associated with AS. B*2709 differs from B*2705 by a single substitution (His *v* Asp) at position 116, which is located in the F pocket of the peptide-binding site. In the opinion of D'Amato and his colleagues the substitution at position 116 might exclude the acceptance of arthrogenic peptide from the B*2709.

Our patient was born in the south of Italy, she is B27 positive, and has uSpA with an erosive and disabling peripheral arthritis. Our case, also, suggests that the B*2709 might be associated with SpA and that the negative association found in Sardinian patients with AS[10] should be confirmed in other studies. These should include the full spectrum of SpA and not be limited to AS.

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Y chromosome microchimerism in rheumatic autoimmune disease

It is well known that some features of chronic graft-versus-host disease (GVHD) resemble those of other rheumatic autoimmune diseases, such as systemic sclerosis (SSc), Sjögren's syndrome (SS), and primary biliary cirrhosis (PBC). Furthermore, the development of systemic lupus erythematosus (SLE)-like diseases has been seen in murine models of GVHD.[1] The pathogenesis of rheumatic autoimmune diseases is still unknown. One possibility that has been suggested is that these diseases are associated with pregnancy because of their strong female predilection and, especially in SSc, a peak incidence after parturition. In 1996 Bianchi *et al* reported that fetal cells could survive in the maternal circulation for up to 27 years after parturition, a phenomenon termed fetal microchimerism.[2] These observations led the hypothesis that persistent fetal cells in the maternal circulation could mediate a graft-versus-host reaction, resulting in autoimmune disease.

Nelson *et al* have previously carried out a quantitative assay for male DNA in women with SSc and normal women who had delivered at least one son.[3] They indicated that the mean number of male cell DNA equivalents among controls was 0.38 cells/16 ml whole blood and 11.1 among patients with SSc. In addition, Artlett *et al* have shown Y chromosome-specific sequences in the DNA extracted from peripheral blood in 32 of 69 women with SSc (46%) as compared with 1 of 25 normal women (4%).[4] They also reported that those allo-cells were T lymphocytes and infiltrated lesional skin. These findings support the hypothesis that fetal microchimerism may contribute to the pathogenesis of SSc. However, this is still controversial because Murata *et al* have recently reported that there is no significant difference in the presence of fetal DNA in peripheral blood between Japanese patients with SSc and healthy women with non-quantitative assay.[5] Here we report further studies of fetal microchimerism in SSc, SLE, and SS.

We assayed for a specific Y chromosome sequence in the DNA extracted from peripheral blood by a nested polymerase chain reaction (PCR) in 20 patients with SSc, 21 patients with SLE, 18 patients with SS, and 41 healthy volunteers. All patients and healthy volunteers were Asian-Japanese women who had delivered at least one son. The nested PCR was done using the primers Y1–1, Y1–2, Y1–3, and Y1–4, which are specific for a part of the Y chromosome sequence, DYZ1, as described previously.[4 6] The identity of the detected PCR product was confirmed by nucleotide sequencing. The results from healthy volunteers and test groups were compared by Fisher's extract probability test.

Table 2 Comparison of clinical findings of DYZ1 positive and negative systemic sclerosis groups

	DYZ1		
	Positive (n=10)	*Negative (n=10)*	*Total (n=20)*
Barnett's type,			
I	3	4	7
II	3	5	8
III	4	1	5
Autoantibodies			
Antinuclear factor	10	8	18
Topoisomerase I	4	1	5
Centromere (PBC*)	3 (3)	8 (0)	11 (3)
RNP	4	0	4
SS-A(Ro)	2	3	5
SS-B(La)	0	0	0
RA	3	1	4
ssDNA	2	1	3
Mitochondria	2	0	2
Smooth muscle	1	0	1

*PBC = primary biliary cirrhosis.

Y chromosome-specific DNA was detected in 10 of the 20 patients with SSc (50%), eight of 41 healthy volunteers (20%, p=0.017), and six of 18 patients with SS (33%). No Y chromosome-specific DNA was detected in any of the patients with SLE (table 1). The DYZ1 was most commonly found in Barnett's type III (four of five). The DYZ1 positive patients with SSc also had a variety of antibodies including anti-RNP, antimitochondrial, and anti-smooth muscle antibodies that may reflect polyclonal activation of immune cells. Anticentromere antibodies were detected more commonly in the DYZ1 negative group (eight of 10). All three patients with SSc who had PBC were DYZ1 positive and had anticentromere antibodies (table 2).

Our data confirm that male DNA is found more commonly in women with SSc than in normal women. Interestingly, DYZ1 was not detected in patients with SLE and there was no significant difference between patients with SS and healthy volunteers. These data suggest that fetal microchimerism may be a phenomenon which is strongly associated with the pathogenicity of SSc and not with the related autoimmune diseases, SLE and SS.

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Table 1 Patients' characteristics

	SSc	*SLE*	*SS‡*	*Healthy controls*
Patients (n)	20	21	18	41
Age (years, mean (range))	56.1 (44–74)	50.2 (34–82)	54.8 (27–74)	53.2 (39–59)
Duration of illness (years, mean (range))	10.2 (1–26)	11.9 (1–24)	8.7 (1–19)	
DYZ1 positive (No (%))	10* (50)	0† (0)	6 (33)	8 (20)

*p=0.017, systemic sclerosis (SSc) *v* healthy volunteers.
†p=0.028, healthy volunteers and systemic lupus erythematosus (SLE).
‡SS = Sjögren's syndrome.

