophageal hypomotility. None of the study participants had thrombocytopenia or a history of deep venous thrombosis. Twenty two per cent of the group with Raynaud's disease had aCL, which is higher than the 8.7% reported by Vayssairat *et al*.[10] Patients with positive tests did not differ from those who had negative clinical manifestations or laboratory values.

All of the patients with SSc and RP and 13% of the healthy controls had positive IIF tests on HEp-2 substrates. None of the patients with SSc had antibodies to topoisomerase I (Scl-70) or SS-A/SS-B. No IIF pattern correlated with $a\beta_2$GPI or aCL.

In our study we found that the frequency of antibodies to β_2GPI and aCL was low in scleroderma, 8% and 12% respectively. There were no clear clinical or laboratory correlations with a positive test.

Table 1 Demographics and laboratory results in patients with SSc, RP, and normal controls

	Scleroderma (n=26)	Raynaud's phenomenon (n=23)	Normal controls (n=21)
Women	21	22	13
Men	5	1	8
Age groups		*(p=0.02)	*(p=0.005)
20–30	2	4	6
31–40	8	12	7
41–50	6	4	5
50+	10	3	3
Disease duration (months), mean (range)	69 (6–244)	89.7 (1–364)	N/A
Anticentromere antibodies	14 (54%)	5 (22%)	0 (0%)
Nucleolar antibodies	5 (19%)	4 (17%)	1 (5%)
Haemoglobin (g/l)	129 (SD 32)	134 (SD11)	N/A
Platelets (cells×10^9/l)	339 (SD 126)	293 (SD 61)	N/A
CK (μmol/l)	128 (SD 144)	79 (SD 38)	N/A
BUN (mg/l)	140 (SD 40)	130 (SD 30)	N/A
Creatinine (mg/l)	9.1 (SD 1.3)	9.2 (SD 1.0)	N/A

BUN, blood urea nitrogen; CK, creatine kinase.
*Comparison of age distribution versus SSc.

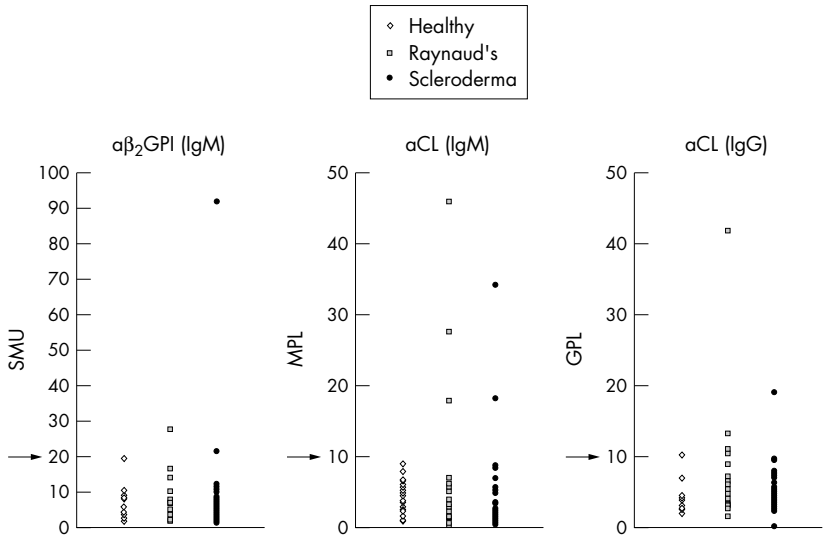

Figure 1 Comparison of $a\beta_2$GPI and aCL antibody levels in patients with SSc, RP, and normal controls. The numbers on the ordinate represent optical density values converted to SMU (standard IgM β_2GPI units), MPL (1 MPL unit = the binding of 1 μg/mL IgM aCL), or GPL (1 GPL unit=the binding of 1 μg/ml IgG aCL). The arrows indicate the cut off values for each dataset.

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Recurrence of reactive arthritis after a booster dose of tetanus toxoid

We report the case of a 24 year old man who developed a recurrence of reactive arthritis after receiving a booster of tetanus toxoid.

Case report

A 24 year old man presented with acute swelling of the right ankle. Two weeks before presentation, he had been given a booster tetanus toxoid vaccination. Within a few days of the injection, he felt pain and noticed swelling of the right ankle. The swelling and pain worsened, such that at presentation he was walking with a pronounced antalgic gait. There was no preceding history of trauma, infection, or any past history of psoriasis, iritis, inflammatory bowel disease, or inflammatory back pain. There was no family history of ankylosing spondylitis.

