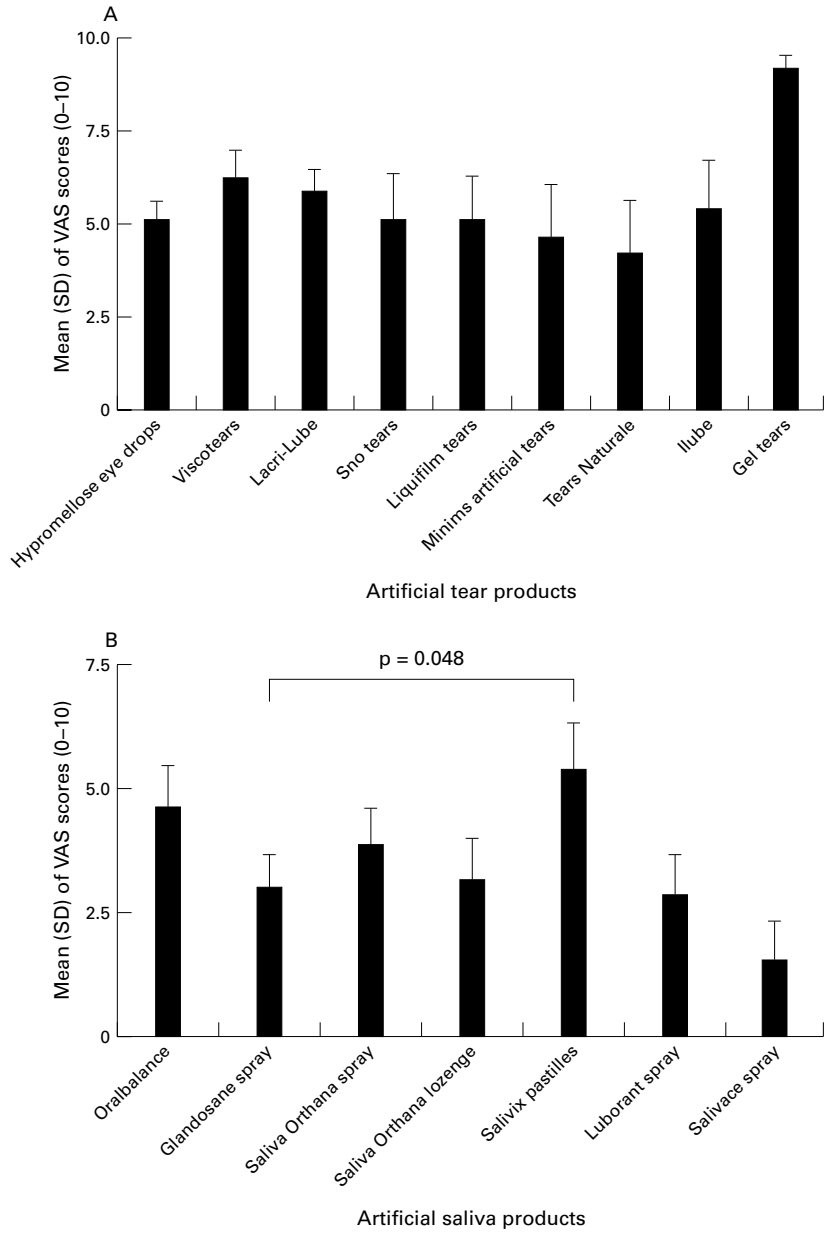

Figure 1 Patients' ratings of the effectiveness of (A) tear and (B) saliva replacement treatments for ocular or oral dryness. Patients were asked to rate any product, which they had ever used, on a 10 cm visual analogue scale (VAS), for each product. Results are shown as mean (SD) VAS scores. The p value refers to a comparison of results for Glandosane spray and Salivix pastilles (Mann-Whitney U test).