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Marker of erosive progression in RA

Urokinase plasminogen activator (uPA) catalyses the formation of the proteolytic enzyme plasmin, which plays a part in tissue degradation and remodelling,[1] and seems to have an important role in the erosive growth of pannus in rheumatoid arthritis (RA).[2] The action of uPA is localised and intensified by a cell bound receptor (uPAR),[3] expressed by some malignant cells and some inflammatory cell types, including activated synoviocytes in the marginal zone between pannus and cartilage in RA synovial tissue.[4]

The uPAR may become cleaved at the cell surface bound anchor, forming a free soluble receptor (suPAR) which is detectable in steady, low concentrations in healthy controls, but with raised concentrations in patients with disseminated malignant disease.[5]

Recently, in a cross sectional study, we found increased concentrations of suPAR in plasma of patients with RA compared with controls and patients with other types of inflammatory rheumatic disorders.[6] This finding raises the question, whether suPAR might be an easily accessible plasma marker of erosive activity in the synovial joint space in RA.

In a pilot study we followed up outpatients with RA to evaluate the relation between suPAR and disease activity. Plasma suPAR was measured and other clinical and paraclinical variables of disease activity determined in these patients on two or more occasions during a 12 month period. The present study included all patients (n=16) for whom comparable radiographs of the wrists and hands were obtainable, and also, when relevant, other symptomatic joints, taken before and after the period of suPAR measurements. The *x* ray films of participating patients were read independently by a radiologist unaware of the patient's clinical status and suPAR values. An enzyme linked immunoabsorbent assay (ELISA) was used to measure suPAR in plasma, as previously described.[5 6]

Table 1 Period average values of corresponding paraclinical and clinical variables of 16 patients with rheumatoid arthritis followed up prospectively and subsequently divided into two groups with or without progressive erosive changes on radiographs. Values are medians with range

	Erosive progression (n=5)	*No erosive progression (n=11)*
suPAR† (μg/l)	1.51 (0.93–2.73)*	1.03 (0.56–2.09)*
CRP† (mg/l)	11.4 (6.1–30.1)	11.0 (4.2–29.5)
ESR† (mm/1st h)	24 (15–24)	16 (7–58)
Tender joints (of 28)	6 (3–20)	4 (0–17)
Swollen joints (of 28)	4 (1–8)	2 (0–10)

*$p<0.05$, non-parametric Mann-Whitney test.
†suPAR = soluble urokinase plasminogen activator in plasma; CRP = C reactive protein; ESR = erythrocyte sedimentation rate.

The study group comprised 11 women and five men with a median age of 53.5 years (range 25–80) and a median disease duration of 57 months (range 5–360). Fifteen patients were rheumatoid factor positive and 10 had bony erosions on prestudy radiographs. Antirheumatic treatment included methotrexate (11 patients), hydroxychloroquine (two), sulfasalazine (one), and low dose steroids (eight). Clinical evaluation and measurement of suPAR, erythrocyte sedimentation rate (ESR), and C reactive protein (CRP) were done a median number of three times, and the time interval between radiographs was a median of 22 months.

Table 1 shows the results of the study. We found significantly higher suPAR concentrations ($p<0.05$) in plasma from those patients with RA whose *x* ray findings showed disease progression than in the patients who had no radiographic signs of progression, but the differences in ESR, CRP, and clinical variables were not significantly different.

This study was a pilot study in a clinical setting and conclusions must be drawn cautiously. The main problems, apart from the small number of patients, are, firstly, that in some of the patients prestudy radiographs were one to two years old. However, this would tend to diminish the differences found between the erosive progressive and non-erosive progressive groups as patients in remission, or with low activity in the study period, could be classified as progressive due to previous activity. Secondly, another possible bias, tending to increase the difference in suPAR between the two groups in this study, is that patients with high clinical activity would probably have had more extensive *x* ray examinations, increasing the chance of finding new erosions. We did not, however, find a difference in the number of radiographically investigated joints between our two groups of patients.

In conclusion, we find that this study indicates that plasma suPAR may be an easily accessible plasma marker of erosive progression in RA, and further studies on the subject are warranted.

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CORRECTION

Epidemiology of whiplash (Barnsley L. Ann Rheum Dis 2000;59:394; Reply: Ferrari R, Russell AS. Ann Rheum Dis 2000;59:395–6.)

The Editor of the *Annals* regrets that we inadvertently published a reply to Dr Barnsley from Drs Ferrari and Russell that contained some misinformation, and offers his apologies to Dr Barnsley.

Possibly, Drs Ferrari and Russell were confusing Dr Barnsley with someone else. Firstly, Dr Barnsley is a man and not a woman, as they stated. Secondly, Dr Barnsley did not attend the World Whiplash Congress in Vancouver and has not read the transcripts of it and thus could not be, as Drs Ferrari and Russell commented, “well aware of an impressive study presented there”.

(Note: Corrections printed in the journal also appear on the *Annals* web page (www.annrheumdis.com) and are linked to the original publication.)