females. The mean age of onset of psoriasis in our cohort was 29.27 yr (s.d. 14.16 yr). Overall, 98% of the samples were genotyped successfully, and all of the genotypes for the controls satisfied the Hardy–Weinberg equilibrium.

With respect to single locus associations, none of the variants examined from SLC22A4, SLC22A5, SLC9A3R1 and RUNX1 were significantly associated with PsA in the Newfoundland population either by genotype or minor allele frequencies. We then analysed two marker haplotypes for markers of interest in rheumatoid arthritis [SLC22A4 (rs3792876) and RUNX1 (rs2268277)] and Crohn’s disease [SLC22A4 (rs1050152) and SLC22A5 (rs2631367)] and noted no association (P = 0.342 and P = 0.81, respectively). We also examined two marker combinations for the remaining SNPs in SLC22A4 (rs3792876 and rs1050152, P = 0.48; rs3792876 and rs3763112, P = 0.580) as well as haplotypes for all four SNPs in SLC22A4 on chromosome 5 (P = 0.90). Finally we assessed the relationship of all six markers on three different chromosomes and again found no association (P = 0.74).

Thus in our study, we noted no association between the organic cation transporter genes and PsA in the Newfoundland population. This is in contrast to a recent British study that investigated 471 Caucasian PsA patients and 605 population controls for similar variants in SLC22A4 and SLC22A5 [4]. They noted two SNPs, rs3763112 mapping to SLC22A4 and rs2631367 mapping to SLC22A5, to be significantly associated with PsA (P = 0.001 and P = 0.007, respectively). Furthermore, the same haplotype as Crohn’s disease between SNPs (rs1050152 and rs2631367) was strongly associated with PsA (P = 0.002) in their population. The lack of association of these SNPs and the Crohn’s disease haplotype in our study may reflect a difference in the PsA populations, as Newfoundland is a homogeneous founder Caucasian population, while the British population was admixed. A potential benefit of studying the Newfoundland population is the possibility of an amplified genotype relative risk due to the enhanced signal to noise ratio that exists in the population as a result of genetic and relative environmental homogeneity. However, as locus homogeneity is also likely to exist in the Newfoundland population, not all genes of potential importance to PsA will be implicated in the Newfoundland population. We therefore were unable to implicate SLC22A4, SLC22A5, SLC9A3R1 and RUNX1 in the Newfoundland PsA population, even though there is significant epidemiological, clinical and immunological overlap between PsA, psoriasis, rheumatoid arthritis and Crohn’s disease.

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Successful treatment of steroid-resistant
Weber–Christian disease with biliary
ductopenia using cyclosporin A

Sir, Weber–Christian disease (WCD) is an unusual idiopathic disorder characterized by non-suppurative nodular panniculitis with fever and cutaneous lesions [1]. The aetiology of WCD remains unknown, and systemic WCD, associated with severe liver damage, is often fatal [2]. Hepatic injury associated with WCD is characterized by steatohepatitis [3, 4]. To our knowledge, however, WCD with biliary ductopenia has not yet been reported. We report the first case of systemic WCD with biliary ductopenia that was successfully treated with cyclosporin A (CyA).

The patient was a 27-yr-old Japanese man with recurrent episodes of subcutaneous nodules on both legs since 1995. In January 1998 he was admitted to the Department of Dermatology at our hospital because of a middle-grade fever, bilateral pitting oedema and subcutaneous nodules. Laboratory tests showed the following results. A complete blood count revealed a leucocyte count of 2.3 x 10^3/µl (89% band cells, 6% lymphocytes, 2% monocytes). Haemoglobin level was 10.7 g/dl and haematocrit 33.5%. Platelet count and coagulation tests were normal. The patient was found to have severe malnutrition with extremely low serum concentrations of total protein and albumin (5.8 and 2.3 g/dl, respectively). The serum concentrations of aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase, γ-glutamyl transpeptidase and creatine kinase were elevated to 173, 74, 1506, 745, 113 and 199 IU/l, respectively. The serum concentrations of total bilirubin (T-Bil), pancreatic enzymes and α1-antitrypsin were within the normal range. Serum ferritin level was markedly increased (34 783 ng/dl). ANA was positive, while the other antibodies and microbiological tests were negative. A small amount of bilateral pleural effusion, moderate fatty liver, a moderate amount of ascites and diffuse intestinal oedema were detected by abdominal ultrasonography or CT. Bone marrow aspirate showed no histiocytic infiltration. A skin biopsy showed panniculitis, which included infiltration of lymphoid cells and granulomatous inflammation of epithelioid cells. He was diagnosed with WCD and treated unsuccessfully with pulse steroid
therapy (intravenous methylprednisolone, 1 g/day for 3 days). He was transferred to our department because of his worsening clinical condition and laboratory tests (Fig. 1A). Gastrointestinal bleeding associated with disseminated intravascular coagulation (DIC) and severe jaundice were observed. T-Bil and soluble interleukin-2 receptor (sIL-2R) concentrations were extremely high at 23.5 mg/dl and 13,500 U/ml, respectively. In February 1998, the patient was treated with intravenous CyA and plasma exchange therapy, achieving a plasma CyA concentration of 100 ng/ml. Three weeks later oral CyA therapy (225 mg/day) was started instead of intravenous CyA infusion because of almost complete recovery. Before steroid therapy, a liver biopsy showed periportal steatosis with infiltration of neutrophils, lymphocytes and macrophages. Note also the lack of bile ducts (haematoxylin–eosin stain, ×100). (C) High-power photomicrographs of liver histopathological findings 40 days after commencement of CyA therapy. Note the reduction in hepatic steatosis and infiltrated lymphoid cells and histiocytic cells, and the significant increase in the number of bile ducts (arrows) in comparison with panel B (haematoxylin–eosin stain, ×400). Parts (B) and (C) of this figure may be viewed in colour as supplementary data at Rheumatology Online.
improvement, CyA and corticosteroid treatment was discontinued in 1999. He has been symptom-free and has maintained a normal life style for more than 5 yr without CyA and steroids.

