

gastroduodenoscopy was normal. Biopsy of rectal tissue was normal and negative for amyloid. Liver and spleen scan confirmed hepatosplenomegaly. Splenoportography showed normal splenic and portal veins with no varices. Liver biopsy showed aggregates of inflammatory cells around portal tracts. Splenomegaly is a feature not previously described in Behçet's disease. The possibility of the patient having a lymphoma led to a diagnostic laparotomy. The spleen weighed 1330 g but showed no specific histological abnormality.

(2) A 17-year-old girl presented in November 1973 with a 10-year history of oral and genital ulcers. She also complained of facial swelling, intermittent fever with temperature up to 40 C, and transient rashes. She had erythema nodosum-like lesions on her legs. On admission she had a tachycardia of 130 beats/min. The spleen was palpable 3 cm below the costal margin. Haemoglobin was 13.7 g/dl, white blood count  $7.5 \cdot 10^9/l$  ( $7500 \text{ mm}^3$ ) with relative lymphocytosis, and ESR 20 mm in the first hour. The serum aspartate aminotransferase (serum AST; SGOT) was 70 IU/l. Alkaline phosphatase was normal. Chest x-ray examination showed peripheral areas of consolidation in both upper lobes. Paul-Bunnell toxoplasma and brucella tests were normal. The tachycardia, fever, and facial swelling settled within 24 hours of starting treatment with prednisone 40 mg/day. Over the course of the next year she was readmitted on four occasions with facial swelling, fever, tachycardia, and pulmonary infiltrates that always responded to prednisone in high doses. The splenomegaly persisted throughout the illness. On one occasion the spleen was palpable at the umbilicus, but rapidly regressed with prednisone treatment to 3 cm below the costal margin by the next day. Two years later, when aged 19, she was admitted elsewhere with an exacerbation of Behçet's disease, and subsequently died. At necropsy the spleen weighed 560 g: its histology was normal.

### Comment

Gastrointestinal manifestations of Behçet's disease are ill-defined. Apparently the small intestine is most often affected.<sup>3</sup> Radiological examination of 85 Japanese patients, 50 of whom had symptoms such as diarrhoea, abdominal pain, and distension, showed dilatation, gas and fluid retention, and segmentation.<sup>3</sup> Lymphangiectasia of the small intestine and ulcerative colitis have been reported. But no gastrointestinal symptoms were recorded in a series of 41 patients from Israel.<sup>2</sup> The gastrointestinal tract was affected in three out of a recent series of 32 patients—one had Crohn's disease, another a resection of the caecum for a non-specific ulcer, and a third recurrent anal ulceration.<sup>4</sup> Two other cases of Behçet's disease and splenomegaly have been reported.<sup>2,5</sup> In both a cause other than Behçet's disease was considered responsible for the splenomegaly—namely, thalassaemia trait<sup>2</sup> and superior vena cava thrombosis.<sup>5</sup>

We thank Professor D O'B Hourihane, Trinity College, Dublin, for the necropsy details in case 2.

<sup>1</sup> Behçet, H, *Dermatologische Wochenschrift*, 1937, **105**, 1152.

<sup>2</sup> Chazek, T, and Fainaru, M, *Medicine*, 1975, **54**, 179.

<sup>3</sup> Oshima, Y, et al, *Annals of the Rheumatic Diseases*, 1963, **22**, 36.

<sup>4</sup> Chamberlain, M A, *Annals of the Rheumatic Diseases*, 1977, **36**, 491.

<sup>5</sup> Kansu, E, et al, *Quarterly Journal of Medicine*, 1972, **41**, 151.

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## Serum ferritin during unmaintained remission in acute lymphoblastic leukaemia

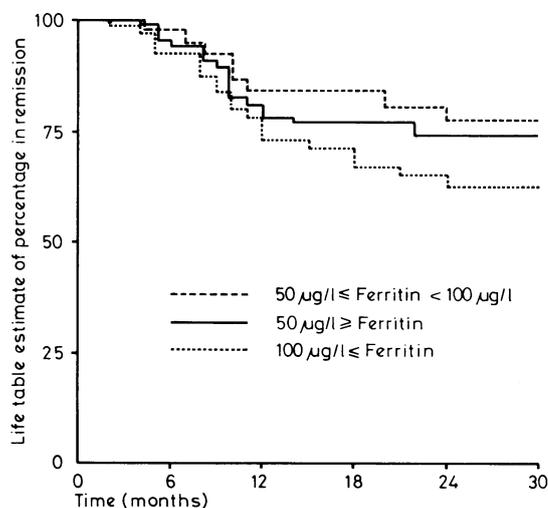
In children with acute lymphoblastic leukaemia (ALL) serum ferritin concentrations are often raised at presentation before treatment. During chemotherapy much higher values may be reached but they often return to normal in patients who remain in remission after stopping treatment.<sup>1</sup> A raised serum ferritin concentration in ALL might therefore be useful as a guide to prognosis and as a sign of early relapse in patients in remission and off chemotherapy.<sup>1</sup> To test this

hypothesis we carried out a prospective study of serum ferritin concentrations in patients with ALL in unmaintained remission.

