abnormality of SS. However, any conclusion must await a further extensive study.

Optimal thresholds of gland function were insufficiently accurate for diagnosis of SS, as they failed to discriminate between SS and controls, probably owing to different degrees of dysfunction in the patients with SS and the small sample size. We noted that tracer accumulation by the parotid gland decreased in sicca syndrome, but failed to show similar changes in submandibular uptake.⁹⁻¹⁰ A decreased excretion fraction in all glands compared with normal is characteristic of sicca syndrome and not exclusive to SS as has been described.⁹⁻¹⁰

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Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) as recurrence of aborted PMR

A comparison of clinical and laboratory findings in patients with RS3PE alone, PMR alone, and RS3PE associated with PMR has been recently published by Cantini *et al*.¹

Figure 1 Dorsal hand swelling, mild synovitis, tenosynovitis of the extensor carpi ulnaris (arrow) and of the flexor tendons (arrowhead). Axial STIR image of the left wrist (TR/TE 1840/30; TI=85; NEX=1; matrix=180 × 180).

Their results suggest that the three conditions might represent a continuum, with PMR, a more severe condition, at one end and, RS3PE alone, at the other. PMR has a longer duration, is more commonly associated with systemic symptoms, requires higher doses of steroids for a longer time, and shows more relapses and recurrences. Although Cantini *et al* emphasised the similarities between PMR and RS3PE, they concluded that RS3PE alone is a separate entity. Other studies by the same group of authors have shown that RS3PE may be a feature of different diseases, such as spondyloarthropathies, psoriatic arthritis, rheumatoid arthritis (RA), acute sarcoidosis, and neoplasms.² Whether RS3PE is a distinct syndrome or a clinical feature of different inflammatory diseases is still unknown.

We have recently followed up a patient, whose disease course might help in interpreting the relation between PMR and RS3PE. This 76 year old man had a sudden onset of pain and stiffness in the shoulder and pelvic girdles in September 1997. Two days afterwards, he was seen by his general practitioner, who prescribed intramuscular betamethasone (4 mg daily for six days). A few days after completion of treatment, the patient was seen by one of us. At this time, physical examination was completely normal. In particular, no joint pain could be elicited and there were no signs of arthritis or tenosynovitis. His clinical history was unremarkable except for mild hypertension. Routine laboratory examinations performed before the onset of the disease, in January 1997, were normal with an erythrocyte sedimentation rate (ESR) of 1 mm/1st h. No further treatment was given and it was suggested that the patient called us if his symptoms recurred.

At the end of October, the patient again complained of joint pain and was admitted to our unit. At physical examination, there was pain at movement of the wrists and dorsal hand swelling with pitting oedema. There were no skin lesions compatible with psoriasis and no personal or family history of psoriasis. ESR was 38 mm/1st h and C reactive protein 12 mg/l (normal <5 mg/l). IgM rheumatoid factor, antinuclear antibodies, and a panel of antiviral antibodies were negative. Radiographs of hands and sacroiliac joints were normal. Magnetic resonance imaging (MRI) of the hands was performed by a dedicated extremity 0.2 T system (Artoscan, Esaote, Genova, Italy). Sequences included axial and coronal T₁ weighted gradient echo and short τ inversion recovery (STIR). Section thickness was 3.5 mm, interslice gap was 0.3 mm,

and the field of view was 11 cm. Tenosynovitis of the flexor and extensor tendons was seen in both hands, with mild synovitis in the left wrist (fig 1). A diagnosis of RS3PE was made and treatment with prednisone 5 mg/day and indometacin 50 mg at night was started. The signs and symptoms resolved completely after one week. Treatment was stopped after three months. Recently (June 2000), the patient is completely well with no recurrences of his disease.

This case report suggests that RS3PE may be the only clinical sign of recurrence in a patient with PMR. With the exception of the indexes of inflammation, which were not tested at disease onset, our patient fulfilled all the commonly accepted criteria for PMR.³ Clinical features and MRI imaging of the recurrent disease were typical of RS3PE. It is tempting to speculate that early treatment of PMR might have aborted disease by downgrading the inflammatory response. If this is true, recurrence might have occurred at a more localised level of inflammation, represented by RS3PE. Two patients with PMR described by Healey had three subsequent episodes responsive to steroids, with typical signs of PMR, RS3PE, and seronegative RA.⁴ In their series of RS3PE, Olivé *et al* studied two patients with PMR before RS3PE.⁵ However, no precise description of the clinical features of these patients was given. These data confirm the view that PMR and RS3PE may be different manifestations of the same disease.

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Antiphospholipid antibodies and RA: presence of β_2 GP1 independent aCL

Anticardiolipin antibodies (aCL) are found in many conditions, such as lupus erythematosus, but also in other connective tissue diseases like rheumatoid arthritis (RA). To determine the prevalence and significance of aCL in RA, we evaluated the frequency of anticardiolipin and anti- β_2 glycoprotein 1 (β_2 GP1) antibodies in patients with RA.