Three years previously he had presented to another rheumatologist with acute synovitis of the left ankle, mid-foot, metatarsophalangeal joint of the left big toe, and tenosynovitis of the long flexor of the right middle finger. This was associated with conjunctivitis and chlamydial urethritis, with raised levels of chlamydia-specific IgG. His plasma viscosity was raised at 1.69 mPa.s; haemoglobin was 139 g/l, rheumatoid factor negative, and HLA-B27 positive. Plain radiographs of the left ankle, foot, and right hand showed no abnormalities. He was treated with indometacin and an intra-articular injection of triamcinolone to the left ankle as well as minocycline for himself and his partner. The conjunctivitis settled within a few days, the urethritis within a fortnight, but the joints took six months before becoming quiescent, by which time he was able to stop the indometacin. Chlamydia IgG was negative by this time.

Physical examination at the second presentation showed swelling of the right ankle joint, with tenderness and synovial thickening. The subtaloid, mid-tarsal, and metatarsophalangeal joints were fully mobile with no swelling. The erythrocyte sedimentation rate was raised at 36 mm/1st h.

Initially, triamcinolone was injected into the right ankle, indometacin 50 mg three times a day was prescribed, and he was given elbow crutches to stop him weight bearing on the right leg. Two weeks later there was partial improvement. Prednisolone (20 mg a day decreasing by 5 mg weekly) and enteric coated sulfasalazine (500 mg twice daily) were added. One month later the ankle synovitis and pain had settled.

Discussion

Several strands of evidence link different vaccines to the development of a spectrum of arthritides. Often, a close temporal relation between vaccination and the onset of arthritis exists, allowing an inference about the influence of a particular vaccine. On this basis, tetanus toxoid injection has been associated with the development of rheumatoid arthritis, comprising a symmetrical inflammatory polyarthritis and positive rheumatoid factor.[1] Recombinant hepatitis B vaccination can also produce a similar picture.[2] Symmetrical small joint polyarthritis but with negative rheumatoid factor has been described in association with intravesical Bacillus Calmette-Guérin (BCG) vaccine used as immunotherapy for bladder carcinoma.[3]

The spectrum of arthritis associated with vaccination is illustrated by the induction of large joint monarthritis by combined diphtheria, poliomyelitis, and tetanus toxoid vaccine.[4] In one of these cases, synovectomy was curative until a booster vaccination five years later caused recurrence and, indeed, it has been suggested that rechallenge with vaccine may be associated with more severe symptoms.[5] Further evidence for the role of vaccines in arthritis comes from the monitoring of adverse drug reactions, with one survey indicating a causal link between rubella vaccination and acute and chronic arthritis, especially in women.[6]

The mechanisms underlying arthritis associated with vaccination are not yet fully understood. A cross reaction between bacterial lipopolysaccharide epitopes and synovial antigen, leading to an idiotype-anti-idiotype immunological response enhanced by HLA-B27 expression, may provide one model.[7] However, HLA-B27 expression is not a prerequisite for arthritis linked to vaccines[8] although its presence may predict a more prolonged and severe episode.[5] Vaccines may also trigger autoimmune responses by binding to critical antigen binding clefts on the major histocompatibility complex class II molecule, thereby triggering T cell proliferation.[2 9]

The impact of arthritis associated with vaccination can be severe, with prolonged and significant morbidity lasting many months. Hassan and Oldham reported Reiter's syndrome with joint pains and conjunctivitis lasting many months,[5] whereas Bracci and Zoppini additionally reported fevers and lymphadenopathy with the hepatitis B surface antigen vaccine (Engerix B).[10] However, as with our case, appropriate treatment, including non-steroidal anti-inflammatory drugs and intra-articular or oral steroids, can be useful in limiting the duration and degree of symptoms.

Vaccination has also been shown to cause necrotising vasculitis. Leucocytoclastic vasculitis has been induced most often, but polyarteritis nodosa-like and systemic vasculitides have also been reported in a few instances.[11–16]

In children, two other syndromes may occur after rubella vaccination (and natural infection): (*a*) the "arm syndrome", in which brachial radiculoneuropathy causes arm and hand pain, and dysthesias that are worse at night; (*b*) "catcher's crouch", a lumbar radiculoneuropathy causing pain in the popliteal fossa on arising in the morning, which is exacerbated by knee extension and improves in a "catcher's crouch" position. Both syndromes occur one to two months after vaccination. Although the initial episode may last up to two months, relapses may occur for up to a year, eventually resolving completely without permanent sequelae.[17]

Our case highlights a relationship between vaccination and arthritis and the ability of vaccine to retrigger a reactive arthritis in a susceptible person. Although the mechanisms of vaccination induced arthritis are not clear, there is sufficient evidence to suggest that some vaccines may cause joint disease or adversely affect pre-existing joint problems. It would therefore be prudent to warn patients awaiting vaccination about the possible adverse effect on joint symptoms.