### Patients, methods, and results

Serum samples were obtained after the end of chemotherapy from all patients in the UKALL trials I-III throughout the United Kingdom between October 1974 and January 1977, and subsequent samples were requested at three-monthly intervals until the patients relapsed. A total of 202 patients were studied (116 males and 86 females). Their ages ranged from 2 to 28 years (mean 8.3 years). Serum ferritin concentrations were measured by immunoradiometric assay.<sup>2</sup> Serum iron, total iron binding capacity, and serum aspartate aminotransferase were also measured in each patient. The relationship between length of remission and initial serum ferritin concentration was investigated using the log-rank test.<sup>3</sup>

Out of the 202 patients in the trial, 53 (26%) relapsed during the follow-up period, which varied from 4 to 45 months. In 151 of them, including 42 who relapsed, an initial serum ferritin value was obtained within six months of stopping treatment. There was no significant difference between the distributions of initial values in those who relapsed and those who did not (Kolmogorov-Smirnov test  $D = 0.126$ ,  $P > 0.10$ ). The duration of remission was not related to the initial ferritin value when patients were divided into two groups using 50 or 100  $\mu\text{g/l}$  as the dividing line ( $\chi^2 = 0.18$ ,  $P > 0.6$  and  $\chi^2 = 1.88$ ,  $P > 0.10$  respectively) (figure). When the 24 patients with serum



Life table estimate of percentage of patients in remission for patients with serum ferritin concentrations less than 50  $\mu\text{g/l}$  (—), patients with serum ferritin concentrations between 50 and 100  $\mu\text{g}$  (---), and patients with serum ferritin concentrations greater than 100  $\mu\text{g/l}$  (....). Time scale represents months from cessation of chemotherapy.

ferritin concentrations greater than 200  $\mu\text{g/l}$  were compared with the remaining 127 there was still no significant difference in relapse rate ( $\chi^2 = 0.06$ ,  $P > 0.8$ ). Two or more sequential ferritin measurements were performed in 156 of the 202 patients studied, including 36 who relapsed. There was a significant fall in ferritin concentration between the first and last measurement (sign test,  $P < 0.001$ ). In the 36 patients who relapsed the fall in serum ferritin concentration was continued when the two values immediately before relapse were compared (Wilcoxon matched pairs signed rank test,  $P = 0.035$ ). The serum ferritin concentration was not related to age, sex, or serum iron or aspartate aminotransferase concentrations.

### Comment

In an earlier study<sup>1</sup> we showed that the serum ferritin concentration in children with newly diagnosed ALL was over 10 times higher than normal and that after the completion of successful chemotherapy the concentration fell to normal levels. The low concentrations found in long-term survivors suggested that the serum ferritin might be a useful prognostic indicator and aid in predicting relapse. The results of the present study provide no evidence that the serum ferritin concentration within six months after the beginning of an unmaintained remission in ALL is related to length of remission or that serial measurements of the concentration could be used in predicting relapse. One explanation for these negative findings may be that the ferritin assay using an anti-spleen ferritin antibody is not sensitive

enough to detect small amounts of possibly abnormal serum ferritin derived from leukaemic cells. Isoelectric focusing techniques have shown characteristic isoferritin profiles for several normal tissues and immunological differences can also be shown using specific antisera.<sup>1</sup> If immunological differences between leukaemic and normal ferritins exist it may be possible to produce an antibody directed against leukaemic cell ferritin; assays using such an antibody might be expected to yield data of clinical relevance in acute leukaemia.

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<sup>1</sup> Parry, D H, Worwood, M, and Jacobs, A, *British Medical Journal*, 1975, **1**, 245.

<sup>2</sup> Jones, B M, and Worwood, M, *Journal of Clinical Pathology*, 1975, **28**, 540.

<sup>3</sup> Peto, R, *et al*, *British Journal of Cancer*, 1977, **35**, 1.

<sup>4</sup> Wagstaff, M, Worwood, M, and Jacobs, A, *Biochemical Journal*, 1978, **173**, 969.