WCD is a primary panniculitis, which is a histiocytic disorder described as a form of lobular panniculitis with infiltration of haemophagocytic benign histiocytes [1]. In our patient, the diagnosis of WCD was made based on the clinical features, histopathological findings of the skin and liver biopsy specimen. His WCD was steroid-resistant and he developed several complications, including DIC and severe jaundice, after steroid pulse therapy. However, CyA was remarkably effective and the clinical condition showed almost complete recovery except for mild fatty liver. Successful treatment of WCD with CyA was first described in 1987 [5] and several additional reports described a similar response to CyA [6–9]. The aetiology of WCD remains unknown. However, it has been related to an immunologically mediated reaction because of sIL-2R elevation [8, 9]. In the present case, we also observed high serum concentration of sIL-2R, which represents T-cell activation, and successful response to CyA, which acts primarily on helper T cells and interferes with the production of various cytokines. CyA therapy resulted in a dramatic decrease in the serum concentration of sIL-2R followed by rapid clinical improvement.

In addition, a striking feature of this case was the hepatic involvement. Liver biopsy before steroid pulse therapy showed periporal steatohepatitis with biliary ductopenia. Ductopenia is a rare cause of prolonged, progressive cholestatic liver disease [10]. It is mainly associated with chronic allograft rejection, graft-versus-host disease, primary biliary cirrhosis, drugs and toxins. Ductopenia associated with WCD is rare and our report is the first to describe ductopenia as one of the pathological features of WCD and to show that CyA is significantly effective in ductopenia associated with steroid-resistant WCD.

In conclusion, we report a case of WCD with biliary ductopenia successfully treated with CyA. Ductopenia should be included as a possible pathophysiological factor of hepatic lesion in WCD.

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**Leflunomide-induced subacute cutaneous lupus erythematosus**

Sir, Leflunomide is a disease-modifying anti-rheumatic drug (DMARD). It is effective in monotherapy and/or in combination with TNF-α blockers in the treatment of RA. Leflunomide inhibits pyrimidine metabolic pathways in lymphocytes and other rapidly proliferating cells. Its active metabolite, A771726, inhibits dihydroorotate dehydrogenase, a key enzyme of de novo pyrimidine synthesis.

Variable leflunomide-related adverse events have been reported. Diarrhoea is the most frequent one. It usually occurs within the first 3 months of treatment and resolves in most cases after symptomatic treatment or after decreasing the leflunomide dose [1]. Pancytopenia [2] and liver dysfunction with elevated serum levels of transaminases [3] have also been described, necessitating the monitoring of blood cell count and liver function.

Adverse cutaneous reactions due to leflunomide have also been reported, including alopecia and skin ulceration [4]. A case of leflunomide-induced subacute cutaneous lupus erythematosus (SCLE) has been reported [5]. Here we report two other cases of SCLE occurring in RA patients treated with leflunomide.

Patient 1 was a 59-yr-old woman who had had RA since 1987, with progressive joint destruction despite successive treatments with gold salts, sulphasalazine and methotrexate (MTX). MTX was subsequently combined with infliximab in September 2000. In January 2002, MTX and infliximab were stopped because of persistent active RA. The patient was then treated with leflunomide (20 mg daily after a 100 mg daily loading dose for the first 3 days) associated with prednisone (5 mg daily), ketoprofen and tramadol. In December 2002, the patient presented an annular eruption on the back, neck and face suggestive of SCLE (Fig. 1). Neither arthritis nor other systemic involvement was observed. A blood test showed an inflammatory state (ESR 84 mm in 1st h, CRP 121 mg/l), antinuclear antibodies (ANA) 1/1000 with homogeneous fluorescence, and anti-Ro antibodies