Desferrioxamine and Acute Iron Poisoning

SIR,—A reference to the iron-chelating agent desferrioxamine occurs in the *British Medical Journal* of 17 October, p. 993, under the heading "Current Practice—To-day's Drugs." The author correctly describes desferrioxamine as a water-soluble compound having a strong avidity for iron, and reproduces a table of chelating agents for heavy metal poisoning, in which the compound is again correctly described as the antidote of choice for iron poisoning, being remarkably non-toxic.

However the further statement that desferrioxamine needs to be given by intramuscular or intravenous injection requires modification in the light of clinical experiences in several countries. Intramuscular injection is entirely safe and provides effective blood levels within 20 to 30 minutes. Rapid intravenous injections have been reported to cause anaphylactic-type hypotensive reactions in several cases, and we therefore recommend that this method of administration should be avoided.

For the benefit of casualty officers and others who may be required to deal with iron-poisoning emergencies, we suggest the following procedure:

- (1) Inject 2,000 mg. desferrioxamine dissolved in Water for Inj. B.P. intramuscularly.
- (2) Perform gastric lavage followed by the oral administration of 5,000 mg. desferrioxamine in 50–100 ml. water (by stomach tube if necessary).
- (3) Set up an intravenous drip and administer desferrioxamine by continuous intravenous infusion at a rate of not more than 15 mg./kg. per hour. Maximum dosage 80 mg./kg. in 24 hours.
- (4) Repeat intramuscular injections of 2,000 mg. desferrioxamine at 12-hourly intervals, if necessary.

Used as described, hypotensive reactions are not to be expected.—I am, etc.,

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Anticoagulants: Another View

SIR,—Professor John McMichael's comments on long-term anticoagulant therapy (17 October, p. 1007) seem to reflect undue animus, and his manipulation of the data appears to be inconsistent. He first removes one group (deaths in the first three months), and later says that such selection (in this case the grouping into sexes) is "not permissible." It is difficult to see why he makes one selection and disallows another, particularly when separate consideration of the results in men and women would seem almost obligatory in a disease in which the incidence and mortality differ in the sexes. The fact that 80% of the treated group of men returned to work compared with 64% of the control group is surely a result worth striving for.

Professor McMichael calls the incidence of haemorrhage ominous. In my experience this word in well chosen. I have seen eight instances of haematuria among patients on long-term anticoagulant therapy. In one this was due to an unduly low prothrombin level, associated with the use of Atromid (clofibrate).

In the remainder the control was regarded as satisfactory. Four cases were found to have a silent renal stone, one a renal-tract infection, one a hypernephroma, and one case was not explained. The report criticized by Professor McMichael makes no mention of possible factors predisposing to haemorrhage, but my experience is that haematuria in a patient whose prothrombin index is 2 to 2.5 is an indication for careful renal-tract investigation.

The subject of this trial is an important one. The conclusions appear to be based on an experience with less than 400 patients. Would it not be reasonable to extend the observations if the existing facts do not suffice to convince? It may show that what is good for the gander is also good for the goose.—I am, etc.,

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Treatment of Xanthomatosis

SIR,—I was most interested in Dr. B. W. Roper's report (17 October, p. 990) of two cases of essential hypercholesterolaemic xanthomatosis treated with Atromid. I have treated nine cases in this way, together with three cases of essential hyperlipaemia, and reported my findings earlier this year.¹

These patients have now been treated for periods varying from eighteen months to two years. The blood cholesterol is normal in all of them, and the skin lesions have resolved in all but one. This patient, who had gross cutaneous involvement, continues to progress satisfactorily, improvement to date being assessed at 75%.

There seems little doubt that at present Atromid is the best treatment for essential hypercholesterolaemic xanthomatosis.—I am, etc.,

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REFERENCE

- ¹ Borrie, P., *Brit. J. Derm.*, 1964, 76, 53.

Functional and Imagined

SIR,—Dr. Ronald Gibson's paper (17 October, p. 965) was full of stimulating thought and will surely be widely read and deeply considered. It is unfortunate, therefore, seeing what influence it may well have, that some of the references therein are so evidently symptomatic of an essential misunderstanding of the nature of psychosomatic illness.

"I am quite sure in my own mind that the symptoms are real and that there is no emotional overlay here" are the words that, with approval, he puts in the mouth of an exemplary G.P.

"I can find no cause for this pain; therefore I do not believe that it exists; therefore it must be imagined. . . ." This, one understands, is the G.P.'s interpretation of a letter received from a specialist colleague, which letter presumably read something like this. "I can find no organic cause for this pain, which I believe is due to anxiety or stress (or to be functional, or to be psychosomatic in origin)."