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## Antibiotics and respiratory illness in general practice: prescribing policy and work load

Twenty-five million prescriptions for antibiotics are written by general practitioners annually for new episodes of respiratory illness.<sup>1</sup> Apart from the treatment of relevant morbidity the belief remains that withholding antibiotics creates extra subsequent work, particularly work "out-of-hours." This retrospective study examines the relationship between antibiotic prescribing policy on new respiratory illness and consulting patterns in a group practice.

### Patients, methods, and results

The practice was a three-partner one caring for some 6000 city patients. A fourth doctor worked in the practice on a regular part-time basis and a trainee was employed. The following three groups of patients, all registered continuously with the practice since birth, were studied: (1) all 50 born in 1970, (2) all 60 born in 1960, (3) all 43 born in 1950 and 1951. The study covered the seven years 1970-6. For each consultation for a new respiratory symptom a note was made of the doctor consulting, any antibiotic prescribed, and any further consultation within two weeks and what was then prescribed. "Failure" of treatment was defined as the prescription of either an antibiotic within two weeks of a new consultation at which no antibiotic had been prescribed or a change of antibiotic for a patient who had received an antibiotic at a new respiratory consultation within the previous two weeks. Out of 856 new respiratory consultations antibiotics were prescribed at

639 (75%); 53 "failures" of treatment were noted, an incidence of 6%. The "failure" rate was the same for all doctors working in the practice although the antibiotic prescribing policies ranged widely from 48% to 88% (table). Antibiotics were prescribed at 73% of 521 consultations with the youngest group of patients and 8% of consultations were failures. The trainees had double the failure rate (11%) of the more experienced doctors (6%) in this age group. There were only five failures in the 216 consultations with the intermediate age group (77% received antibiotics). Out of 119 consultations with young adults 79% received antibiotics and 7% failed. Twenty of the 53 failures occurred after not prescribing an antibiotic at the first consultation and 33 arose despite prescribing an antibiotic at the first consultation. An expected new respiratory illness consultation rate for the patients studied was estimated from the National Morbidity Study.<sup>2</sup> The ratio of actual to expected consultations in the 0-6 age group was 521:392 (an excess of 33%), in the 10-16 age group 216:156 (an excess of 38%), and in the 20-26 age group 120:102 (an excess of 18%). The overall expected figure of 650 consultations was exceeded by 31%, at a total of 856 consultations.

### Comment

Only limited conclusions may be drawn from a retrospective study of even good practice records. The apparent discrepancy in the amount of work attributed to the three partners is explained thus: partner one sees more elderly patients; partner two consults faster than his colleagues and sees more patients overall; partner three joined the practice three years after the start of the study period (there is no evidence that his prescribing to very young infants was different from his overall prescribing policy for young children). A policy of high antibiotic prescribing apparently does not reduce the number of patients seeking further consultation and change of treatment in the acute phase of the illness. An overall policy of prescribing antibiotics to three patients out of four with new respiratory illness (three out of five is the area average<sup>3</sup>) apparently creates more follow-up work attributable to changing antibiotics than to having to initiate them. Trainees seem less able to prescribe effectively to children (or to "sell" their initial management policy to the parents) than are more experienced doctors. An above average practice antibiotic prescribing frequency appears to be associated with an above average respiratory illness consultation rate.

The absence of any support for the belief that prescribing antibiotics on a large scale saves work may, in conjunction with other recent work,<sup>4,5</sup> encourage doctors to make the initial move towards educating and away from prescribing that should eventually snowball to the benefit of doctor, patient, and society.

We thank Drs J Gauld, I Ross, and R Strachan for their interest and for access to their practice records.

<sup>1</sup> *British Medical Journal*, 1974, **3**, 1.

<sup>2</sup> Office of Population Censuses and Surveys, *Morbidity Statistics from General Practice, Studies on Medical and Population Subjects No 26*. London, HMSO, 1974.

<sup>3</sup> Howie, J G R, *et al*, *Journal of the Royal College of General Practitioners*, 1971, **21**, 657.

<sup>4</sup> Marsh, G N, *British Medical Journal*, 1977, **2**, 1267.

<sup>5</sup> Thomas, K B, *British Medical Journal*, 1978, **1**, 1327.

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Number of consultations for new respiratory illness by doctors in a group practice and frequency of antibiotic prescribing and of treatment "failures"\*

	Partner 1	Partner 2	Partner 3	Part-time doctor	Trainees	Total
Consultations	132	340	104	65	215	856
Antibiotics prescribed	97 (73%)	298 (88%)	71 (68%)	31 (48%)	142 (66%)	639 (75%)
Failures	10	16	7	4	16	53
Percentage of failures	8%	5%	7%	6%	7%	6%

\*As defined in text.