**LETTERS TO THE EDITOR**

Negative antineutrophil cytoplasmic antibodies in Behçet's disease

Sir: Antineutrophil cytoplasmic antibodies have been detected in patients with idiopathic necrotising and crescentic glomerulonephritis, active Wegener's granulomatosis, and microscopic polyangiitis. \(^1\)

Behçet's disease, an inflammatory disorder of unknown cause, is characterised by oral and genital ulcers associated with systemic manifestations due to large and small vessel vasculitis, ocular, cutaneous, and arthritic symptoms. \(^2\) In the central nervous system involvement are often the translation of small vessel vasculitis. \(^3\) Crescentic glomerulonephritis has also been reported. \(^4\)

Polymorphonuclear leucocytes have been implicated in the pathophysiology of Behçet's disease. Lesions are characterised histologically by acute inflammation and an intense infiltration of polymorphonuclear leucocytes with small vessel necrosis, especially at mucosal and cutaneous sites. \(^5\) The increased chemotaxis and random motility of polymorphonuclear leucocytes in Behçet's disease have been confirmed in several studies, and it has been suggested that a cytoplasmic polymerase dysfunction in neutrophils is responsible for this increased activity. \(^6\) To appreciate better the role of polymorphonuclear leucocytes in this disease it would be informative to study antineutrophil cytoplasmic antibodies in patients with active and inactive Behçet's disease.

Twenty eight patients (27 male, one female) with a mean (SD) age of 40 (3) years (range 28-56) were studied. \(^7\) All patients had buccal aphthosis associated with at least two of the following criteria: genital aphthosis, cutaneous lesions, uveitis, and positive paucity testing. The incidence of clinical manifestations with reported vasculitis is as follows: uveitis (12 cases), central nervous system disease (six cases), thrombophlebitis (six cases), erythema nodosum-like lesions (five cases), and antinuclear antibodies (one case). \(^8\) The disease was active in 15 patients and inactive in 13.

Indirect immunofluorescence on human neutrophils was used to detect antineutrophil cytoplasmic antibodies, according to the method of Van der Woude. \(^9\) None of the 28 serum samples from the patients with Behçet's disease was positive for these antibodies (titres >1/10). The fluorescence was negative in 27 patients and positive in one at a titre of 1/10.

This study strongly suggests that antineutrophil cytoplasmic antibodies cannot be incriminated as contributing to the abnormalities of polymorphonuclear leucocytes in Behçet's disease. 

---

**Pregnancy loss, menopause, and the onset of rheumatoid arthritis**

Sir: Spector and Silman suggest that spontaneous abortion may have a protective effect on the development of rheumatoid arthritis (RA). \(^1\) This seems at odds with a previous study from the same group reporting that first degree relatives of women with RA who are destined to develop RA themselves have more frequent adverse pregnancy outcomes in the form of perinatal deaths. \(^2\) The authors attempt to reconcile the two studies by suggesting that late reproductive loss is only important in those 'primarily susceptible to rheumatoid arthritis'. Although this is an interesting concept, further information to support this hypothesis has not been obtained. In the first study the obstetric histories of the female probands were not given, yet it may be informative to know how they compared with those reported for their relatives who were either affected or non-affected with RA. In the second study the family histories of the patients with RA were not stated, although presumably some first degree relatives are likely to have RA. A study performed by us supports the findings of the second study. After interviewing a large number of women with RA and other autoimmune disorders we found that pregnancy loss is not a risk factor for the later development of RA. \(^3\)

Undoubtedly, pregnancy loss has an ameliorating effect on the activity of RA. Most women develop RA having completed their pregnancies, however. \(^4\) The influence of other hormonal factors, such as the menopause, deserves more attention. From an interview of 117 women with RA in our previous study it was noticeable that a large number had onset of their arthritis about the time of menopause, an observation not included in our paper. Age of onset of first symptoms of RA and age at menopause (for this purpose defined as cessation of menses) were obtained from all women in the study, in different sections of a questionnaire, with confirmation by recourse to hospital notes when possible. Seventeen women who had undergone hysterectomy and 17 women who had premenopausal women were excluded from this analysis.

There seemed to be a broad peak of age of onset of arthritis coinciding with the expected age of menopause (fig 1). When the onset of arthritis was analysed in relation to the menopause in individual patients there were a larger number reporting onset of arthritis and menopause within an encompassing five year interval (fig 2). Undoubtedly this finding is due partly to an unconscious bias in relating major life events to each other, especially considering our crude definition of the menopause. Nonetheless, it is biologically plausible that hormonal fluctuations occurring during the menopause may trigger onset of RA in some women, perhaps by the same mechanism as that occurring in postpartum flares of arthritis in younger women.

These observations at least merit a prospective study, including of appropriate, as a further investigation of the role of hormone function in women developing RA. Our epidemiological colleagues may also be able to tell us eventually whether hormone replacement therapy is more advantageous than imagined, or perhaps the opposite.

---

**Correspondence to: Dr M Hamza, BP 45, El Menzeh 104, Tunisia.**


---

**Figures**

1. *Age of onset of arthritis.*

2. *Onset of arthritis in relation to the menopause.*
Negative antineutrophil cytoplasmic antibodies in Behçet’s disease.

M Hamza and O Meyer

Ann Rheum Dis 1990 49: 817
doi: 10.1136/ard.49.10.817-a

Updated information and services can be found at:
http://ard.bmj.com/content/49/10/817.1.citation

These include:
Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/