Correspondence

High-dose immunoglobulin in Felty's syndrome

SIR, Felty's syndrome comprises rheumatoid arthritis, splenomegaly, and neutropenia and is regarded as a distinct clinical entity.¹ The mechanism of the neutropenia is obscure. One hypothesis suggests an autoimmune neutropenia involving the spleen as the site of either antibody production or antibody coated neutrophil destruction.² Studies of circulating neutrophils from patients with Felty's syndrome have demonstrated increased levels of neutrophil bound IgG compared with normal individuals and patients with rheumatoid arthritis alone.³ In addition, sera from Felty's patients have increased binding of IgG to normal neutrophils in vitro, postulated to be due either to immune complexes⁴ or to anti-neutrophil antibodies.⁵ Patients with autoimmune thrombocytopenic purpura demonstrate similar immunological abnormalities, with the target cell being the platelet.⁶

Encouraged by previous reports of transient reversal of auto-immune thrombocytopenia⁷ and autoimmune neutropenia⁸ following the infusion of high-dose intravenous IgG, we conducted a pilot study to assess the effects of this treatment in 4 patients with Felty's syndrome. The clinical and laboratory data of the 4 patients are summarised in Table 1. The patients were taking nonsteroidal anti-inflammatory drugs only.

A total dose of 1.2 g of immunoglobulin per kilogram of body weight was infused over 3 days. Daily doses ranged from 15 g to 29 g and were administered over a period of 4 hours. The immunoglobulin was provided by Blood Products Laboratory, Elstree. No side effects were observed in any of the patients under observation. Neutrophil counts were performed daily on a Coulter S Plus (Technicon).

Only one patient demonstrated an increase in the neutrophil count (case 2). This occurred between days 22 and 25, but only by 50% to a maximum count of 820/mm³ ($0.8 \times 10^9/l$). The patient who had a splenectomy showed no change in his neutrophil count. The half life of the infused IgG was 9 days, even shorter than that for homologous IgG in patients with uncomplicated rheumatoid arthritis (13 days), a condition in which hypermetabolism of homologous IgG has been demonstrated.⁹

We conclude that high-dose immunoglobulin infusion is unlikely to be beneficial in patients with Felty's syndrome.

Royal National Hospital
for Rheumatic Diseases,
Bath

MICHAEL AHERN
JAMES HARKNESS
PETER MADDISON
SUSAN FORSKITT

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Table 1 Clinical and laboratory data of 4 patients

Case	Age	Sex	Clinical features	Prior Therapy	Neutrophil count
1	77	F	RA 25 years, neutropenia 5 years, septic arthritis 1976, pneumonia	Gold 1974-76 Corticosteroids 1972	310/mm ³
2	60	F	RA 42 years, numerous chest infections	NSAID	550/mm ³
3	71	M	RA 25 years, splenectomy 1975 for recurrent infections, recurrence of neutropenia 6 months postoperatively	NSAID	220/mm ³
4	61	F	RA 20 years, septic arthritis 1974	Gold 1973	320/mm ³

RA=rheumatoid arthritis. NSAID=nonsteroidal anti-inflammatory drugs.
SI conversion: number of neutrophils/mm³ $\times 10^6$ = number/l.

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Septic arthritis due to *Bacteroides fragilis*

SIR, We read with interest the report of Hart *et al.*¹ of a case of *Bacteroides fragilis* septic arthritis of the wrist in a patient with rheumatoid arthritis (RA). They made the claim that this was probably the first case report of wrist joint involvement due to this organism. By coincidence we reported a similar case of septic polyarthritis due to *Bacteroides fragilis* in a patient with RA earlier in 1982.² This patient had bacteroides sepsis in 9 joints including both wrists, and also responded well to metronidazole treatment.

A joint infection in a patient with RA should not only be considered when one joint suddenly flares up, but should also be borne in mind with a generalised flare-up, and anaerobic cultures should be done after joint aspirations as a routine investigation.

1640 Volkskas Centre,
Van der Walt Str.,
0002-Pretoria,
South Africa

D. SCHORN
J. A. PRETORIUS

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Polymorphonuclear function in Behçet's syndrome

SIR, The recent report by Fordham *et al.*¹ has drawn attention to the role of polymorphonuclear leucocytes (PMN) in the pathogenesis of Behçet's disease. While the aetiology of Behçet's disease remains unknown, immune complex-induced vasculitis with associated systemic inflammatory lesions are recognised key events in its pathogenesis. The occurrence of systemic inflammatory lesions has prompted studies of PMN function in Behçet's disease. Several investigators have found an increased PMN chemotactic response,¹⁻⁵ although a reduced chemotactic response to inulin-activated serum and a normal chemotactic response to casein have also been described.⁶ Phagocytic and adherent properties of Behçet PMN are normal,¹ while leucocyte oxygen consumption in the resting state and after stimulation by phagocytosis of *Staphylococcus albus* are diminished.³ Spontaneous nitroblue tetrazolium reduction

is normal, whereas reduction after endotoxin stimulation is depressed.³

These studies have prompted us to study the production of the toxic superoxide radical O_2^- in response to stimulation with the chemotactic peptide N-formylmethionyl-leucyl-phenylalanine (FMLP) in the PMN isolated from a 27-year-old female suffering from Behçet's disease of 8 years' duration. She had a present or past history of mouth and genital ulcerations, arthritis, and vasculitic skin lesions, thus fulfilling 3 major and one minor diagnostic criteria for Behçet's disease.⁷ At no time did she have eye or neurological involvement. Current treatment consisted of 15 mg of prednisone and 20 mg of piroxicam daily. For the assay of O_2^- produced by the activated PMN, a ferricytochrome C reduction procedure was used.⁸ The production of O_2^- was measured on 2 separate occasions comparing results with those obtained in 2 concurrently studied age and sex-matched healthy controls and with the normal ranges of the rate and quantities of O_2^- production earlier established in our laboratory for 33 normal controls.⁹ After prewarming the isolated PMN for 30 minutes 6-8 duplicate assays of O_2^- production were performed during an approximate 3-hour period. Results are as follows:

	Rate of O_2^- production (nmol O_2^- / 10^6 cells/min)	Total quantity of O_2^- produced (nmol O_2^- / 10^6 cells)
Behçet patient (1st experiment)	9.42, SD 3.68	22.0, SD 4.58
Concurrent control	9.46, SD 2.33	23.9, SD 3.13
Behçet patient (2nd experiment)	9.0, SD 0.42	21.5, SD 0.74
Concurrent control	9.11, SD 0.81	23.08, SD 2.08
Normal controls (33)*	8.90, SD 1.7	22.8, SD 5.7

In this Behçet's patient both the rate as well as the total quantity of O_2^- produced in response to stimulation with FMLP was clearly within normal limits when compared with both concurrent and previously tested controls. Abnormal production of toxic O_2^- radical, a facet of PMN function, which to the best of our knowledge has not been studied before, may therefore not contribute to the generation of the systemic inflammatory lesions encountered in Behçet's disease.

Clinical Sciences Building,
University of Alberta,
Edmonton,
Alberta,
Canada T6G 2G3

CLAES FRIMAN
PAUL DAVIS

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