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Serum IgE concentrations in complete Behçet's disease

Behçet's disease is a multisystem panvasculitis of unknown aetiology.¹ An immune complex vasculitis is thought to be the basic pathological process in Behçet's disease.² The type of the antigen which occurs in the formation of the immune complex is not yet clear.

This study was designed to clarify the pathogenesis of the disease and suggests a possible link between increased serum IgE concentrations and Behçet's disease.

Four women and 14 men with complete Behçet's disease (age range 22-39 years, mean (SD) age 31.4 (2.09) years) and 12 healthy subjects were examined. There wasn't any age or sex difference in these groups. The serum IgE concentrations, total eosinophil counts in peripheral blood, and peripheral blood film were studied.

The classification and the diagnostic

Results of patients and control studied

Mean (SD) values	Patient	Control	p value
IgE (IU/ml)	132.36 (9.39)	42.94 (4.69)	p < 0.01
Total eosinophil counts (mm ³)	195.67 (0.89)	200.75 (7.80)	p > 0.05
Eosinophils in peripheral blood film	2.56 (0.2)	2.67 (0.30)	p > 0.05
Duration of the disease (years)	8.77 (0.89)		

criteria of the disease were described in 1972 and have gained world wide acceptance.³ According to this classification when four major signs (oral and genital ulcers, non-ulcerative skin lesions, and ocular disease) are present it is accepted as complete Behçet's disease. The diagnosis of Behçet's disease was made according to the diagnostic criteria established by the Research Committee on Behçet's disease.³ The patients studied had no evidence of a personal or family history of atopy. The stools of the patients and healthy subjects were examined microscopically three times over six months. Patients receiving medication who had parasites in their stool were excluded from the study. All the patients were given a complete physical, ophthalmic, and dermatological examination in addition to the routine laboratory tests. Total number of eosinophils in the peripheral blood and peripheral blood film were counted. Serum IgE concentrations were measured with a radioimmunosorbent assay, using a slight modification of the Ceska and Lunk method.⁴

The table shows the total number of eosinophils in the peripheral blood; the peripheral blood film didn't show any significant difference between patients with Behçet's disease and controls (p > 0.05). Serum IgE concentrations in Behçet's disease were higher than those of the controls (p < 0.01). Duration of the disease varied from four to 18 years and there was a positive correlation between serum IgE concentrations and the

duration of the disease (r = 0.85 ± 0.26; p < 0.05).

It has been reported that thrombosis in the great veins and arteries can occur at any stage of Behçet's disease.⁵ IgE mediated antigenic response, probably by action on mast cells or basophils, can induce platelet activation and this activation results in platelet aggregates and perhaps arterial smooth muscle hyperplasia. Such evidence may suggest a reasonable biological pathway linking increased serum IgE concentrations and Behçet's disease.

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MATTERS ARISING

New spiral bacterium in the gastric mucosa: *Gastrospirillum hominis*

We read with interest the paper by McNulty et al¹ and note that they considered *Gastrospirillum hominis* to be responsible for the symptoms of only one of their five patients. We have seen two patients in whom we believe *Gastrospirillum* was a clinically important pathogen.

Case 1

A previously fit woman of 56 presented in March 1987 with a four month history of nausea, malaise, abdominal pain and weight loss. She did not smoke and drank 20 units of alcohol a week. Examination and routine blood tests gave normal results but endoscopy showed widespread submucosal haemorrhages and thickened yellow mucosal folds. Histological examination showed an active

gastritis which was associated with many long tightly coiled spiral organisms. The patient's symptoms resolved spontaneously over six weeks and she refused further endoscopy.

Case 2

In February 1989 a 40 year old man presented with a six year history of recurrent burning epigastric pain and nausea. There were no abnormal signs and routine blood tests provided normal results, but endoscopy showed a mild antral gastritis. Histological examination showed a mild chronic gastritis with many long coiled spiral organisms adjacent to the mucosa. His symptoms worsened and he was treated with bismuth subcitrate (Denol) 1 g only for four weeks. After this he improved and both repeat endoscopy and subsequent histology were normal, with no gastric spiral organisms seen.

Both patients had a gastritis compatible with infection by *Gastrospirillum hominis* and bismuth subcitrate may possibly be an effective treatment. Clarification of this problem must await successful methods of culture.

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Dr McNulty comments:

I do not agree with the conclusions drawn by Dr Logan and his colleagues from their two case histories of "*Gastrospirillum hominis*" in patients attending endoscopy for the investigation of abdominal pain and nausea. They suggest that *Gastrospirillum hominis* was clinically important in these patients—by this I assume they meant that the organism was responsible for their presenting symptoms. The case histories do not bear this out. The symptoms of case 1 resolved spontaneously over six weeks: we do not know whether the organism was present when the woman was asymptomatic, but it is likely that they were as we and others (Heilmann KL, Borchard F. Gastric spiral bacteria. Second International symposium on *Campylobacter pylori*, Bad Nauheim, August 1989, to be published) have shown that the infection is chronic. The second patient's symptoms improved with bismuth subcitrate in parallel with his gastritis, suggesting that the organism, like *C*

pylori, may cause chronic active gastritis. Like *C. pylori*, the number of organisms can probably be suppressed but complete eradication will probably be difficult. Was case 2 endoscoped and assessed symptomatically at a later date? If so, organisms may well have been detectable. Dr Logan and his colleagues may be right that "*Gastrospirillum hominis*" causes non-ulcer dyspepsia, but larger studies are needed, and I think it is still premature to draw conclusions from single patient histories.