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Asymptomatic splenic infarction in Wegener's granulomatosis

Wegener's granulomatosis (WG) is a necrotising, granulomatous vasculitis that classically involves the clinicopathological triad of upper and lower respiratory tracts and the kidney.[1] Less frequently, the disease may affect other organs as well. Serious and occasionally fatal complications within the spleen occur in many autoimmune rheumatic diseases,[2] and prompt recognition of these complications is important. In a necropsy series of patients with WG, the spleen was commonly affected: 78–100% of patients had splenic lesions with a combination of necrosis, vasculitis, and granuloma formation.[3 4] Clinically apparent splenic disease is rare, however.[1] We wish to report briefly the case of a 47 year old woman who presented with manifestations of classical WG and radiological evidence of splenic infarcts.

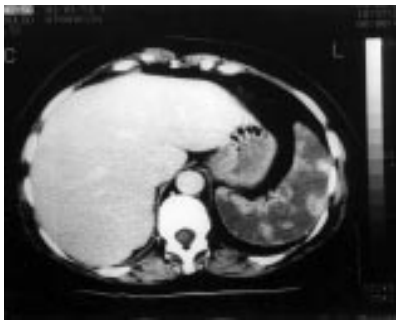

Figure 1 Abdominal CT scan showing a normal liver and a spleen with well defined areas of low attenuation, consistent with infarction.

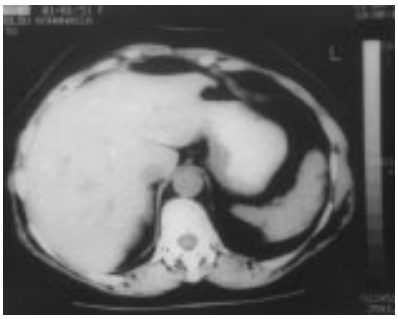

Figure 2 Abdominal CT scan three years later shows volume reduction and scarring of the spleen.

Case report

A 47 year old woman during the past month developed fevers to 38.6°C associated with weight loss, diffuse arthralgias, anaemia, and erythrocyte sedimentation rate of more than 100 mm/1st h. During the past three months she complained of nasal congestion and occasional episodes of epistaxis. A chest *x* ray examination showed a left upper lobe density, and her family doctor prescribed oral amoxicillin in combination with clarithromycin, without improvement. Ten days before admission gross haematuria was noted and a freshly collected urinary sediment showed the presence of red blood cell casts. Renal function declined rapidly with a serum creatinine level of 600 μmol/l and the patient was referred to the hospital for further investigation. A positive cANCA titre (1/160) was found using the indirect fluorescence technique and a positive antiproteinase 3 result on enzyme linked immunosorbent assay (ELISA; 66 U/ml). WG was considered on the basis of ANCA analysis results and the multisystemic nature of the disease and a percutaneous renal biopsy was performed under computed tomography (CT) guidance. Evaluation of renal biopsy specimens with light microscopy and immunofluorescence showed an acute necrotising segmental pauci-immune glomerulonephritis with crescent formation in more than 50% of the glomeruli. An impressive and rather unexpected CT finding was the presence of well defined areas of low attenuation within the spleen, consistent with infarction, with small areas of enhancement within the larger hypodense lesions (fig 1). A search for lupus anticoagulant and anticardiolipin antibodies was negative and no abnormalities of blood clotting could be detected. A trans-oesophageal echocardiogram failed to detect cardiac sources of emboli.

Treatment was started with 500 mg methylprednisolone intravenously per day for three consecutive days together with cyclophosphamide at a dose of 2 mg/kg body weight per day orally. After three days methylprednisolone was continued at 48 mg/day orally. Pulmonary and renal function progressively recovered and serum creatinine was 150 μmol/l on discharge.

Today, three years after the initial presentation, the patient is in stable remission and serum creatinine is 125 μmol/l. A recently performed CT scan showed a considerable volume reduction and scarring of the spleen (fig 2).

