

# Abnormal polymorphonuclear leucocyte chemotaxis in Behçet's syndrome

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**SUMMARY** Experiments both *in vitro* and *in vivo* have been performed to study the chemotactic response of polymorphonuclear leucocytes (PMNs) in Behçet's syndrome. The experimental results were apparently contradictory. Using modified Boyden chambers we found that the PMNs from patients with Behçet's syndrome responded to a greater extent *in vitro* than normal cells, but with skin chambers placed over abrasions the *in vivo* response was less than normal. The significance of these findings is discussed and related to the histological appearances that may be seen in this condition.

The first evidence of the increased chemotactic activity of polymorphonuclear leucocytes (PMNs) from patients with Behçet's syndrome was reported by Matsumura and Mizushima (1975), and because of this they used colchicine in the treatment of Behçet's syndrome, with apparent success (Mizushima *et al.*, 1977). These findings of increased PMN chemotaxis were supported by Sobel *et al.*, (1977). Using an agarose plate technique these workers produced evidence that both serum and intrinsic cellular mechanisms are responsible for this increase in the chemotactic response.

One patient (case 3), having severe uveitis only, was included, as his sibling has 'definite' Behçet's syndrome, fulfilling the criteria of Mason and Barnes, (1969).

The 21 controls for the *in vitro* study were suffering from noninflammatory diseases such as osteoarthritis and low back pain, having a mean age of 51 years. The 16 controls for the *in vivo* study were either healthy normal persons or patients with osteoarthritis or low back pain, having a mean age of 44 years.

For the methods used see Walker *et al.* (1979).

## Patients and methods

Six patients with Behçet's syndrome were studied by *in vitro* methods, and 5 of these patients were studied by *in vivo* methods. The details of the disease manifestations and treatment are shown in Table 1.

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Table 1 Details of patients, symptoms and treatment

Case no.	Sex	Age	Mouth ulcers	Genital ulcers	Uveitis	Skin lesions	Arthritis	Venous thrombosis	CNS	Treatment
1	F	58	+	+		+	+	+		Colchicine
2	M	36	+		+	+	+	+		Levamisole
3	M	33			+					Topical steroids
4	M	42	+	+	+	+	+	+	+	Colchicine
5	F	50	+			+	+	+	+	Steroids
6*	M	37	+	+	+			+		Steroids

\*Case 6 not studied *in vivo*

## Results

### IN VITRO

The PMNs from patients with Behçet's syndrome migrated to a significantly greater degree towards normal activated plasma than did control cells, as shown in Fig. 1.

Control: Mean  $\pm$  SE =  $66 \pm 3$  PMNs/high power

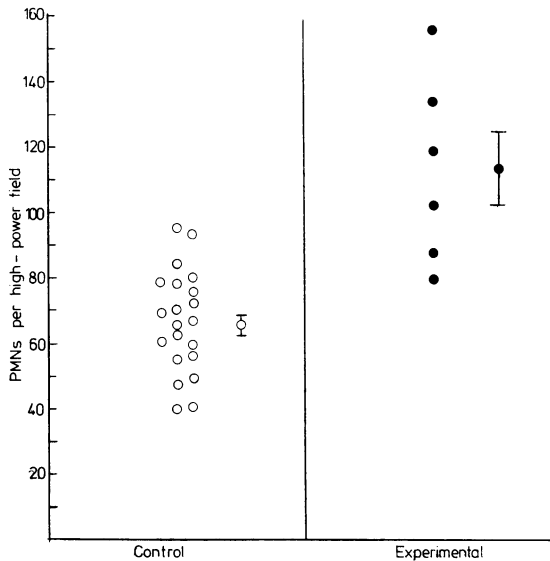


Fig. 1 Response of PMNs from control and experimental groups to activated control plasma. ○ PMNs from control group. ● PMNs from experimental group. Mean ± standard error indicated by circles with bars.

field. Behçet's syndrome: Mean ± SE = 113.1 ± 11.8 PMNs/high power field. 72% increase, P < 0.001 (Student's *t* test).

There was no significant difference in the response of normal cells towards activated plasma of either control patients or of patients with Behçet's syndrome.