Y chromosome microchimerism in Sjögren's syndrome

There are many similarities between graft versus host disease (GVHD) and some rheumatic autoimmune diseases, such as systemic sclerosis (SSc), Sjögren's syndrome (SS), and primary biliary cirrhosis. Bianchi *et al* reported that fetal cells could survive in the maternal circulation for up to 27 years after parturition. This phenomenon is called fetal microchimerism.[1]

Some observations led the hypothesis that persistent fetal cells in the maternal circulation could mediate a graft versus host reaction, resulting in autoimmune disease. It is known that during a chronic GVHD, a Sjögren-like syndrome, is often observed: a salivary gland biopsy sample from patients with chronic GVHD showed lymphocytic infiltration, similar to that found in SS.[2] Nlson and colleagues have studied male fetal microchimerism in skin lesions and peripheral blood from women with SSc and at least one male pregnancy. They found that male DNA is more commonly associated with women with SSc than the healthy ones.[3]

Miyashita and colleagues have recently studied, by a nested polymerase chain reaction (PCR), fetal male microchimerism in peripheral blood from women with SSc, SS, and systemic lupus erythematosus.[4]

They confirmed that male DNA is found more commonly in women with SSc than in normal women, whereas there was no significant difference between patients with SS and healthy women.[4]

Also, Toda and colleagues have examined microchimerism in the circulation of patients with SS. A Y chromosome-specific sequence was detected as a marker for fetal cells by a nested PCR and by DNA hybridisation combined with PCR using specific primers and probes. The authors concluded that circulating fetal cells in patients with SS are uncommon, if they exist, but they may migrate preferentially into target organs of the disease rather than into the circulation.[5]

We have recently searched for male microchimerism in minor salivary glands tissue from six women with SS and at least one male pregnancy or miscarriage (table 1, patients 1–6). A diagnosis of SS was made according to EEC criteria.[6] As control we used DNA from minor salivary biopsy samples of three women with SS and with only a female pregnancy (patients 7–9), one woman with SS without a previous pregnancy (patient 10), and two healthy women, one with a male pregnancy and one with a female pregnancy (patients 11, 12). Table 1 gives details of the patients.

We assayed by PCR for a specific Y chromosome sequence, SRY, and for the homologous gene of amelogenin.[7 8] We tested our primers by diluting male peripheral blood DNA with female blood DNA. The sensitivity of our methodology was 10 pg for SRY primers and 100 pg for amelogenin. Given the sensitivity of the method, a cautionary note has to be made about laboratory personnel. When a male operator performed the DNA extraction and PCR a random positive case was obtained.

We have not found any male DNA either in the tissue from women with SS and a male pregnancy or in the controls. As far as we know this is the first study of fetal microchimerism in minor salivary gland tissue from a patient with SS.

Although this preliminary study does not seem to support the hypothesis that microchimerism has a role in the pathogenesis of Sjögren's syndrome, we cannot exclude the possibility that the time lag between the last pregnancy and sampling might have influenced the result. On the other hand, Evans and colleagues found male microchimerism in women with scleroderma even up to 38 years after pregnancy.[9]

In conclusion, a larger number of patients, with a more recent pregnancy, should be evaluated in order to confirm or refute the role of fetal microchimerism in women with primary SS.

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Table 1 Patients' data

Patients	*Age*	*Pregnancy*		*Miscarriage**	*Age last pregnancy*	*Transfusions**	*SS**	*M**
		Male	*Female*					
1	59	1	1	No	28	No	Yes	No
2	76	1	1	Yes	33	No	Yes	No
3	49	1	0	Yes	22	No	Yes	No
4	53	1	0	Yes	32	No	Yes	No
5	71	3	0	No	29	No	Yes	No
6	58	2	0	Yes	28	Yes	Yes	No
7	54	0	2	No	23	No	Yes	No
8	58	0	1	Yes	35	Yes	Yes	No
9	64	0	1	No	39	No	Yes	No
10	33	0	0	No	–	No	Yes	No
11	66	0	1	No	38	Yes	No	No
12	52	1	0	No	28	No	No	No

*Miscarriage = considered as a possible source of microchimerism; transfusion = considered as a possible source of microchimerism; SS = Sjögren's syndrome; M = microchimerism.

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Pitting oedema in early diffuse systemic scleroderma

The term "puffy skin" is not infrequently noted at initial presentation of patients with systemic scleroderma. However, this is generally described as "non-pitting" oedema. The following case history challenges the latter widely held assumption, showing that its measurement is simple and may offer a more sensitive method of assessing response to treatment than the modified Rodnan skin score.[1]