We studied serum samples from 50 consecutive patients (36 women, 14 men) with RA

Table 1 Correlation of anticardiolipin antibodies (aCL) with serological and clinical findings in 50 patients with rheumatoid arthritis. Results are given as number (%) of patients

	aCL+ patients (n=9)	aCL- patients (n=41)	p Value
Age (years)	63.2 +/- 4	63.5 +/- 12	NS
ANA* positive (titre >160)	7 (77)	30 (73)	NS
Sicca syndrome	4 (44)	12 (29)	NS
Extra-articular manifestations	4 (44)	6 (14)	NS
Thrombosis history and/or abortion	1 (11)	3 (7)	NS
Steroid treatment	7 (77)	32 (78)	NS
DMARD* treatment	8 (88)	26 (63)	NS

*ANA = antinuclear antibody; DMARD = disease modifying antirheumatic drug.

satisfying the 1987 American College of Rheumatology criteria for RA. Serum IgG and IgM aCL were characterised by enzyme linked immunosorbent assay (ELISA)¹ using microtitre plates (Immunosorb, Nunc, Roskilde, Denmark) coated with cardiolipin purified from bovine heart (Sigma, St Louis, MO). Wells were saturated with 1% bovine serum albumin (BSA; Diamed, Cressier/Morat, Switzerland) in phosphate buffered saline solution (PBS). Serum samples diluted 1/100 in PBS-BSA were incubated for one hour at 37°C. The blocking and sample diluent buffer did not contain β_2 GP1 and differed from those using fetal calf serum, which are considered to add exogenous β_2 GP1. aCL levels were expressed in IgM and IgG units (U), calculated by including serum samples calibrated with Harris's standards on every plate.² A search was made for IgG and IgM β_2 GP1 antibodies by an ELISA using human β_2 GP1 antigen coated on irradiated plates, according to Arvieux *et al.*³ aCL and β_2 GP1 antibody levels were considered to be positive when greater or equal to 20 U. Rheumatoid factors (RF) (detected by nephelometry) and antinuclear antibodies (ANA) (detected by indirect immunofluorescence (IIF)) were determined for each patient. Additionally, antikeratin antibodies (detected by IIF on sections of rat oesophagus) and the presence of HLA-DR4 or HLA-DR1 were determined for 25 patients. The patients were assessed to determine the presence or absence of extra-articular manifestations of RA and sicca syndrome. A history of arterial or venous thrombosis, recurrent fetal loss, and current treatment—for example, steroid treatment, treatment with disease modifying antirheumatic drugs, and treatment for other diseases, were reviewed. Statistical analysis was performed with the χ^2 test or Fisher's test, as appropriate.

Nine patients (18%) had low titre IgG isotype aCL, but no β_2 GP1 antibodies. There was no correlation with thrombosis or recurrent fetal loss. There was an increase in sicca syndrome and extra-articular manifestations of RA in the aCL+ group, but this was not statistically significant (table 1). No significant association was found between aCL and other autoantibodies (RF, ANA, antikeratin antibodies). No statistically significant association was found between any drug inducing aCL and the presence of aCL. In contrast with our patients, another study found IgG aCL in only 2% of healthy subjects.⁴

β_2 GP1 antibodies were found in 8% of patients with RA, belonging to the IgM class in 75% of these cases. The sera containing IgM β_2 GP1 antibodies also contained positive levels of RF. There was no correlation with any clinical manifestation. β_2 GP1 antibodies were not found in healthy subjects.⁴

The frequency of aCL, all of them β_2 GP1 independent in this study, was close to⁵ or lower than in other studies (39–49%).^{6,7} We found no association with clinical manifestations such as thrombotic events,⁸ or extra-articular manifestations,⁹ or with other autoantibodies (ANA).^{7,9} The relation between IgM β_2 GP1 antibodies and RA remains to be determined; it might be due to non-specific binding with RF.

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Ethical aspects of new medicines targeted at treatment of RA

We read with interest the article reported by Kreutz *et al* "European regulatory aspects on new medicines targeted at treatment of rheumatoid arthritis".¹ The use of placebo studies for the development of new medicines in patients with rheumatoid arthritis (RA) remains controversial.² Placebo studies are useful when testing the effectiveness of new drugs. However, in two studies that compared two active disease modifying drugs with placebo the radiological deterioration was about four times higher in those patients with placebo.^{3,4} In view of this, in 1999 Emery and Smolen suggested that long term placebo studies should be a thing of the past in patients with active RA.⁵ Nowadays, there is enough evidence that single or combined treatments can modify RA. Thus, for example, in a recent prospective and observational study patients with severe RA who responded to methotrexate had a reduced mortality.⁶ Also, in three randomised controlled trials Sharp *et al* demonstrated retardation of radiographic progression by the use of leflunomide.⁷ Observations like these support the possible discontinuation of placebo in studies of active RA. Moreover, patients enrolled in placebo control studies should receive information on the potential risk of permanent and irreversible damage in those receiving placebo without any active disease modifying drug. Finally, at present it is difficult to establish whether six months without any active disease modifying drug in those receiving placebo is acceptable.

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