of the disease, or that the levels of circulating B cells may not reflect their levels in tissues. Although B cells are present in low amounts in rheumatoid synovial tissues, some investigators have recently shown a considerable number of activated B cells in bone marrow adjacent to penetrating synovial tissue in bony erosions.¹¹ Future studies, including biopsies, may provide important information on the B cell-depleting action of rituximab in target tissues.

The side effects of rituximab were similar to those described in previous studies.³ The only infectious complication was a foot abscess that occurred 8 months after administration of rituximab in a patient with a 15-year history of diabetes and antecedent of osteomyelitis.

In conclusion, B cell depletion may represent an efficacious and safe alternative in the treatment of patients with rheumatoid arthritis resistant to TNF α inhibitors.

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Soluble fractalkine in the cerebrospinal fluid of patients with neuropsychiatric lupus

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Proinflammatory cytokines increase in concentration in the cerebrospinal fluid (CSF) of patients with neuropsychiatric syndromes of systemic lupus erythematosus (NPSLE), and some reports have shown that cytokines are elevated intrathecally.^{1–3} Recently, levels of Th1 chemokines, monocyte chemoattractant protein 1 (MCP-1; CCL2) and interferon inducible protein-10 (IP-10; CXCL10) have been reported to be raised in the CSF of patients with NPSLE, implicating important roles for these chemokines in the pathogenesis of NPSLE.^{4–5} Here we study the role of soluble fractalkine (CX3CL1) in NPSLE.

A total of 165 patients (161 women and 4 men, aged 16–58 years; mean age 32.4 years) fulfilling the criteria of the American College of Rheumatology for systemic lupus erythematosus (SLE) classification were selected. NPSLE was diagnosed under the American College of Rheumatology criteria for neuropsychiatric lupus syndromes.¹ In all, 84 patients were diagnosed with NPSLE and 81 patients did not fulfill our criteria for NPSLE.¹ Of the 84 patients with NPSLE, samples were collected from 12 patients before NPSLE treatment, whereas samples from the remaining 72 patients were collected during or after glucocorticoid treatment specifically for neuropsychiatric symptoms. Levels of soluble CX3CL1 in the CSF and the serum were determined using an

enzyme-linked immunoassay (DuoSet human fractalkine/CX3CL1 ELISA developing kit, R&D Systems, Minneapolis, Minnesota, USA). Statistical comparisons were carried out using the non-parametric Mann–Whitney U test. Results are presented as the mean (standard error of the mean).

The CX3CL1 concentration in the group with NPSLE was not higher than that in the group without NPSLE ($p = 0.4267$; fig 1A). In untreated patients either with newly diagnosed NPSLE or without NPSLE, the CX3CL1 concentration in the group with NPSLE was not higher than that in the group without NPSLE ($p = 0.9769$; fig 1B). We concluded that the levels of soluble CX3CL1 in the CSF of patients with NPSLE were as high as those in patients without NPSLE. No correlation was found between levels of CX3CL1 and those of other Th1 chemokines (IP-10/CXCL10 ($r = -0.0525$, $p = 0.5963$); MCP-1/CCL2 ($r = -0.0508$, $p = 0.6018$)), which have been reported to be high in the CSF from patients with NPSLE.^{4–5}

To further study the role of soluble CX3CL1 in SLE, serum levels of soluble CX3CL1 were measured in patients with SLE and in patients with other autoimmune disorders. Serum levels of soluble CX3CL1 in patients with SLE (402.28 pg/ml (SD 1119.00)) were higher than those in patients with other autoimmune disorders (rheumatoid arthritis, primary

Figure 1 (A) Levels of soluble fractalkine (CX3CL1) in the cerebrospinal fluid of patients with systemic lupus erythematosus, with neuropsychiatric syndromes of systemic lupus erythematosus (NPSLE) and without (non-NPSLE) neuropsychiatric involvement. The concentration of soluble CX3CL1 in the CSF from patients with NPSLE (n = 84) was 2.426 pg/ml (SD 5.738) and that in the CSF from patients without NPSLE (n = 81) was 1.879 pg/ml (SD 5.017) ($p = 0.4267$). (B) Levels of soluble CX3CL1 in the CSF of patients with untreated SLE, with (NPSLE) and without (non-NPSLE) neuropsychiatric involvement. The concentration of soluble CX3CL1 in the CSF from patients with NPSLE (n = 12) was 4.492 pg/ml (SD 8.787) and that from patients without NPSLE (n = 12) was 4.892 pg/ml (SD 10.073) ($p = 0.9769$).