I do not feel that there is any other conclusion to be drawn from these two quota-

tions than that Dr. Gibson believes a functional pain (or a psychosomatic ailment, or a symptom due to stress or emotion) to be an *imagined one*. This is unfortunately all too common an interpretation both by patient and by doctor, and for as long as the misunderstanding exists so long will the doctor who has a predominantly, if not totally, organic orientation towards disease fail to understand the ideas and opinions of the doctor who attributes at least some symptoms to psychological causes, and indeed so long will the former's patients be without real support and help.

I would urge Dr. Gibson to reconsider the matter in this light—to picture for a moment a novice soldier on the battlefield, with his underlinen soiled by the effects of uncontrollable intestinal hurry. Such diarrhoea and such catastrophe are not imagined. They are both psychosomatic in aetiology and very real. Perhaps more commonplace is the medical student awaiting a viva voce examination. He does not *imagine* that he has frequency; he *has* frequency of micturition, but the cause is not organic. I feel sure that if Dr. Gibson were to dissociate in his mind the words "functional" and "imagined" he would find opinions attributing symptoms to tension and anxiety and emotional difficulty, in the absence of organic disease, and in the presence of a suitable aetiology, far more acceptable.—I am, etc.,

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HUJOHN RIPMAN.

Laevadosin for Muscular Dystrophy

SIR,—In the *B.M.J.* of 10 October (p. 915) the preliminary results of a trial of therapy (Laevadosin) in Duchenne-type muscular dystrophy have been reported, and the conduct of this trial appears more interesting than its results. So far from being "purposely designed to replicate closely" our earlier assessment,¹ very different approaches and methods make comparison impossible.

When serum-enzyme values are used as a parameter, one must remember that physical activity in health causes corresponding variations in those of aldolase and the transaminases,² that this effect is greatly magnified in muscular dystrophy,³ and that continuous serial assays of very numerous specimens successively obtained under standard conditions are thus obligatory for valid statistical analysis of the disease state.⁴ Serum creatine-kinase (C.K.) activity, also a sensitive index of the disease process, likewise shows similar variations not only in health⁴ but also in muscular dystrophy⁵ by assay methods more dependable than those used here.⁶ This present trial seems founded, however, on previous work by the same collaborators, who, failing to detect an immediate increase in serum C.K. after very brief exercise in a few normal individuals,⁷ then supposed that similar findings in dystrophic patients were thereby proved without actual investigation⁸—thus conferring validity on casual outpatient assay.⁹ This erroneous assumption is matched by the incidental statement that elevated serum-C.K. values are found in hepato-cellular disease⁸ despite the dearth of C.K. in liver tissue.¹⁰ On that basis, instead of our standard morning pre-ambulatory blood specimens thrice weekly for some four months in the hospital ward, specimens once a week only for about a month have been

deemed adequate, without definition of the circumstances, which might be, for all one can tell, during attendance as an out-patient. It does seem strange that, during such a "rigidly designed and strictly controlled" trial, one of the control group should have "died suddenly at home before completion of treatment"; or that histological confirmation of the disease at biopsy has not been offered in either the control or treatment group.

Objective serum-enzyme assay can scarcely be replaced by muscle-strength measurements, admittedly crude and subjective, and even then with no attempt to assess the pelvic girdle musculature so characteristically affected in this condition. Nor can these findings be submitted for valid statistical analysis, since the authors have confounded the type of treatment with the mode of administration, the latter implying obvious immobility for intravenous infusion in one group but not for the oral placebo in the other, physical differences additionally capable of influencing muscle power in the dystrophic child. Invocation of Bradford Hill's approval¹¹ of the M.R.C. Streptomycin Trial cannot restore double-blind status, since here the question of five-day intravenous infusions never arose; nor can dressings on an intact arm suddenly confer all the variables such an infusion must introduce, to say nothing of the extra variables on muscle-strength testing due to differences in the dressings themselves. Further, in a disease capable of much ill-defined individual variation, a control group of ten is much too small a sample for adequate statistical treatment. It is surely more scientific to avoid these numerous pitfalls by realizing that in some diseases the use of multiple objective parameters with the patient as his own control has proved accurate, valid, and rewarding in therapeutic and metabolic investigations.¹²—I am, etc.,

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Addiction to Dextromoramide

SIR,—I wish to report a case of addiction to Palfium (dextromoramide), which I believe to be of rare occurrence.