CASE REPORT

A premenopausal computer analyst first presented in May 1998 with a two month history of finger stiffness. The next 10 months were spent investigating and treating the cause of her iron deficiency anaemia—gastric ectasia (watermelon stomach). The diagnosis of diffuse systemic scleroderma was made in March 1999. At this time she presented with persisting symptoms of skin stiffness, burning and pruritis, especially in the early morning, affecting the skin of her arms and legs, face, and upper chest. Clinical examination showed finger clawing, sclerodactyly, and scleroderma affecting her arms to the mid-upper arm, the face, neck, upper chest, thighs, and calves. Pitting oedema, noted in the forearms, upper arms, chest, and thighs, had the following characteristics: it occurred in areas of affected skin—typically it occurred in the advancing front of skin involvement, was slow to induce (of bees' wax consistency), and it affected non-dependent areas. Her skin was also erythematous in parts. Livedoid patterning over the knees was also noted. The rest of the clinical examination, including musculoskeletal cardiac, and respiratory systems, was unremarkable. A skin biopsy specimen from the upper right forearm and dorsum of the left fifth proximal phalanx showed dermal sclerosis and perivascular lymphocytic inflammation around superficial dermal vessels, consistent with scleroderma. Both skin biopsy sites healed with keloid scarring. Her antinuclear antibody titre was 1/640, speckled pattern, and extractable nuclear antigens were negative for RNP, antitopoisomerase, anticentromere, SSA, SSB, and Sm antibodies.

A simple bedside test (the skin pitting oedema time test or "SPOT" test) was devised to quantify the duration of skin pitting and see whether its measurement paralleled response to treatment. A small diameter coin was placed over an area of oedematous skin on the arm, the site being recorded for future reference. A sphygmomanometer cuff was placed over the coin and around the arm, inflated to 100 mm Hg for 60 seconds, and then released. The sphygmomanometer cuff and coin were removed, leaving the coin's impression in the skin. From this time (time 0) the impression was palpated every minute by two independent observers (patient and author) until it was no longer palpable. This time was noted and recorded as the skin oedema time. Both interobserver and intraobserver variation were assessed over three consecutive days (coefficient of variation 6.8% and 6.8% respectively). The patient's skin oedema time was compared with that from a similar area of skin on a control matched for age, sex, and menopausal status (24 minutes).

At the patient's request, treatment with clindamycin over two consecutive days was started on 3 May 1999, at which time the skin oedema time measured 40 minutes. Clindamycin was stopped owing to marked diarrhoea and abdominal tenderness, which settled over five days. The patient was readmitted for pulse methylprednisolone on 13 May, by which time her skin had become increasingly sensitive and pruritic.

Figure 1 outlines her treatment with pulse steroids and cyclophosphamide. Cyclosporin

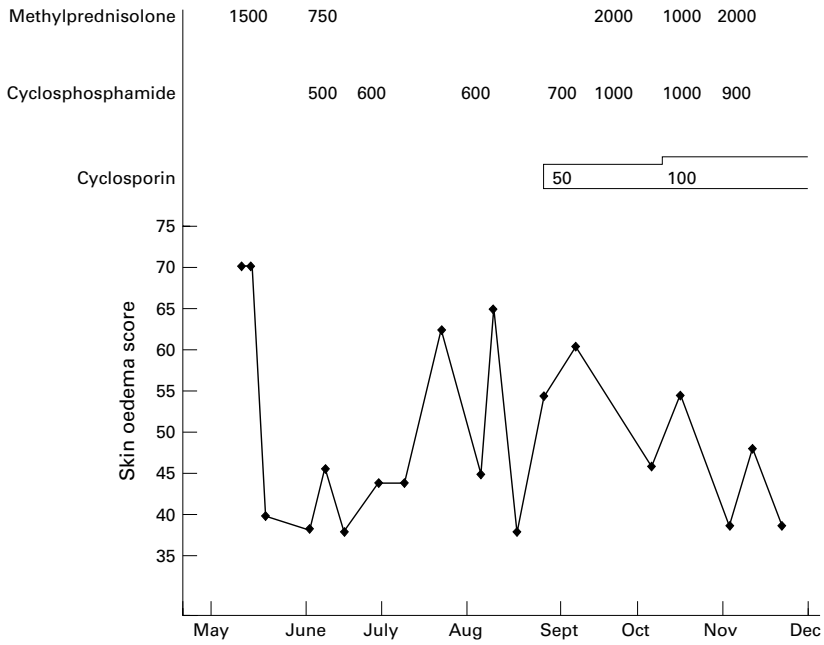

Figure 1 Patient's treatment with pulse steroids and cyclophosphamide.