ORAL IRON COMPOUNDS

SIR,—I have read with interest last week's article by Dr. O'Sullivan and his colleagues. I must congratulate them on a careful presentation of very interesting figures. I would, however, in view of their references to my work, and as I was the first to introduce ferrous succinate into therapeutics, make the following remarks:

Cases refractory to oral iron.—Has the phosphate metabolism been investigated in these cases? It is theoretically possible for an excess of phosphate in the alimentary tract completely to vitiate all iron absorption. Has this condition been excluded, assuming that it does exist? If it has not been excluded, has any attempt been made to protect the iron administered from interaction with phosphates in order to improve the uptake of iron? I need not emphasise that iron phosphates are insoluble and ferric phosphate is completely insoluble.

Inclusion of ascorbic acid.—This is incorrectly termed a "supplement." It is found that the inclusion of ascorbic acid tends to protect ferrous salts from oxidation. This may account for the better uptake of iron preparations administered coincidentally with ascorbic acid. We are here, therefore, not concerned with vitamin-C deficiency.

The criticism that ferrous sulphate was given for 42 days, compared with ferrous succinate for 24 days.—I would make the point that many of us are dealing with *patients requiring treatment.* If one has embarked on a particular line of treatment, one is loth to discontinue therapy in the absence of intolerance. Some of these cases were obviously improving slowly on ferrous sulphate, which was continued until clinical improvement justified its discontinuance. Had ferrous succinate been employed, shorter treatment would have been required.

Tolerance.—The salient feature here is not whether diarrhœa or constipation of "sufficient severity" was present. The criterion should be, is it present at all? Acceptable forms of therapy should produce no, or minimal, side-effects. The patient's well-being must be considered primarily. Home-treated cases will only persevere with a form of treatment which does not upset them. This is the crux of the matter.

I should welcome any observations on these matters.

London, W.1. DAVID HALER.

PYRETOGENIC EFFECT OF LYSERGIC ACID DIETHYLAMIDE

SIR,—Lysergic acid diethylamide (L.S.D.) has been found by Horita and Dille [1] to possess a pyretogenic effect in rabbits, cats, and dogs when injected intravenously in amounts as small as 0·5 μg. per kg. body-weight. This action was prevented by transection of the cervical spinal cord or administration of *d*-tubocurarine or sodium pentobarbitone. Administration of antipyrin, 'Dibenamine,' 'Hydergine,' or dihydroergotamine did not influence the pyretogenic effect, which Horita and Dille concluded was of central origin.

L.S.D. is a very potent and specific antiserotonin,[2] but this action does not manifest itself on the central nervous system.[3] If the pyretogenic effect of L.S.D. is of central origin we should not expect it to be inhibited by serotonin.

We have used 16 rabbits, weighing 2·5–3 kg., divided in two groups. All were given 20 μg. per kg. of L.S.D. intravenously. Group B were given simultaneously 5 mg. per kg. of serotonin creatinine sulphate intravenously. The rectal temperature was measured by a mercury thermometer. The results are summarised in the accompanying table. In both groups there is a significant increase in the temperature after the injection of L.S.D. The pyrexia does not differ significantly between the two groups, thus showing that in these conditions the serotonin does not inhibit the pyretogenic action of L.S.D.

This supports the opinion that the pyretogenic effect of L.S.D. is of central origin.

L.S.D. was kindly supplied by Messrs. Sandoz Ltd., Basle, and serotonin by Abbott Laboratories, Chicago.

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1. Horita, A., Dille, J. M. *J. Pharmacol.* 1955, **113**, A29.
2. Gaddum, J. H., Hameed, K. A. *Brit. J. Pharmacol.* 1954, **9**, 240.
3. Woolley, D. W., Shaw, E. *Brit. med. J.* 1954, ii, 122.

CLINICAL TESTS OF PASSIVE JOINT SENSE

SIR,—I agree with Sir Charles Symonds and Dr. Gooddy (July 16) that testing the sense of position and motion in the usual way is an indispensable and fairly reliable part of the neurological examination, although there are some differences in performing the test. Although we have to consider the possibility that the patient may be able to judge movement from some distortion of the skin, as Dr. Lee and Mr. Browne (July 9) point out, I feel that grasping the toe laterally with as little pressure as possible is preferable to gripping the dorsal and plantar surfaces, because of the greater variations in pressure by using the latter method. Many patients will attempt to move their toe up and down in order to judge the position of the toe, and they should be instructed to avoid these movements. I was struck, however, by the fact that Lee and Browne as well as your correspondents consider only the great toe and do not mention the small toes. Yet it is well known that the sense of position, then that of motion, is lost in the small toes before it disappears in the great toe. Therefore testing deep sensation only in the great toe and omitting the small toes would appear incomplete and would decrease the value of the test in a case where the sensation has been found normal in the great toe.

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ADENOSINE AND THE HEART

SIR,—As I understand from Dr. Somló's letter of May 28, the effects of adenosine triphosphate in this case are attributed to the production of a state of shock similar to that produced by histamine, adrenaline, or insulin.

May I suggest another explanation—namely, that A.T.P. speeds up the polymerisation of actin, which, in the whole muscle, means the relaxation of the muscle. Your annotation in the same issue states that Mg phosphate is the most active member of the group, and this supports my view, since the presence of Mg is absolutely vital to the polymerisation of actin (in other words, to the relaxation of muscle). Hence, A.T.P. without Mg does not bring about polymerisation, while additional traces of minimum amounts of Mg—combined with A.T.P.—increase the polymerisation (and thus relaxation) enormously.

I was very interested in the ideas expressed in Dr. Somló's letter and your annotation, and in the light of them I would suggest that the effect of A.T.P. in paroxysmal tachycardia may be produced in both ways by the induction of shock and actin polymerisation.

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INFLUENCE OF SEROTONIN ON THE L.S.D-INDUCED PYREXIA IN RABBITS

Group	No. of animals	Temp. (deg. Centigrade) before injection	Temp. (deg. Centigrade) after injection				
			1 hr.	2 hr.	3 hr.	5 hr.	24 hr.
A (L.S.D.)	8	39·59 ±0·08	41·37 ±0·12	41·20 ±0·06	40·41 ±0·11	40·15 ±0·16	39·57 ±0·14
B (L.S.D. + serotonin) ..	8	39·66 ±0·08	41·24 ±0·14	41·44 ±0·10	40·81 ±0·16	40·49 ±0·18	39·41 ±0·08