A male patient, aged 61, developed severe pain in back and down the left sciatic nerve in January 1963. X-ray showed gross narrowing of L5-S1 disk space, with some narrowing of other lumbar disk spaces also. Paracetamol tablets were prescribed for analgesia but failed to ease the pain and Palfium tablets were prescribed. He reached the stage of taking 50 Palfium tablets per week, and had been doing

so from June 1963 until April 1964, when he found himself quite unable to stop his tablets for more than a few hours. I then tackled him about this large dose and told him he was addicted to them and that he must cease taking them. He stated that he wished to be helped and was prepared to co-operate fully. I referred him to the Bethlem Royal Hospital and the Maudsley Hospital and he was admitted on 10 May 1964, where the dextromoramide tablets were stopped abruptly and he was heavily sedated with chlorpromazine 200 mg. tablets and sodium amytal 3 gr. (192 mg.) every four hours. He developed quite severe withdrawal symptoms. Within a few hours he became extremely agitated and tense, complaining of "twitchings" in all four limbs and pacing restlessly up and down, smoking continuously. He remained extremely miserable for 24 hours, but his symptoms had largely subsided within 48 hours and did not recur even when all his sedatives were stopped. He was discharged home on 29 May. He has not required any tablets since and has remained symptom-free and is delighted that he is no longer an addict.

—I am, etc.,

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Propranolol for Angina

SIR,—Dr. R. Mulcahy (10 October, p. 942) seems to attribute to us a more sanguine view of our findings of the effect of propranolol (19 September, p. 720) than expressed in our summary, in which we state "this study suggests that beta-adrenergic blockade may be helpful in angina pectoris." In planning the trial we considered the possibility of a "second wind" effect leading to an increase in exercise tolerance, as suggested by Dr. Mulcahy. However, we felt that an interval of from 30 to 50 minutes between the exercise tests was sufficient to preclude this type of response.

We were led to report our results by the finding that any striking increase in exercise tolerance was confined to the patients limited by angina during the test. The absence of major improvement in other patients suggested that any favourable effect from the therapeutic suggestion of an intravenous injection was outweighed by the effort required to exercise to the limit of tolerance for a second time within an hour. In these circumstances we feel that our tentative conclusions as to the possibility of benefit from the drug were justified.

Subsequent work in seven patients with seriously impaired exercise tolerance has, in fact, shown that a saline injection is followed by an average increase in exercise tolerance of only 6%, a response similar to that found after propranolol in patients who were not limited by angina.—We are, etc.,

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Sarcoidosis of the Parotid

SIR,—I have recently had occasion to review our experience of inflammatory conditions of the parotid in the department of surgical studies at the Middlesex Hospital, and I was therefore particularly interested in the article by Dr. G. Greenberg and others (3 October, p. 861) on enlargement of the parotid gland due to sarcoidosis. In an

analysis of 120 cases we found two examples of sarcoid, one presenting as a lump simulating a tumour, the true diagnosis not being suspected until a routine pre-operative chest x-ray was taken, the other being an incidental histological finding in the wall of a cyst removed by operation. Neither showed the clinical features of inflammation, and so much is this our experience that we warn against a common tendency to raise the diagnosis of sarcoid too readily as a cause of parotitis. It would be interesting to know in how many of Dr. Greenberg and her colleagues' patients the parotid was the primary presenting condition, and in how many of these the clinical symptoms were inflammatory rather than the development of a diffuse or localized inert swelling.—I am, etc.,

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Professional Patients

SIR,—The term professional patient requires elaboration. The patients described by Dr. T. L. Dunn (3 October, p. 879) share some features in common with cases of hospital addiction. This is a well-documented condition in the medical¹⁻⁴ and lay press.

In his concept of "Illness as a Hobby," Dr. Richard Asher (who introduced the term Munchausen syndrome⁵) has proposed a spectacular but realistic practical classification of some of the commoner types of perennial patients⁶:

- (1) *The "serious self-student"*: not necessarily a hypochondriac; e.g., the T.B. patient knowledgeable about pneumoperitoneums, artificial pneumothoraxes, and phrenic crushes.
- (2) *The rich hypochondriac*: grand-tour type who consults eminent specialists throughout the world.
- (3) *The poor hypochondriac*: perpetual outpatient.
- (4) *The pharmaceutical collector*.
- (5) *The jaddist apostolic*: visits a "little man" who is "just off" some street seeking royal jelly, acupuncture, wholemeal, etc.
- (6) *The lonely person*: chat with doctor plus glass of medicine (equivalent to chat with landlord plus glass of beer).
- (7) *Sufferers from chronic autogenous disease*: e.g., anorexia nervosa, dermatitis artefacta, and Munchausen syndrome.
- (8) *Genuine malingerers*.

The alleged increasing abuse of psychiatric services by professional patients is a problem requiring cautious interpretation, for it may be more apparent than real. Furthermore, all the above types of patients are world-wide and existed long before 1948, which precludes them from being merely "products of the extension of social and psychiatric services under the National Health Service." The patients Dr. Dunn describes are undoubtedly true malingerers; the implications of this are that we should make our psychiatric hospitals less comfortable and less attractive than at present and less freely available, to discourage those people from taking advantage of us. This is obviously unthinkable. I suspect, however, that the majority are motivated by more subtle considerations and fall into the categories 1-7.

The alleged increasing abuse of psychiatric services by professional patients is a problem