Management of Acute Iron Poisoning

SIR,—Drs. D. G. D. Barr and D. K. B. Fraser (6 March, p. 657) suggest that there may be potential danger in giving large doses of the chelating agent Desferal (desferrioxamine B mesylate) by mouth in the management of acute iron poisoning, because of the possible tissue toxicity of the ferrioxamine complex which is formed when the chelating agent combines with inorganic iron.

Acute iron poisoning consequent on the ingestion of inorganic iron is a dangerous and frequently lethal condition: it may be unwise to be too cautious in its treatment; energetic treatment is called for when it is known that a large amount of inorganic iron has been taken by a child. The first essential is to deal with iron, circulating either freely ionized or loosely combined with plasma proteins, by chelation to a form in which it is completely non-ionized and highly stable. This is achieved by intramuscular injection of intravenous infusion, and this aspect of the use of Desferal would seem to be justified beyond doubt and often life-saving.

With regard to oral therapy, the use of Desferal in high dosage would appear to offer an alternative between the further absorption of large amounts of inorganic iron and the possible absorption of similar amounts of iron chelated as ferrioxamine.

Even if the chelate were known to have minor toxic properties in high dosage it would still be preferable to chelate the iron in the intestine rather than accept the continued absorption of large amounts of inorganic iron. However, the position is rather more favourable than this, since ferrioxamine appears to be a compound of quite low toxicity. The first suggested use for ferrioxamine was as a possible therapeutic agent in the management of iron-deficiency anaemia, and very large quantities were injected intramuscularly for this purpose without harmful effects.¹ We have also found that intravenous injections of up to 150 mg. ferrioxamine in adults have produced no toxic effects other than occasional transient facial flushing, and in the intensive treatment of iron overload with intravenous Desferal up to 800 mg. of ferrioxamine has been recovered from the urine in 24 hours. These findings indicate that ferrioxamine circulating in quite high amounts appears to be without toxic effect.

It cannot be too strongly emphasized that acute iron poisoning is a serious medical emergency which calls for vigorous treatment. We would agree that the present scheme of dosage recommended² for the use of Desferal in the management of this condition must in the present state of our knowledge be tentative and may have to be modified in the light of experience.—We are, etc.,

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REFERENCES

- 1 Wöhler, F., *Acta haemat.*, 1963, 30, 65.
- 2 *Ciba Information*, 1964.

Chromosome Studies in Chronic Myeloid Leukaemia

SIR,—In the paper "Chromosome Studies During Early and Terminal Chronic Myeloid Leukaemia," by Dr. N. H. Kemp, Dr. J. L. Stafford, and Miss Rosemary Tanner (18

April 1964, p. 1010), on page 1013 in the second paragraph of the discussion there is the statement, "The findings from Case 1 clearly illustrate that Ph¹+ cells are already present in the bone marrow before there is any evidence of a leukaemic process in the peripheral blood. . . ." According to Table I, on the day that the marrow culture was made the leucocyte alkaline-phosphatase (L.A.P.) score on peripheral blood granulocytes was 6, which is excellent and probably pathognomonic evidence of chronic myeloid leukaemia in the peripheral blood.

Furthermore, in this case¹ the diagnosis of the polycythaemia vera alleged to precede the chronic myeloid leukaemia evidently was made on the basis of a packed-cell volume of 59% and haemoglobin of 19.4 g./100 ml. in a patient with 25,200 W.B.C./c.mm. (68% neutrophils, 25% lymphocytes, 7% monocytes), and 486,000 platelets/c.mm. in March 1959. This is insufficient evidence upon which to make a definite differential diagnosis of chronic myeloid leukaemia *v.* polycythaemia vera. The failure of the white count to rise until September 1961 is ascribable to treatment with ³²P and is of no value in differential diagnosis. The authors' contention would have been better validated had they demonstrated an increased L.A.P. and a marrow typical of polycythaemia vera in this patient prior to treatment with ³²P. Their contention that the patient had polycythaemia vera would have been further strengthened by demonstrating lack of iron in the marrow and hypochromic microcytic red cells. With the evidence at hand it is just as likely that Case 1 had chronic myeloid leukaemia in March 1959.—I am, etc.,

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** We have shown Professor Block's letter to Dr. Kemp and his colleagues, who reply as follows:

