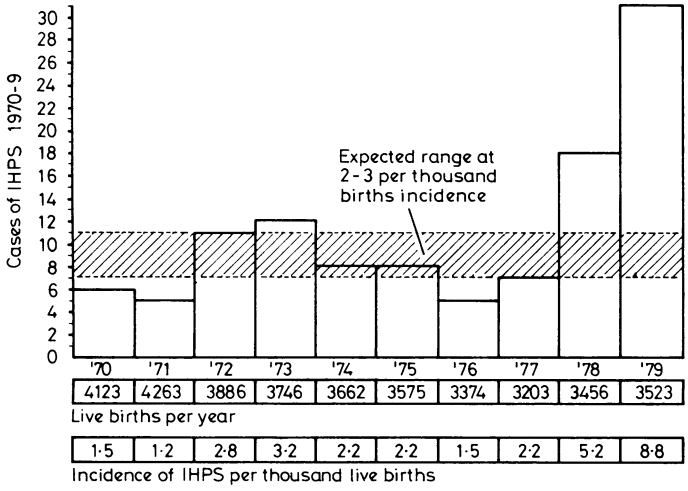
through the decade ($\chi^2 = 57{\cdot}7$, df = 9, $p \ll \ll 0{\cdot}001$), mainly owing to the high incidences in 1978 and particularly 1979.

I analysed the 31 cases occurring in 1979 in more detail to see whether the expected associations had been distorted. The male to female ratio was 27:4 (6·8:1). Firstborn children constituted 42% of cases (13/31) compared with 31% of live-born children. The number of affected infants born each month, expressed as a percentage of births in that month, rose throughout the year, being lowest in February and highest in October. These findings agree with those of Dodge,[2] but the cases are too few to permit statistical analysis.

Information on stress in pregnancy was obtained by postal questionnaires from 27 mothers of affected infants and 17 control mothers taken at random from women whose infants were admitted to hospital in the first weeks of



Number of cases of infantile hypertrophic pyloric stenosis (IHPS) during 1970-9 and incidence per 1000 live births.

life with a serious acquired disorder during 1979. Questions on stress were based on those used by Revill and Dodge.[3] No significant difference was found between the two groups.

Information on drugs given to the mothers when pregnant and the affected infants was obtained from obstetric notes and from questionnaires sent to general practitioners and mothers of affected infants. The only drugs received by more than four of the 31 women were iron and vitamin preparations during pregnancy and promazine hydrochloride, pethidine, and nitrous oxide during labour. These have been used routinely in all women for many years. No one drug was received by more than three of the 31 infants, so that no drug can be implicated in causing the condition.

The addresses of affected infants were evenly distributed throughout the area in proportion to population density. The fathers of cases were in 20 different types of employment. Twenty-four general practitioners referred the 31 cases.

Comment

The incidence of infantile hypertrophic pyloric stenosis in the Central Region of Scotland was remarkably high in 1979. The cases show no divergence from the usual patterns of association of the disorder that might suggest a new factor in its aetiology. It will be interesting to find out whether the change in incidence is transient or permanent, local or national.

I wish to thank Dr A L Speirs and Dr J Inall, consultant paediatricians, Stirling and Falkirk Royal Infirmaries, for their encouragement and permission to make these observations on their patients, and Mr R J Prescott, Medical Computing and Statistics Unit, Edinburgh Medical School, for statistical advice.

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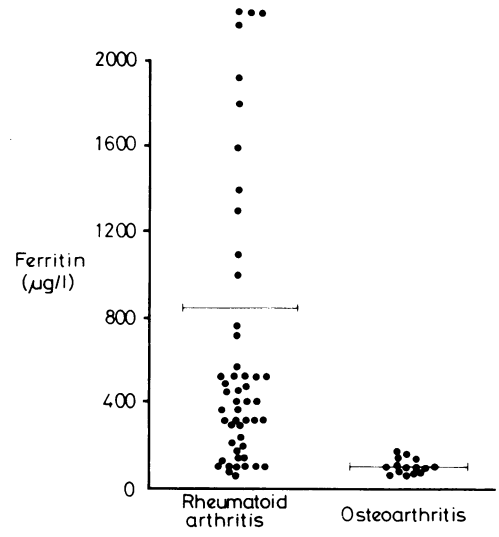
Stirling and Falkirk Royal Infirmaries, Scotland
ALISON M KERR, DCH, MRCP, paediatric registrar (present appointment: paediatric registrar, Royal Hospital for Sick Children, Glasgow, Scotland)

