arthritis (ReA), rheumatoid arthritis (RA) and osteoarthritis, and correlate them with the HLA-B27 haplotype in a subset of ReA patients positive for *Chlamydia trachomatis*. The results did not reveal significant differences in cytokine levels and ratios among the groups, although lower levels of interferon γ (IFN-γ) in SF were found in the HLA-B27-positive ReA patients than in the negative ones.

The data presented are striking, but they merit comment. First, the Quantikine ELISA kits used are not validated for use with SF. Therefore, it is fair to ask why these kits were used to analyse the SF.

Secondly, the lower levels of SF interleukin (IL) 10 in ReA than in RA are at variance with other reports. In addition, how do the authors explain the higher ratios of IFN-γ to IL-10 among the ReA patients? Animal models of *Chlamydia* infection have shown that the clearance of the organism is affected by the balance between IFN-γ and IL-10, and IL-10 gene knockout mice clear *Chlamydia* infection more rapidly than normal [2–4].

We also wonder why IL-4 and IL-17 were not analysed. Considering that the immune response to *Chlamydia* requires a Th1 response, it would have been of interest to demonstrate the adequacy or inadequacy of this response by determining the presence of IL-4. In addition, IL-17 is relevant to joint destruction, and its presence in the joints of ReA patients is of obvious interest and importance [4].

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Reply

We thank Drs Cuchacovich and Espinoza for their interesting comments.

Commercial ELISA kits, including the Quantikine kit, developed for serum or plasma measurements, have been widely used to determine levels of cytokines in synovial fluid (SF) [1]. In a comparative study, cytokine measurements have been performed in SF, plasma and culture supernatants with commercial ELISA kits from seven companies (one of them being R & D Systems) and similar findings were obtained with the three kinds of samples [2].

The lower levels of SF interleukin (IL)-10 in reactive arthritis (ReA) patients compared with rheumatoid arthritis (RA) patients have also been reported by other groups (spondylarthropathies, mean 4.5 U/ml *vs* RA, mean 84.6 U/ml [3]; ReA, median 10 pg/ml *vs* RA, median 30.3 pg/ml [4]; seronegative spondylarthropathies, mean 9.2 pg/ml *vs* RA, mean 88.4 pg/ml [5]). In two of these studies, where the SF levels of interferon (IFN)-γ were reported the SF IFN-γ/IL-10 ratios were also higher in ReA [4] patients and seronegative spondylarthropathy [5] patients.

These data are in contrast to the relative abundance of synovial IL-10 mRNA reported by Kotake *et al*. [6] in patients with *Chlamydia*-associated arthritis. However, our patients with *Chlamydia trachomatis* ReA had a mean duration of arthritis (1.4 months) shorter than that of the patients in this report (3 months). Thus, the discrepant results could be explained if IL-10 production was delayed in patients with ReA or if there is regulation at the level of translation. These differences could also be explained by differences in drug therapy.

IL-10 gene knockout mice clear *Chlamydia* infection more rapidly than normal mice. However, lung infection with the mouse pneumonitis biovar of *C. trachomatis* [7] probably differs from human ReA because there are human serovars of *C. trachomatis*. For instance, Perry *et al*. [8] showed that all human serovars of *C. trachomatis* were much more sensitive to the direct inhibitory actions of IFN-γ than the mouse pneumonitis strain.

The low IL-10 concentrations and high IFN-γ/IL-10 ratios observed in SF from ReA patients could indicate an autoimmune response to self heat shock protein (hsp) 60. Indeed, in mice immunized with both mouse and *C. trachomatis* hsp60, lymphocytes proliferated strongly in response to mouse hsp60, secreted 6-fold less IL-10 and exhibited a 12-fold increase in the IFN-γ/IL-10 ratio compared with mice immunized with mouse hsp60 alone [9]. These findings suggest than an increased IFN-γ/IL-10 ratio, as observed in ReA patients, may contribute to the *Chlamydia*-induced immunopathology.

IL-4 and IL-17 are certainly cytokines of interest but we could not determine their levels because sufficient SF was not available.