Discussion

Splenic involvement in WG has included such abnormalities as splenomegaly, capsular adhesion, impaired splenic function, and infarcts.[2] Infarction may occur as a result of a distal occlusion of the splenic artery or its branches, because splenic parenchymal arteries are end vessels that do not communicate with one another.[5] There are few reports on splenic infarction on post mortem in patients with WG.[3 4] Histological examination frequently shows massive or multiple areas of splenic necrosis, usually associated with extensive central arteritis, splenic trabeculitis, follicular arteriolitis and necrosis, disseminated visceral granulomata, and capsulitis. On CT, splenic infarcts classically and more commonly appear as peripheral, well defined, wedge shaped areas of low attenuation.[5] However, other patterns of infarction have been recognised. These include multiple heterogeneous low attenuation lesions; regions of normal enhancement centrally with peripheral low attenuation; and large, low attenuation hypodense lesions that may have a rim of enhancing tissue peripherally.[5 6] Examination with ultrasound in combination with duplex sonography of splenic blood supply permits non-invasive diagnosis of splenic infarction.[7] The diagnosis can be confirmed by magnetic resonance imaging or CT scan, which permits assessment of the extent of splenic infarction.

Splenic involvement in WG may be more prevalent than previously believed.[6–10] Pain in the left upper quadrant and left shoulder and fever may be present after splenic infarction, but many patients remain asymptomatic.[5 7] Consequently, cross sectional imaging is not often carried out and the lesion may frequently go unrecognised. Unless there are signs of imminent rupture of the spleen or bleeding,[11] a conservative approach is justified. In the long term these patients may be more susceptible to pneumococcal infection because of the functionally asplenic condition.[7] This possibility provides further help in the diagnosis of this rare condition in vivo.

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Two cases of *Mycobacterium avium* septic arthritis

The "unusual and memorable" case reported by Ter Borg and Tersmette[1] serves as a useful reminder that atypical mycobacterial infections, although uncommon, need to be considered in immunocompromised patients.

We present here two case reports of patients with pre-existing rheumatic disease receiving immunosuppressive treatment, who developed septic arthritis due to *Mycobacterium avium intracellulare*.

Case one

A 51 year old woman presented in 1999 with Raynaud's phenomenon, facial telangiectasia, sclerodactyly, and a positive antinuclear antibody. She complained of exertional dyspnoea, and subsequent high resolution computed tomography of the chest disclosed a ground glass appearance, indicative of active alveolitis. A diagnosis of scleroderma with interstitial lung disease was made, and treatment with prednisolone 30 mg and azathioprine 100 mg daily was started. In August 2000, she complained of pain and stiffness in the left shoulder, and this was treated with an intra-articular steroid. Six months later, she developed a left shoulder effusion, from which 50 ml of serosanguinous fluid was aspirated. Gram stain and initial bacterial cultures of the fluid were negative, and Ziehl-Neelsen stain did not show acid fast bacilli. Microscopy showed the presence of calcium hydroxyapatite crystals, and hence the shoulder was again injected with corticosteroids. Two months later, *M avium* was identified from the synovial fluid culture. The patient was treated with clarythromycin and ethambutol, and has made a good clinical response.

Case two

A 36 year old man presented in 1993 with arthralgia, proximal muscle weakness, and a creatine kinase of 12 000 U/l. Muscle biopsy confirmed the diagnosis of polymyositis. Treatment with prednisolone (initially 60 mg daily) and azathioprine 150 mg was started. In 1997 he developed axillary lymphadenopathy, and subsequent biopsy showed *M tuberculosis.* A good clinical response was achieved with rifampicin, isoniazid, and ethambutol.

In 1999 synovitis developed in the left knee and right wrist. Both joints were aspirated and injected with corticosteroids after initial Gram stain, Ziehl-Neelsen stain, and bacterial culture were negative. Eight weeks later, *M avium* was cultured from fluid in the left knee, and treatment with clarythromycin, ethambutol, and rifampicin was started. Histology from a right wrist tenosynovectomy six months later demonstrated granulomas, and culture confirmed the presence of *M avium*. At present, the patient continues to receive treatment with prednisolone 7.5 mg daily and azathioprine 150 mg daily, together with the antimycobacterial therapy, but clinical evidence of septic arthritis remains.

Discussion

Infective arthritis due to *M avium* is rare, most commonly occurring in immunocompromised subjects, such as those receiving immunosuppressive drugs, or HIV positive patients [2]. The most commonly affected joint is the knee. Up to 40% of patients with atypical mycobacterial septic arthritis have received prior intra-articular corticosteroid injection in the affected joint [3]. Diagnosis of these infections rests on culture of the synovial fluid (approximately 15%), or culture of surgically obtained specimens, though the often insidious nature of the infection may lead to a delay in diagnosis of many years [3]. Antimycobacterial treatment is given (dependent on sensitivities), with or without surgical synovectomy. Prognosis is variable, but most patients can expect to make reasonable or good functional recovery.

In summary, we report two cases of septic arthritis due to *M avium*, in patients with previously diagnosed inflammatory arthritis, who had received azathioprine and systemic and intra-articular corticosteroids. Arthritis with significant synovitis is not a common feature of dermatomyositis or scleroderma and therefore *M avium* should be considered as a diagnosis in patients receiving these drugs.