Synovial fluid ferritin in rheumatoid arthritis

In any inflammatory state a shift of iron occurs from the transferrin and red-cell compartments into reticuloendothelial cells.[1] In rheumatoid arthritis the inflamed synovial membrane shares many features of a reticuloendothelial organ[2] and the type A phagocytic cells contain abundant iron.[3] This iron is stored predominantly as intracellular ferritin, a water-soluble derivative of the protein apoferritin, potentially able to diffuse into synovial fluid. We therefore looked for ferritin within synovial fluid in an attempt to explore the relation between the inflamed synovium and the anaemia so prevalent in rheumatoid patients.

Patients, methods, and results

We studied 50 patients with rheumatoid arthritis and 15 with osteoarthrosis with associated effusion. Ferritin was measured in serum and synovial fluid by radioimmunoassay (Gammadab I^{125} ferritin kit; Travenol Lab). Ferritin was found in all synovial fluid samples. In patients with osteoarthrosis the concentrations were similar to serum concentrations, while in rheumatoid arthritis they were significantly higher ($p < 0{\cdot}0001$) and occasionally 20 times the corresponding serum value. The figure shows the distribution of fluid ferritin between the two groups; the difference is significant ($p < 0{\cdot}0001$). In patients with rheumatoid arthritis a significant correlation existed between serum ferritin and synovial fluid ferritin concentrations ($r = 0{\cdot}4$, $p < 0{\cdot}01$) and a negative correlation between synovial fluid ferritin and haemoglobin concentrations ($r = -0{\cdot}3$, $p < 0{\cdot}05$).



Concentrations of ferritin in synovial fluid in patients with rheumatoid arthritis and osteoarthritis.

Serum ferritin concentrations were not significantly different between the two groups, though both the highest and lowest values occurred in the patients with rheumatoid arthritis (mean ± SD 158 ± 241 μg/l in patients with rheumatoid arthritis and 104 ± 97 μg/l in those with osteoarthritis). No correlation was found between serum ferritin and haemoglobin concentrations.

Comment

The discovery of abundant ferritin within synovial fluid of patients with rheumatoid arthritis is of interest. It has been suggested that iron within the synovial membrane arises from the continued oozing of blood from the vascular granulation tissues into the synovial cavity, and that this may contribute appreciably to the anaemia of rheumatoid arthritis.[3]

Another hypothesis, which we favour, is that the synovial reticuloendothelial cells actively compete with other organs of the reticuloendothelial system for iron derived predominantly from effete circulating blood cells. This iron is stored as ferritin and the amount reflected by the synovial fluid ferritin concentration. The negative correlation between haemoglobin and synovial fluid ferritin concentrations might suggest that iron within the synovium contributes to the anaemia of rheumatoid arthritis. The significantly higher concentrations of ferritin in synovial fluid than serum, and the significant

correlation between the two, suggest that the serum ferritin concentration partly reflects the ferritin load within the synovium. This explains the apparent anomaly, occasionally found in patients with rheumatoid arthritis, whereby serum ferritin concentrations are raised with disproportionately low marrow iron stores. We postulate that in these cases the reticuloendothelial cells within the synovial membrane, stimulated by the inflammatory process, actively take up iron and store it as ferritin, in direct competition with the bone marrow. Here, because of some as yet unspecified block in the release of iron from intracellular ferritin inflammatory states, it is no longer freely available for haemoglobin synthesis.[4]

Thus concentrations of ferritin in synovial fluid may reflect reticuloendothelial activity within the synovial membrane, and these observations merit further study.

We thank Dr M Thompson, department of rheumatology, Royal Victoria Infirmary, Newcastle upon Tyne, for his help with this study.

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Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath BA1 1RL
D R BLAKE, MRCP, senior registrar
P A BACON, FRCP, consultant rheumatologist

Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP
E J EASTHAM, MRCP, senior registrar
K BRIGHAM, FIMLS, senior medical scientific officer

Galactorrhoea after withdrawal of bromocriptine

We describe a young woman with Parkinson's disease who developed transient galactorrhoea and hyperprolactinaemia after withdrawal of treatment with bromocriptine.