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Reply

Sir, We were pleased to read the report of Loo *et al*. in relation to two cases of polyneuropathy associated with Churg–Strauss syndrome (CSS) responding to intravenous pulse cyclophosphamide. The primary purpose of our original article was to raise awareness that the presence of mononeuritis multiplex or, as in these cases, distal motor polyneuropathy, should be regarded as severe disease associated with significant long-term morbidity. In the current literature, the definition of severe disease in CSS is ambiguous as far as peripheral nerve involvement is concerned. While we acknowledge that CSS is associated with a better prognosis when compared with other primary small-vessel vasculitides [1–2], significant neuropathic involvement can result in short- and long-term disability. This may be prevented if we can treat appropriate patients with adequate therapy to induce rapid remission of disease and prevent relapse. Although steroid monotherapy can sometimes achieve this, in our two cases steroid alone was insufficient to achieve complete remission. The use of concomitant pulse cyclophosphamide therapy may also reduce the cumulative dose of corticosteroid required to maintain remission, thus avoiding the bone and metabolic complications of long-term steroid therapy. We agree with Loo *et al*. that prospective outcome studies that address the risk–benefit ratio should be done, especially to take account of functional outcome and quality of life issues in patients with Churg–Strauss syndrome.

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Mononeuritis in Churg–Strauss syndrome in Asians responding to intravenous cyclophosphamide

Sir, We read with interest the letter by Hoi and Morand on the use of intravenous (i.v.) cyclophosphamide in the treatment of mononeuritis associated with Churg–Strauss syndrome (CSS). We agree with them that the presence of mononeuritis multiplex is a serious complication of CSS and warrants more aggressive therapy [1]. We wish to report two further cases of CSS, in Asians, presenting with mononeuritis multiplex. Both patients responded well to monthly pulses of i.v. cyclophosphamide with significant improvement of their neurological signs.

The first patient was a 38-yr-old Indian lady with a 2-yr history of bronchial asthma. She was treated with an inhaled β_2 agonist and inhaled corticosteroid. She presented with a 3-month history of low-grade fever, generalized malaise and symmetrical polyarthralgia. She developed progressive paraesthesiae and weakness affecting all four extremities 2 months after the onset of constitutional symptoms.

On presentation, the patient had bilateral wrist and foot drop and loss of pinprick sensation in a glove and stocking distribution. There were generalized rhonchi on auscultation of her chest. There were multiple purpuric rashes and non-healing ulcers on the dorsum of both feet. Her investigation results are summarized in Table 1. The diagnosis of CSS was made in accordance with the American College of Rheumatology classification criteria [2].

The patient was treated with i.v. methylprednisolone 1 g daily for 3 days followed by oral prednisolone 1 mg/kg daily, which was gradually tapered. In addition, i.v. cyclophosphamide 0.75 g/m^2 (to a maximum of 1 g) was given monthly for 6 months, with subsequent oral azathioprine 2 mg/kg daily. The absolute eosinophil count and elevated inflammatory markers dropped rapidly within days. Her bronchial asthma remained well controlled. There was no progression of her neurological deficits. The vasculitic ulcers were completely healed after 4 months of treatment. After 9 months of treatment, her right wrist extension, hand grip and right foot dorsiflexion muscle power was 5/5 (compared with 3/5 on presentation), the left wrist extension was 4/5 (2/5 on presentation) and the left foot dorsiflexion was 2/5 (0/5 on presentation). Pinprick sensation had returned to normal and paraesthesiae were confined to the tips of her fingers and toes.

The second case was a 68-yr-old Chinese man who had had chronic bronchial asthma and allergic rhinitis since childhood and had a 10-yr history of chronic rhinosinusitis. The patient was diagnosed as having pulmonary tuberculosis in June 2001 and was treated with the standard four-drug regime, consisting of streptomycin, isoniazid, rifampin and pyrazinamide with pyridoxine supplementation. He was on low-dose prednisolone daily for control of his bronchial asthma. The patient presented in August 2002 with a 2-week history of progressive bilateral lower limb weakness and paraesthesiae, low-grade fever and arthralgia. On examination, he had complete bilateral foot drop, loss of pinprick sensation over the sole and dorsum of both feet and lateral aspects of both calves, consistent with the L5 and S1 dermatomes, and loss of proprioception in both feet. His investigation results are summarized in Table 1.

CSS was diagnosed in the absence of other causes of hypereosinophilia. The patient was treated with the same regime as in case 1, with additional i.v. methylprednisolone 500 mg on each pulse of i.v. cyclophosphamide (0.75 g/m^2, to a maximum of 1 g). He completed 6 months of anti-tuberculous treatment and subsequently had isoniazid and pyridoxine prophylaxis until he finished the six i.v. cyclophosphamide pulses. The hypereosinophilia and elevated inflammatory markers resolved within days,