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Successful radiosynoviorthesis of an olecranon bursitis in psoriatic arthritis

We describe the case of a 45 year old male patient who for more than 10 years had had psoriasis with typical manifestations at knees and elbows. The family recalled psoriasis of the grandfather. Without any trauma or special straining, an olecranon bursitis and an arthritis of the left elbow developed in 1999 as the initial manifestation of psoriatic arthritis. Three months after developing the bursitis, the patient came to the rheumatological outpatient clinic for his first visit.

The clinical findings showed a patient with good general condition (height 186 cm, weight 93 kg), blood pressure 120/80 mm Hg, rhythmic pulse rate 68 beats/min; psoriatic skin lesions at knees and elbows; no reduction of spine mobility. The left elbow showed an olecranon bursitis with a diameter of 50 mm. The remaining musculoskeletal system was not affected.

The laboratory results were within the normal ranges, HLA-B27 was negative, antinuclear antibodies negative, functional tests of liver and kidney were normal.

Radiographic findings showed that sacroiliac joints and the left elbow joint were normal. Sonography showed an olecranon bursitis with a large effusion (fig 1A).

Diclofenac 100 mg twice daily was given for the first two weeks but did not produce any effect. After that, the olecranon bursa was punctured aseptically, and a crystal suspension of 10 mg triamcinolone hexacetonide was injected. Two days later, the bursitis relapsed completely. Further therapeutical options were surgical bursectomy or, alternatively, radiation synovectomy. After having received complete information, the patient gave his consent to treatment by radiosynoviorthesis. After aspiration of 9 ml of a serous effusion, 55 MBq rhenium-186 was instilled into the olecranon bursa, and then, to avoid radiosynovitis, 5 mg triamcinolone was injected. Radioisotope scanning immediately after the injection and three days later showed that the radionuclide was distributed uniformly in the bursa. There were no local signs of an infection.

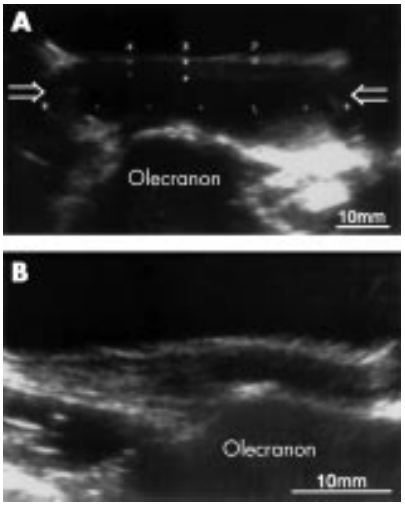

Figure 1 Sonography of the left elbow (A) showing an olecranon bursitis (58.1 mm; 17.7 mm; 3.3 mm; 2.5 mm) and (B) three months after radiation synovectomy.

A physical examination three months after radiation synovectomy of the olecranon bursitis showed regular clinical findings. Arthrosonographic results had also normalised (fig 1B). Even six months later the bursitis was not reactivated.

Radiation synovectomy is often used as an alternative, or in addition to, surgical synovectomy. Definite indications are chronic persisting synovitis, intermittent hydrops, relapsing synovitis after surgical synovectomy, haemophilic arthropathy, and activated osteoarthritis resistant to other treatments. Some studies have reported successful concomitant treatment of Baker's cysts in the treatment of gonarthritis,[1] but radiosynoviorthesis solely for the treatment of Baker's cysts is not usual. It is possible, however, by infusion of a radioisotope into the knee joint, but the popliteal cyst must not be punctured directly. Due notice should be taken of contraindications.[2] Other reports disagree about the success rates of radiosynoviorthesis in treating psoriatic arthritis compared with rheumatoid arthritis.[3 4] A few years ago, only patients aged over 40 were treated with radiosynoviorthesis. Today, this treatment is used in an increasing number of younger patients. The success rate for radiosynoviorthesis of olecranon bursitis is between 50 and 80%, depending on the localisation and the amount of inflammatory activity.[5–7]

Up to now, no studies of the treatment of chronic inflammation of the bursa by radiosynoviorthesis have been reported. In our patient, neither the treatment with a nonsteroidal anti-inflammatory drug (200 mg diclofenac daily) nor the local treatment with triamcinolone hexacetonide after a decompression aspiration led to improvement. As an alternative to surgical bursectomy, radiosynoviorthesis with rhenium-186 was performed. The patient improved quickly and started working again the following day. The follow up examinations, after intervals of three and nine months, confirmed the continuing success.