Professor Block's comments raise two distinct issues. Firstly, whether there was any evidence of a leukaemic process in the peripheral blood of Case 1 at the time when the Ph¹ chromosome was first detected in the bone marrow. This is largely a matter of semantics. It is very likely that the polymorphonuclear neutrophils circulating at this time were derived from Ph¹+ve cells in the bone marrow; this is indeed supported by the low L.A.P. score. However, the white cell count and differential at this time was unexceptional for polycythaemia vera, (W.B.C. 16,500/c.mm., neutrophils 76%, lymphocytes 18%, monocytes 4%, eosinophils 1%, and basophils 1%) and, by itself, would scarcely permit a confident diagnosis of leukaemia. Certainly Ph¹+ve cells were present in the bone marrow before any granulocyte precursors could regularly be detected in the peripheral blood.

The second point is more crucial. In effect, did Case 1 ever suffer from polycythaemia vera? The relevant time is the period of six months between the time of diagnosis and the first dose of ³²P. Certainly the patient was polycythaemic, the highest recorded haemoglobin level (24 March 1959) being 19.6 g./100 ml. and the P.C.V. 61%: without regular venesection it proved impossible to maintain the P.C.V. below 55%. Indeed, venesection was necessary for the same reason, despite treatment with ³²P, for a period of two years until 16 March 1961.

Clinical, radiological, and laboratory investigations, and, finally, necropsy, failed to reveal any underlying cause for the polycythaemia.

During this initial six months the white cell count varied, except during an attack of lobar pneumonia already referred to, between 17,000 and 34,000 cells/c.mm. (mean 23,900/c.mm.—a range quite acceptable for polycythaemia vera.¹ Granulocyte precursors were only present in the peripheral blood during the pneumonia. The platelet count, although not diagnostic, was always above the normal range, and reached its peak of 680,000/c.mm. as early as March 1959.

Until the W.B.C. began to rise rapidly in October 1961 the clinical and haematological picture of this patient was very convincingly that of polycythaemia vera. Only in retrospect, with the final events in mind, can the original diagnosis reasonably be questioned, and we too gave this due consideration. With Professor Block we also wish that the L.A.P. had been estimated earlier in the disease, but at that time the technique was not established in this laboratory. Perhaps even more pertinent would have been a cytogenetic analysis of the bone marrow at the time of the original diagnosis, possibly revealing the Ph¹ chromosome to be uniformly absent, but in 1959 this was not within our repertory. There is, unhappily, no diagnostic marrow pattern in polycythaemia vera: we are, however, conversant with the vagaries of this disease, and, indeed, this patient had been subjected to detailed investigation as one of a series of cases of polycythaemia vera studied in this laboratory.^{2,3} In our experience a hypochromic microcytic blood picture is the result of treatment by venesection rather than an initial finding in polycythaemia vera.

The available evidence tends to support the initial diagnosis: albuminuria, the presenting symptom, has not uncommonly been observed in this disease⁴; the spleen was not palpable until November 1961, again a feature more characteristic of polycythaemia vera than of chronic myeloid leukaemia; and the episodes of gout and the presence of gouty tophi add further support.

As Professor Block well knows, the issues that he raises are favourite debating points among haematologists. Discussion such as this can demonstrate where clarification is still required, even where it is not yet possible.—Ed., *B.M.J.*

REFERENCES

- 1 Wintrobe, M. M., *Clinical Haematology*, p. 799, 5th ed., 1961. Henry Kimpton, New York.
- 2 Anstey, L., Kemp, N. H., Stafford, J. L., and Tanner, R. K., *Proc. 8th Congr. Europ. Soc. Haem. Vienna*, 1961, 1, 91.
- 3 Kept, N. H., Stafford, J. L., and Tanner, R. K., *ibid.*, 1961, 1, 92.
- 4 Atamer, M. A., *Blood Diseases*, p. 276, 1963. Grune and Stratton, New York.

Hypersensitivity to Neomycin

SIR,—In your instructive article on "Drugs in the Treatment of Ear Infections" (6 March, p. 637) it is pointed out that many cases are not of bacterial origin. External otitis is often a manifestation of "idiopathic" eczema; idiopathic denoting our uncertainties about the pathogenesis. Other sites subject to this common and often recurrent malady are the fingers and palms ("cheiropompholyx"), the scalp ("seborrhoea"), the eyelids ("blepharitis"), the perineal region ("pruritus vulvae et ani"),