Lack of significant effect of therapeutic propranolol on measurable platelet function in healthy subjects

Pamphilon and colleagues have shown that propranolol, a non-selective β blocker, does not significantly inhibit platelet function when therapeutic doses are administered to healthy subjects.¹ They suggest that a different response might be obtained in patients with cardiovascular disease and hyperactive platelets. Some additional comments may be of interest.

The authors discuss the possibility that β blockers exert their action in situations where circulating catecholamine concentrations are very high. We assessed the effect of acute hypoglycaemia (during insulin stress tests) on various metabolic and haemostatic variables in healthy subjects who had been given either placebo, nadolol, or propranolol, orally, for 10 days.² These non-selective β blockers significantly inhibited some catecholamine-mediated effects (hypokalaemia; a rise in factor VIII), but only propranolol had a marginal inhibitory effect on platelet aggregation.

In another study we found that platelet aggregation induced by adrenaline was significantly decreased in samples obtained from patients with a diagnosis of acute myocardial infarction or ischaemic heart disease who were taking β blockers when compared with a similar group of patients not taking such medication.³ Beta blockade may, indeed, be associated with platelet antiaggregatory effects but that these may only be elicited in conditions associated with pronounced platelet hyperaggregability such as myocardial infarction and ischaemic heart disease.³

There are also important methodological considerations in assessing the effect of drugs on platelet function. For example, whole blood platelet aggregometry (impedance or "free" cell count techniques) allows the effects of drugs on platelet, red, or white cell interactions to be measured. This has occasionally resulted in a better definition, even at lower doses, of the effects of several drugs, such as nifedipine, dipyridamole, heparin and ethanol, on platelet aggregation.⁴ Mean platelet volume, measured by very sensitive techniques (using a Coulter C256 channelyser), may also be another very sensitive method to assess the effect of a variety of agents on platelets.⁵

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Dr Pamphilon et al comment:

The comments of Barradas and Mikhailidis are of interest and point to the relevant mechanism whereby β blockers may exert a beneficial effect in patients with myocardial infarction and ischaemic heart disease—that is, modulation of platelet hyperaggregability in susceptible subjects.¹ The observation that propranolol but not metoprolol enhances platelet aggregatory responses to adrenaline remains unexplained.² Thus it seems likely that blockade of the effects of high concentrations of circulating catecholamines is of central importance. We did not observe significant changes in the mean platelet volume in either group of subjects using the Coulter S Plus 4 rather than the Coulter C256 channelyser.

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Leukaemic phase of mantle zone (intermediate) lymphoma: its characterisation in 11 cases

In his parody of lymphoma classifications a distinguished editor of the *Journal of Clinical Pathology* reflected the confusion and cynicism of the average pathologist at the perceived hair-splitting of the lymphomaniacs in their attempts to categorise non-Hodgkin's lymphomas.¹ The confusion over the classification of low grade non-Hodgkin's lymphomas is well illustrated by the report on the leukaemic phase of mantle zone (intermediate) lymphoma by Pombo de Oliveira et al.² The category of intermediate cell lymphoma was first proposed by Berard et al.^{3,4} It was noted that, "these tumours contain some lymphocytes resembling those of well differentiated lymphocytic tumours and some atypical cells more closely resembling the poorly differentiated lymphocytes of nodular or follicular lymphoma".⁵ It is now widely accepted that lymphocytic lymphoma of intermediate differentiation (INT) and mantle zone lymphoma (MZL) are the same tumour, perhaps at different stages of evolution,⁶ and Jaffe et al have proposed that MZL should be the preferred term.⁵

The category of centrocytic lymphoma was introduced into the Kiel classification to describe a diffuse lymphoma of small, slightly irregular lymphoid cells that were originally thought to be of follicle centre derivation (hence the name centrocyte).⁷ Subsequent studies have shown that centrocytic lymphoma is a distinct entity, clinically, morphologically, and phenotypically distinct from follicle centre cell lymphoma.^{8,9} It is unfortunate and confusing that the term "centrocytic lymphoma" is still applied to this tumour even after it has been shown not to be of centrocyte origin.

Many authors have suggested that INT/MZL is the same entity as centrocytic lymphoma.

In a review of INT/MZL, Jaffe et al concluded that this tumour, "clinically, morphologically, and immunophenotypically appears virtually identical to centrocytic lymphoma of the Kiel classification".³ Pombo de Oliveira et al seem to have retreated slightly from that position and conclude that, "centrocytic lymphoma and INT are clearly closely related morphologically and phenotypically but may not be entirely interchangeable pathological entities".² The authors further state that, "perhaps the application of molecular, genetic, or cytogenetic markers may allow such cases to be appropriately classified in future". In fact, cytogenetic studies suggest a close relation between INT and lymphocytic lymphoma.¹⁰

It is my opinion that the recognition of INT based on the finding of a mixture of cells with round and cleaved nuclei is flawed. It has been recognised for years that quite apart from biological variability, fixation and processing artefacts can induce considerable variation within a single neoplasm. Lymphocytic lymphomas and centrocytic lymphomas have been well described and defined histologically. It can, however, be difficult to separate these neoplasms on the morphology of the lymphoid cells alone, particularly in suboptimally fixed tissues. There are, however, many other features that assist in the differentiation of these two neoplasms, perhaps the most reliable being the identification of paraimmunoblasts which are always present in variable numbers in lymphocytic lymphomas and never found in centrocytic lymphomas. On the basis of this criterion, figs 7 and 8 of the paper by Pombo de Oliveira et al² show a centrocytic lymphoma and figs 10 and 11 a lymphocytic lymphoma. Clearly, the status of INT will not be resolved until a more reliable means of identification, other than variability of nuclear shape, is used to select cases for study.

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