As far as we know this is one of the first reports on radiosynovectomy in an isolated bursitis. This case gives cause for hope that radiosynoviorthesis represents a successful alternative treatment to operational intervention for chronic inflammation of the bursa.

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Multiple sclerosis in the course of systemic sclerosis

We describe the case of a young woman with longstanding systemic sclerosis (SSc), who later developed multiple sclerosis (MS), and discuss the possible explanations for this rare co-occurrence.

A 30 year old white woman was admitted to the department of neurology of our institution with 10 days' history of vertigo and diplopia. A year earlier the patient had had an episode of paraesthesiae of her right leg, which resolved spontaneously within two to three weeks. Since the age of 22, she had been under the care of the rheumatology service of the same hospital for SSc, and her condition remained stable with treatment with D-penicillamine 500 mg daily and methylprednisolone 2 mg daily.

Clinical examination showed an alert woman with normal vital signs and typical appearance of scleroderma—that is, tightness and atrophy of the skin of her face and hands with contractions of her fingers. Examination of the lungs, heart, and abdomen showed no abnormality. Fundoscopy disclosed temporal pallor bilaterally. There was vertical nystagmus on upward gaze and diplopia on looking to the right, without apparent ophthalmoplegia. Deep tendon reflexes were brisk and abdominal reflexes were absent bilaterally. An extensor plantar response was seen on the right but no muscle weakness or sensory loss.

There was no evidence for keratoconjunctivitis sicca, as Schirmer's I, rose bengal, and break up time eye tests were normal. These had been performed routinely several times previously before the present admission. Furthermore, the patient had never complained of xerostomia.

Routine blood tests were normal. Serology showed positive antinuclear antibodies at a titre of 1/640, of the fine speckled pattern, and positive anti-Scl70 antibodies. Antibodies to cardiolipin and the other extractable nuclear antigens, including Ro(SSA), La(SSB), Sm, and nRNP, were absent, as they had been on several occasions in the past.

Visual evoked potentials were abnormal bilaterally. Cerebrospinal fluid (CSF) analysis disclosed increased intrathecal IgG synthesis (IgG index 0.88, normal <0.66) and oligoclonal bands. Magnetic resonance imaging (MRI) studies showed several abnormalities of the brain and the cervical cord (fig 1).

A five day trial of intravenous methylprednisolone 500 mg/day resulted in moderate relief of her symptoms and treatment was started with interferon β to prevent progression of the neurological process. At present, the patient has been receiving interferon β for two years and there is no evidence of any further neurological compromise.

One can suggest three possibilities for the coexistence of the neurological syndrome and the SSc in this patient. Firstly, MS occurring independently from SSc might account for the neurological deficits, given the laboratory findings and the patient's sex and age, and the prevalence of MS in the general population. However, it is also possible that there is an association between the two conditions, because MS, like SSc, is also believed to be autoimmune in nature, and the pathogenetic role of T cells is crucial in both processes.[1] Furthermore, MS has been increasingly reported in association with other autoimmune diseases not primarily affecting the nervous system.[2] If any of the above possibilities is present, the prognosis and therapeutic approach of our patient should match those of typical MS. The coexistence of SSc and MS is rare and, as far as we know, has been described in only four patients. Rapidly progressive and finally gripping MS developed in their early twenties, whereas SSc appeared later in the course of the MS in all four patients.[3–5] Interestingly, unlike these cases, our patient presented in her thirties with a mild form of MS, several years after the onset of SSc.

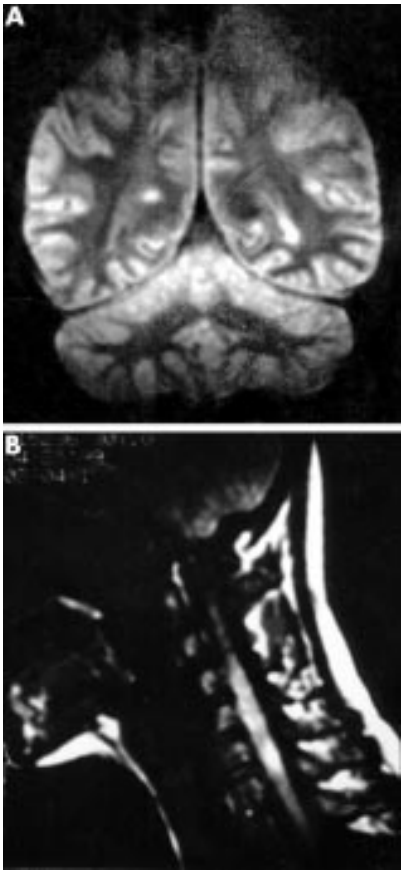

Figure 1 (A) T_2 weighted coronal MRI scan of the brain showing bilateral areas of increased signal intensity (up to 5 mm) into the white matter of the parietal lobes, mainly on the left. (B) Sagittal MRI scan of the cervical cord showing an area of increased signal intensity, which extends from the C3 to C7 level, resulting in focal enlargement of the cord at that level.