Case report

A 21-year-old housewife presented in 1975 with signs of Parkinson's disease limited to the right side. There was no history of encephalitis or treatment with drugs and no relevant family history. Results of the following investigations were normal: skull radiography, electroencephalography, isotope brain scan, computed tomography, slit-lamp examination of the cornea, and serum caeruloplasmin concentration.

In October 1976 she began taking levodopa and carbidopa. In August 1977 she developed involuntary movements of both legs, and her treatment was changed to benzhexol alone. While taking this she became increasingly hypokinetic, and in November 1977 began taking bromocriptine, 5 mg three times daily then 10 mg three times daily after one month.

There was considerable improvement in the hypokinesia without dyskinesia and she remained well until the last quarter of 1979, when she began to show the "on-off" phenomenon in addition to developing signs of Parkinsonism on the left side. Treatment with bromocriptine was stopped on 6 December 1979 and she continued taking benzhexol alone. Three weeks later she noted enlargement of the breasts and could express milk easily from both. Her menstrual periods remained normal. Serum prolactin concentration, first measured on 28 January 1980, was raised at 1950 mU/l (normal range 80-390 mU/l). During the next three months the galactorrhoea resolved spontaneously, and the serum prolactin concentration returned to normal (293 mU/l on 5 March 1980). When the basal prolactin concentration had fallen to 435 mU/l there was a large increase in prolactin concentration after the intravenous injection of 200 μg thyrotrophin-releasing hormone (table).

Tomograms of the pituitary fossa showed no evidence of pituitary tumour. The following were normal: serum total thyroxine concentration, basal serum thyrotrophin concentration, the response of serum thyrotrophin concentration to intravenous thyrotrophin-releasing hormone, basal concentrations of serum gonadotrophins and the response of these to intravenous gonadotrophin-releasing hormone, and diurnal variation in plasma cortisol concentration. An eight-hour water-deprivation test gave a normal result.

Response of serum thyrotrophin and prolactin concentrations to intravenous injection of 200 μg thyrotrophin-releasing hormone

Time after injection (min)	Thyrotrophin (mU/l)	Prolactin (mU/l)
0	2·7	435
20	12·6	4368
60	11·6	2246

Comment

Bromocriptine inhibits the secretion of prolactin from the anterior pituitary. There have been no other reports of hyperprolactinaemia after stopping treatment with bromocriptine for Parkinson's disease. In patients with hyperprolactinaemia, however, serum prolactin concentrations may return to pretreatment values when bromocriptine is withdrawn.

The occurrence of galactorrhoea and hyperprolactinaemia in our patient three weeks after stopping treatment with bromocriptine therefore raised the possibility of an underlying lesion, such as a prolactinoma, that had been masked by giving bromocriptine. Radiography of the pituitary fossa, however, showed no evidence of a tumour; the response of serum prolactin concentration to intravenous thyrotrophin-releasing hormone was not in keeping with a prolactinoma[1]; and the spontaneous resolution of the hyperprolactinaemia was inconsistent with any underlying abnormality of prolactin secretion.

Dopamine inhibits the secretion of prolactin, and brain dopamine is depleted in Parkinson's disease. Serum prolactin concentrations in patients with untreated idiopathic Parkinson's disease, however, are normal or only slightly increased,[2] suggesting that hypothalamic dopaminergic neurones are relatively unaffected by the disease. Galactorrhoea that persisted for five years has been described in one case of classical postencephalitic Parkinson's disease,[3] but the assay for serum prolactin was not then available. The aetiology of our patient's Parkinson's disease is uncertain, but the spontaneous resolution of the hyperprolactinaemia is inconsistent with any association between the high prolactin concentrations and Parkinson's disease itself. We therefore suggest that the transient hyperprolactinaemia in our patient represented an otherwise undescribed rebound phenomenon after withdrawal of bromocriptine.

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Royal Infirmary, Edinburgh EH3 9YW
B PENTLAND, MRCP, lecturer in neurology
J S A SAWERS, MRCP, medical registrar

Correction

Nocturnal enuresis and the buzzer alarm: role of the general practitioner

An error occurred in this article by Dr G C Close (16 August, p 483). In the footnote the address of N H Eastwood and Son Ltd, makers of the Eastleigh alarm, should have read "70 Nursery Road, London N14 5QH."