IN VIVO

As shown in Fig. 2, there was a clear reduction in the number of PMNs which migrated into skin chambers compared to the control results.

Control: Mean ± SE = 41.1 ± 3.7 × 10<sup>6</sup> PMNs/cm<sup>2</sup>/1 ml serum/24 h. Behçet's syndrome: Mean ± SE = 11.8 ± 2.7 × 10<sup>6</sup> PMNs/cm<sup>2</sup>/1 ml serum/24 h. 72% decrease, P < 0.001 (Student's *t* test).

Discussion

There is an apparent paradox in our results. When the PMNs from patients with Behçet's syndrome migrate through filters in vitro there is evidence of increased responsiveness to normal chemotactic stimuli, as has been reported previously (Matsura and Mizushima, 1975; Sobel *et al.*, 1977). This overactivity may explain the marked PMN infiltration into the synovium and synovial fluid which has been reported to occur in patients with Behçet's syndrome who have an arthropathy

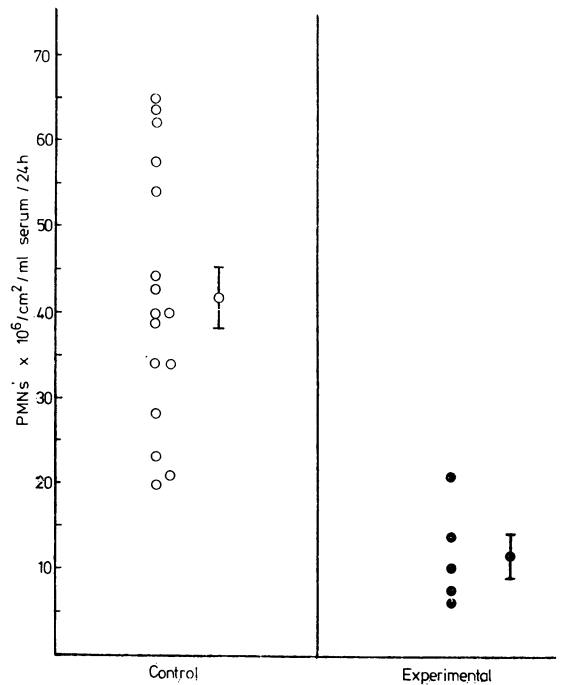


Fig. 2 Comparison of PMN accumulation in skin chambers between control and Behçet's patients. ○ PMNs from control group. ● PMNs from experimental group. Mean ± standard error indicated by circles with bars.

(Vernon-Roberts *et al.*, 1978; Gow, personal communication), and also into the uveal tract and aqueous humour in patients with uveitis (Oniki *et al.*, 1976; Shimada *et al.*, 1972).

Despite the increased responsiveness of PMNs detected in vitro there was a reduction in the number of PMNs which migrated through skin abrasions into chambers in vivo. We have found that in patients with rheumatoid arthritis the in vivo findings reflected the in vitro results (Walker *et al.*, 1979), but the situation in Behçet's syndrome is obviously different.

Histological studies of lesions of the oral mucosa (Lehner 1969) and of induced skin lesions (Haim *et al.*, 1976) show a completely different picture from the synovial histology. The histology of recurrent oral ulceration in Behçet's syndrome shows a predominantly lymphomonocytic picture with a raised mast cell count. Similar appearances are seen in the dermis 12-48 h after a lesion has been induced by needle prick or injection of normal saline.

Skin and oral mucosa are ectodermal in origin, and the synovium and uvea are mesodermal in origin. There are obvious structural differences such as the

absence of basement membrane in the synovium and uvea. It appears that in patients with Behçet's syndrome tissues of these different embryological origins show different inflammatory reactions. A predominantly lymphomonocytic picture is seen in skin lesions and recurrent oral ulceration, which may represent a form of delayed hypersensitivity (Lehner, 1969), responding to an immunomodulatory drug such as levamisole (Lehner *et al.*, 1976).

The predominantly PMN infiltrate in the synovium and uvea, however, may represent an Arthus reaction (Oniki *et al.*, 1976) enhanced by the abnormally high PMN chemotactic response seen *in vitro*, which may be suppressed by colchicine. These histological observations may explain the paradoxical results obtained in this study.

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