A third possibility exists that, the neurological manifestations of this patient might have been part of her primary disease—that is, SSc. Involvement of the central nervous system (CNS) in this disease is considered uncommon, and secondary to vasculopathic damage.[5 6] The fact that our patient had prolonged visual evoked potentials, suggestive of optic neuropathy, is rather in favour of MS, although this abnormality has been reported in SSc.[7] On the other hand, a significant percentage of patients with systemic lupus erythematosus may present with CNS disease and, some of them with oligoclonal banding in the CSF.[8] Brain or spinal cord disease, or both, with clinical features and laboratory findings indistinguishable from MS has been reported in Sjögren's syndrome too, although CNS involvement in this syndrome has been a matter of serious debate.[9 10]

In the absence of guidelines for the management of such patients, we considered our patient as a case of classical MS and, therefore, she was not deprived of the possible benefit of a disease modifying treatment, such as interferon β.

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CORRECTION

Heavy cigarette smoking and RA

(Masi AT, Aldag JC, Malamet RL. Ann Rheum Dis 2001;60:1154.)

The authors of this letter, in a further analysis of their data, found that four heavy smokers in the control group were incorrectly included in the 168 subjects matched to the 42 pre-RA cases who had baseline negative rheumatoid factor (RF–) status. They should be correctly reassigned to the 48 matched controls for the 12 pre-RA cases who had baseline positive rheumatoid factor (RF+) status.

The correct assignments place 11 (23%) heavy smokers in the 48 controls for the 12 pre-RA RF+ cases. Those 12 cases include two (17%) heavy smokers. The 168 controls for the 42 pre-RA cases who had baseline negative rheumatoid factor (RF–) status should correctly include eight (5%) heavy smokers. Those 42 cases include 11 (26%) heavy smokers. The new correct figures are shown in bold in the table.

The correct assignments strengthen the findings in this prospective, community based study that baseline heavy cigarette smoking was an independent risk factor from baseline positive rheumatoid factor status.

Corrections printed in the journal also appear on the *Annals* website www.annrheumdis.com and are linked to the original publication.

Table 1 Numbers of pre-RA cases and matched controls reporting heavy cigarette smoking (CS 30+/day) at baseline by relevant categories and odds ratios (ORs) with 95% confidence intervals (95% CIs) for developing ACR+ rheumatoid arthritis

	Pre-RA cases		Respective matched controls			
Categories	Number	CS 30+/day (%)	Number	CS 30+/day (%)	OR	95% CI
Pre-RA RF+	12	2 (17)*	48	**11 (23)***	**0.7**	**0.1 to 3.5**
Pre-RA RF–	42	11 (26)	168	**8 (5)**	**7.1**	**2.6 to 19.1**
Entry and post-RA RF–	15	4 (27)	60	1 (2)	21.5	2.2 to 210.6
Conversion of pre-RA RF– to RF+†	27	7 (26)	108	7 (6)	5.1	1.6 to 16.0

*No association of CS 30+/day with pre-RA RF+ (p=0.99).
†Conversion of RF– at baseline to RF+ after clinical onset of RA.

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Fax +44 208569 9555
Email: tony@q2q.co.uk or p.brooks@mailbox.uq.edu.au

British Society for Rheumatology XIXth AGM

23–26 Apr 2002; Brighton, UK
Contact: BSR, 41 Eagle Street, London WC1R 4TL, UK
Website: www.rheumatology.org.uk

4th EULAR Sonography Course

25–28 April 2002; Madrid, Spain
The course is entitled "Practical use of musculoskeletal ultrasonography"
Contact: Esperanzo Naredo
Email: enaredo@eresmas.com
Website: www.eular.org/courses and www.sameint.it/eular

10th International Vasculitis and ANCA Workshop

25–28 Apr 2002; Cleveland, Ohio, USA
Contact: Debora J Bork, The Cleveland Clinic Foundation, Desk A50, Center for Vasculitis Care and Research, 9500 Euclid Avenue, Cleveland, OH 44195, USA
Tel: 216 445 8533
Fax: 216 445 7569
Email: borkd@ccf.org
Website for registration and abstract submisssion: www.clevelandclinicmeded.com/courses/Vasculitis2002.asp

International Congress: New Trends in Osteoarthritis

9–11 May 2002; Milan, Italy
Contact: Organising Secretariat, O.I.C. S.r.l., Via Fatebenefratelli 19, 20121 Milan, Italy
Tel: +39 02 65 71 200
Fax: +39 02 65 71 270
Email: osteoarthritis@oic.it

