Correspondence

The Toxicity of Iron Compounds

SIR,—The paper by Dr. Gilbert Forbes (March 22, p. 367) has drawn attention to the toxic action resulting from accidental overdosage of ferrous sulphate taken by mouth. No mention is made of the name of the preparation, but we believe we are correct in saying that it was "fersolate" tablets, of our manufacture.

Experiments in progress in these laboratories indicate that for the more soluble iron compounds the toxicity is closely correlated with the iron content (calculated as ferrous iron) and strongly suggest that the action is due to the formation of ferric chloride in the stomach. The iron compounds were given, either in solution or suspension, to fasting rabbits by means of a stomach tube; the doses were adjusted to body weight. According to the dose, the animals either died in a few hours or recovered completely. The post-mortem findings for those that died were completely in agreement with those of Forbes, the cause of death being haemorrhagic gastritis. The animals that recovered were quite well on the following day; daily blood counts and urinary examination showed no abnormal findings. In some cases, but not all, the stomachs of these animals showed signs of irritation at the great curvature.

The results so far obtained indicate that the fatal dose of ferrous sulphate in rabbits is higher than those reported by Forbes for guinea-pigs. We find that "fersolate" tablets compare favourably for toxicity with other iron compounds so far tested, and the presence of small amounts of copper and manganese sulphates does not increase the toxicity, which is due to ferrous sulphate. The toxic effect of the iron in Bland's pills is less than half that of other ferrous salts; but relatively higher doses are required for haemopoietic action.

The lower toxicity of Bland's pills may be due to the sodium sulphate in this preparation having a cathartic action that hastens the excretion of the iron. Rabbits treated with high doses of Bland's pills had a profuse diarrhoea within half an hour of dosing. It would appear, therefore, that a gastric lavage with an alkaline solution would be of value after accidental overdosage with ferrous sulphate. This would neutralize the acidity of the stomach, cause precipitation of ferrous carbonate, and prevent the formation of ferric chloride and retard the absorption of iron.

The results of further experiments, now in progress, will, it is hoped, be published in detail later.

Ferrous sulphate is one of many medicinal substances having undesirable effects when taken in grossly excessive quantities. We consider that Dr. Forbes's paper serves to emphasize the need to keep such preparations out of reach of young children, and to guard against overdosage.—I am, etc.,

Glaxo Laboratories, Ltd.,
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G. F. SOMERS.

SIR,—Dr. Gilbert Forbes (March 22, p. 367) has written a very important paper which has wide-reaching implications. Have we not been assuming too much that "harmless" drugs are innocuous even in large doses, and that the excess will be excreted without danger? The outstanding example is the vitamins which are found only in traces in natural products, and yet are prescribed medicinally in enormous quantities.

To return to the ferrous sulphate question, I remember some 12 years ago being stimulated by Dr. Helen Mackay's papers on anaemia in infants to order massive doses of ferrous sulphate as a routine procedure during the last months of pregnancy. After some months I abandoned this, as a number of women complained of headache, nausea, and malaise, and, if the iron were continued, developed a mild albuminuria. I was convinced that there was an association between these liver and kidney symptoms, resembling a pregnancy toxæmia, and the excessive iron intake, but I must acknowledge that I did not find anyone to agree with me. However, I have never given large quantities of iron in pregnancy since, and in the light of Dr. Forbes's cases

with the reported damage to liver and kidneys I venture to bring up this theory once more and to ask whether anyone else has had a similar experience?—I am, etc.,

London, W.8.

VIOLET RUSSELL.

Retrodisplacement and Fertility

SIR,—There is not the slightest doubt that retrodisplacement of the uterus is a cause of sterility. A woman with a backward displacement of the uterus *can* become pregnant, but if she is sterile and a backward displacement is present, the correction is followed by pregnancy in a very large number of cases. Needless to say, full investigation of both male and female is a necessity.—I am, etc.,

Dublin.

BETHEL SOLOMONS.

The "Costoclavicular Syndrome"

SIR,—Prof. E. D. Telford and Mr. S. Mottershead raise in their paper (March 15, p. 325) several interesting points and advance new concepts of great importance to a proper understanding of the various factors involved in cases of brachial neuralgia. Probably owing to the paper shortage clarity has been sacrificed to compression in certain places.

The authors describe the operative findings in fourteen cases associated with cervical rib and extensive arterial thrombosis; except in two cases the thrombosis extended no higher than the lower border of the pectoralis major. Are these findings meant to imply that the cervical rib played no part in the syndrome and that no case of arterial damage due to cervical rib was found in this extensive series? Is it believed that the arterial damage was due to compression between the heads of the median nerve and that this was due, either directly or indirectly, to the fact that the cervical rib altered the relationship between the plexus and artery?

The stated "textbook picture of neurovascular bundle compression" fails to convey what is found in practice. In our experience there is no such picture. These cases differ considerably in history, symptomatology, and signs, and this difference has valuable diagnostic implications. The authors are undoubtedly right in casting doubt as to whether their remaining 69 cases of cervical rib were in fact correctly described. Prof. J. R. Learmonth's recent paper in *Thorax* undoubtedly gives a balanced judgment of this problem.

We believe that the case in which the axillary artery was compressed by the two heads of the median nerve is the first to be described and as such is of considerable importance. It might be helpful to consider this concept from its obverse angle. Consideration of the respective resistances of artery and nerve would lead to the expectation that symptoms would arise from the nerve rather than the artery in such a case. From the rather meagre clinical data provided it appears likely that this in fact happened. It might be preferable to contend that the median nerve was compressed by the artery. In fact, quite possibly this man's symptoms might have been alleviated by resection of his first thoracic rib, as this would have led to alteration of the artery-plexus relationship.

The challenging statement that in postural manoeuvres of the shoulder resulting in obliteration of the radial pulse the axillary pulse can still be felt cannot be allowed to pass unquestioned. A small personal experience does not suggest its general validity and it is contrary to certain published evidence. It is not clear from the text or the table whether the authors in fact ascertained, in each case where the radial pulse was obliterated, that the axillary pulse was still present and undiminished. Further information on this point would be welcome and, in particular, if in fact all cases had not been examined, on which cases this statement was founded. Further, the statements in the summary, paragraphs 2 and 4, are contradictory; paragraph 4 is almost certainly a misprint, as the references quoted include several undoubted cases of costoclavicular compression proved at operation. The role of costoclavicular compression in causing a rise in venous pressure in the arm requires consideration (Sampson *et al.*, 1940). The evidence as a whole is suggestive that costoclavicular compression is common and cannot be disregarded. It is noteworthy that the rise of venous pressure on bracing back the shoulders cannot be attributed to median nerve compression. It is considerably lessened if the first rib is missing as in thoracoplasty. In these cases the average rise