Figure 2 Serum levels of soluble fractalkine (CX3CL1) in patients with neuropsychiatric syndromes of systemic lupus erythematosus (NPSLE), without NPSLE, with rheumatoid arthritis (RA) and with primary Sjogren's syndrome (SjS), and in healthy controls (HC). Serum level of soluble CX3CL1 in patients with NPSLE was 629.288 pg/ml (SD 1498.668) and that in patients without NPSLE was 166.198 pg/ml (SD 362.972; $p = 0.0106$). Serum levels of soluble CX3CL1 in patients with RA, with primary SjS, and in HC were 40.160 pg/ml (SD 63.607), 71.170 pg/ml (SD 120.454) and 19.520 pg/ml (SD 46.961), respectively.

Sjogren's syndrome (fig 2). Serum levels of soluble CX3CL1 were higher in patients with NPSLE than those in patients without NPSLE ($p = 0.0106$). No correlations were seen between the levels of soluble CX3CL1 in the serum and in the CSF of the same patients on the same day ($r = -0.0314$, $p = 0.7937$).

The chemokine CX3CL1 is a member of the CX3C chemokine family, and its receptor, CX3CR1, was reported to be preferentially expressed in Th1 cells, but not in Th2 cells, in response to CX3CL1.⁶ Therefore, CX3CL1 may be a Th1 chemokine. However, the levels of CX3CL1 in CSF did not correlate with the levels of other Th1 chemokines such as IP-10/CXCL10 and MCP-1/CCL2 in this study. Further studies, including study with more CSF samples from untreated patients with SLE, are necessary to confirm the exact role of CX3CR1-positive cells in neuropsychiatric manifestations in patients with SLE.

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Psoriasis after treatment of juvenile idiopathic arthritis with etanercept

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We highlight the case of an adolescent who developed psoriasis after starting anti-tumour necrosis factor (anti-TNF) treatment for extending oligo-articular juvenile idiopathic arthritis. The patient, a 13-year-old girl, first presented at 18 months of age with arthritis of both knees and the left ankle. Her initial treatment consisted of non-steroidal anti-inflammatory drugs alone, but the pain, swelling and stiffness continued. Intra-articular and oral steroids led to improvement, but not a complete resolution of her symptoms. Uveitis was detected at an early stage and managed with topical steroid drops.

At the age of 7 years, she underwent surgery for a medulloblastoma. Radiotherapy and chemotherapy were completed in July 2000 and ongoing follow-up showed no signs of tumour recurrence. Her arthritis improved considerably with chemotherapy, but relapsed once treatment ended. The arthritis extended to include the small joints of the hand, wrists, elbows and right ankle, leading to reduced mobility and difficulty at school, with stiffness and fatigue.

The patient developed striking cushingoid features on oral steroids, and, in view of the ongoing difficulty with disease control, was started on methotrexate in 2001 (at the age of 9 years). The methotrexate dose was gradually increased and then given subcutaneously to optimise the effect. Etanercept was introduced in 2003 (at the age of 11 years), owing to continuing difficulty with controlling arthritis. This proved effective, with subsequent clinical findings limited to mild synovitis in the right wrist and left ankle. Steroids were discontinued and the methotrexate was gradually reduced, being given orally once again.

Early in 2005, the patient developed a new rash. Red, excoriated skin was evident behind the ears, around the umbilicus, and in the axillae and groin. An opportunist infection related to immunosuppression was considered, but there was no improvement with systemic or topical antibiotics. The skin changes became increasingly psoriatic, a diagnosis confirmed on review by a consultant dermatologist. No history of psoriasis was noted in the patient or her family.

Psoriasis induced by anti-TNF treatment has previously been reported in adults, with a variety of underlying diagnoses.^{1–6} In a prospective study of 289 adults with rheumatoid arthritis starting anti-TNF treatment, 3 (1%) developed psoriasis or psoriasiform eruptions.⁶ This is perhaps surprising, as an improvement in skin disease is often seen with anti-TNF treatment in psoriatic arthritis or severe psoriasis vulgaris.⁷

One possible explanation would be that the patient had psoriatic arthritis from the outset, with arthritis preceding

the onset of skin signs. However, given the temporal relationship, we believe it more likely that the appearance of psoriasis is related to the introduction of etanercept. Alternatively, a tendency to psoriasis may have been unmasked by anti-TNF treatment, or the drug itself could have induced psoriasis. In predisposed people, inhibition of TNF alters immunity, promoting an inflammatory autoimmune response in the skin.¹

Further investigation is warranted to elucidate the mechanisms whereby anti-TNF treatment can have seemingly contradictory effects on psoriasis in different people. Clinicians should remain aware of the possibility of psoriasis arising de novo in patients treated with anti-TNF agents at any age.

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Abbreviation: TNF, tumour necrosis factor.