IOF World Congress on Osteoporosis

10–14 May 2002; Lisbon, Portugal
Contact: IOF Secretariat, 71 cours Albert Thomas, F-69003 Lyon, France
Tel: +33 472 91 41 77
Fax: +33 472 36 90 52
Email: info@ioflyon.org
Website: www.osteofound.org

5th European Conference on Systemic Lupus Erythematosus

26–30 May 2002; Athens, Greece
Chairman Professor HM Moutsopoulos
Secretariat: Amphitrion Congress Organising Bureau
Email: hmoutsop@med.uoa.gr
Email: congress@amphitrion.gr

Annual European Congress of Rheumatology

12–15 June 2002; Stockholm, Sweden
Contact: Fred Wyss, Executive Secretary EULAR, Witikonerstrasse 15, CH-8032, Zurich, Switzerland
Tel: +41 1 383 9690
Fax: +41 1 383 9810
Email: eular@bluewin.ch
Website: www.eular.org

10th International Congress on Behçet's Disease

27–29 June 2002; Berlin, Germany
Under the auspices of the International Society for Behçet's Disease
Up to eight young investigator awards, each of $500, will be awarded on the basis of abstracts submitted
Contact: Professor Ch C Zouboulis, Department of Dermatology, University Medical Centre Benjamin Franklin, The Free University of Berlin, Fabeckstrasse 60–62, 14195 Berlin, Germany
Fax: 49 30 84456908
Email: zoubbere@zedat.fu-berlin.de
Website: www.userpages.fu-berlin.de/~zoubbere
ISBD website: www.behcet.ws

29th Scandinavian Congress of Rheumatology

15–18 Aug 2002; Tromso, Norway
Contact: Hans Nossent, Department of Rheumatology, University Hospital Tromso, Norway
Tel: 47 776 27294
Fax: 47 776 27258
Email: 29scr2002@rito.no or revhan@rito.no

Translational Research in Autoimmunity

21–22 Sep 2002; Pavia, Italy
Contact: Organising secretariat: eventi S.R.L., Corso Cavour, 18/20 - 27100 Pavia, Italy
Email: tra@e20pr.com
Website: www.e20pr.com
Congress website: www.medicine.ucsd.edu/albani/2001 meeting

OsteoArthritis Research Society International (OARSI) World Congress

22–25 Sep 2002; Sydney, Australia
Contact: OsteoArthritis Research Society International (OARSI), 2025 M Street, NW, Suite 800, Washington DC 20036, USA
Tel: +1 202 367 1177
Fax: +1 202 367 2177
Email: oarsi@oarsi.org
Website: www.oarsi.org

10th International Congress on Antiphospholipid Antibodies

29 Sep–3 Oct 2002; Sicily, Italy
Deadline for abstracts 1 April 2002
Contact: Secretariat, 10th International Congress on Antiphospholipid Antibodies, c/o Kenes International, PO Box 50006, Tel Aviv 61500, Israel
Tel: 972 3 5140018/9
Fax: 972 3 5140077 or 972 3 5172484
Email: aps@kenes.com
Website: www.kenes.com/aps

7th International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation and Related Diseases

14–17 Oct 2002; Nashville, Tennessee, USA
Contact: Lawrence J Marnett, Biochemistry Department, Vanderbilt University, School of Medicine, Nashville TN 37232-0146, USA
Tel: (615) 343 7329
Fax: (615) 343 7534
Website: www.eicosanoids.science.eayne.edu

66th American College of Rheumatology AGM

25–29 Oct 2002; New Orleans, USA
Contact: ACR, Ronald F Olejko, Director of Conferences and Meetings, 1800 Century Place, Suite 250, Atlanta, Georgia 30045–4300, USA
Tel: +1 404 633 3777
Fax: +1 404 633 1870
Email: acr@rheumatology.org
Website: www.rheumatology.org

Third International Meeting on Social and Economic Aspects of Osteoporosis and Osteoarthritis

7–9 November, 2002; Barcelona, Spain
Contact: Yolande Piette Communication, Boulevard Kleyer 108, 4000 Liège, Belgium
Tel: 32 4 254 12 25
Fax: 32 4 254 12 90
Email: ypc@compuserve.com

Certifying Examination in Pediatric Rheumatology

18 Nov 2002
Contact: American Board of Pediatrics, 111 Silver Cedar Court, Chapel Hill, NC 27514-1513, USA
Tel: 919 929 0461
Fax: 919 918 7114 or 919 929 9255
Website: www.abp.org