The solution is easily prepared, is available in enormous quantities, is completely stable, and can be stored at room temperature. It may be administered very rapidly and in large amounts, and no patient seems to have been adversely affected by its introduction.

More detailed haematological and biochemical studies of the effect of its administration in the state of shock, hypoproteinaemia, and protein deprivation and loss are being undertaken, and final judgment must await these results. Despeciated bovine serum would, however, appear to accord with the three precepts given at the beginning as being necessary for a plasma substitute, and as such may have a useful place in the treatment of conditions in which human plasma protein has been of value.

Summary

Substitutes for human plasma hitherto prepared have not fulfilled the three criteria: (a) retention in the circulation and eventual metabolism; (b) exertion of an equivalent osmotic pressure; and (c) non-toxicity, non-antigenicity, and freedom from antibodies.

Bovine serum can be made safe for man by destroying the antibodies by heating to 72° C., while rendering the proteins uncoagulable with the addition of 0.2% of formalin and ammonia. Material so prepared appears to accord with the above precepts.

Clinical trial in 26 cases shows that it can be administered rapidly and in large amounts to man with safety.

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TREATMENT OF ANAEMIA IN SCHOOL-CHILDREN WITH IRON AND ASCORBIC ACID

BY

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In a previous survey of the haemoglobin levels of a cross-section of the population in Edinburgh (Davidson *et al.*, 1942) subnormal haemoglobin values were found in approximately 40% of children from municipal schools as compared with only 4.5% of children examined at private schools. Accordingly a therapeutic test was undertaken in order to evaluate the effect of adding supplements of iron and ascorbic acid to the diet of the municipal-school children. The results of this experiment have been submitted to Dr. A. Bradford Hill for statistical analysis, and the statement that a significant rise in the mean haemoglobin values has occurred in any of the experiments outlined below is based on that analysis. In each experiment the initial haemoglobin levels of the control

and experimental groups were not significantly different. The tests were carried out in three municipal schools on children from 5 to 12 years of age.

School I

The children in both the control and the experimental groups were unselected, but were divided into three groups according to whether they took school or home midday meals. Group A consisted of children who went home for a midday meal; Group B included those who took school dinners, for which they paid; while Group C included those children who had free school dinners. The children in the experimental groups were given 3 gr. of ferrous sulphate in tablet form daily for 5 days a week. Haemoglobin estimations were made at the outset of the experiment and again after three months of treatment. The results of the experiment are shown in the accompanying Table.

Table showing Mean Hb % in Control and Experimental Groups

		Total	Treatment Received	1st Examination	2nd Examination	3rd Examination
School I:						
Group A	{ Control Exptl.	77 85	Ferrous sulphate 3 gr. daily	85.4 85.3	84.6 87.0	
" B	{ Control Exptl.	32 44		77.9 80.3	80.1 85.9	
" C	{ Control Exptl.	41 45	" "	82.2 80.7	82.6 86.3	
School II:						
	{ Control Exptl. A	57 56	Asc. acid 25 mg. daily	81.7 82.4	80.8 82.0	
	{ Exptl. B	57	Asc. acid 25 mg. daily + ferrous sulph. gr. 3 daily	82.4	83.8	
School III:						
	Control Exptl.	27 27	Asc. acid 25 mg. daily + ferrous sulph. gr. 6 daily	78.0 77.8	81.2 87.3	88.3 93.5

Conclusions

(a) *Control Groups*.—There was no significant rise in the mean haemoglobin levels at the second examination.

(b) *Experimental Groups*.—In all three groups the mean haemoglobin levels at the second examination after three months of treatment were significantly higher than the corresponding figures for the control groups. In Groups B and C there was also a significant rise in the haemoglobin levels at the second examination as compared with the original haemoglobin values. In Group A, although there was a rise in the haemoglobin values, it was not statistically significant.

(c) An analysis of the haemoglobin figures of those children whose initial haemoglobin level was less than 80% showed that of 59 such children in the control series 31 (52.5%) still had haemoglobin figures of less than 80% at the second examination; while of 71 receiving iron therapy, only 24 (33.8%) still had haemoglobin figures of less than 80% at the second examination. This improvement in the treated group is statistically significant.

School II

(a) *Control Group*: total, 57 unselected children. (b) *Experimental Group A*: total, 56 unselected children; treated with 25 mg. of ascorbic acid daily for 5 days a week. (c) *Experimental Group B*: total, 57 unselected children; treated with 25 mg. of ascorbic acid daily and 3 gr. of ferrous sulphate daily for 5 days a week. Haemoglobin estimations were made at the outset of the experiment and again after three months of treatment.

Conclusions

(a) *Control Group*.—There was no significant rise in the haemoglobin values when the estimations were repeated at the end of three months.

(b) *Experimental Group A*.—There was no significant rise in haemoglobin levels after three months of treatment with ascorbic acid as compared with the initial haemoglobin values or with the control group.

(c) *Experimental Group B*.—There was a significant rise in the haemoglobin levels of the children on iron and ascorbic acid after three months of treatment as compared with the

control group, but the increase over their own initial haemoglobin values was not significant.

(d) An analysis of the haemoglobin figures of those children whose initial haemoglobin level was less than 80% showed that out of 26 in the control series 15 (57.7%) still had haemoglobin figures of less than 80% at the second examination; of those receiving ascorbic acid alone, 19 had haemoglobin levels below 80% at the first examination, and at the second examination 13 (68.4%) were still below 80%; while of those receiving iron and ascorbic acid 19 were below 80% at the first examination, but only 4 (21.1%) were below 80% at the second examination. The improvement noted in this last group is statistically significant.

School III

Only children whose original haemoglobin level was 80% or less were included in this experiment. (a) Control group: total 27. (b) Experimental group: total 27.

The children in the experimental group were given 25 mg. of ascorbic acid daily and 6 gr. of ferrous sulphate in tablet form daily for 5 days a week. It should be noted that the dosage of iron was double that given in Schools I and II, and the children were selected because clinical anaemia was present. Treatment was given for six months. Haemoglobin estimations were made at the outset of treatment and repeated at intervals of three and six months.

Conclusions

(a) *Control Group*.—A significant rise in haemoglobin levels was found at the second and third examinations as compared with the levels found at the first examination.

(b) *Experimental Group*.—This series also showed a significant rise in haemoglobin levels at the second and third examinations. The mean levels in this treated group were, however, significantly greater than those found in the control group at the second and third examinations.

Discussion

Investigations into the Hb levels of large numbers of persons in different areas of Great Britain, including Aberdeen (Davidson *et al.*, 1935) and Edinburgh (Davidson *et al.*, 1942), have clearly demonstrated the frequency with which anaemia occurs in infants, school-children, and women, both pregnant and non-pregnant. The anaemia is almost universally of the hypochromic type, which responds excellently to iron therapy. It leads to a feeling of fatigue and exhaustion, to a loss of appetite, and to a reduction in efficiency. In the case of the infants it has been shown to be associated with an increased liability to infection. The family doctor should constantly be on the watch for the development of anaemia in his patients. The improvement in their general well-being which will rapidly result from the administration of the ferrous salts of iron will amply reward him for the time spent on making the necessary examinations. For the prevention of anaemia, reliance should be placed primarily on securing an adequate intake of iron by instructing the patient to eat sufficient quantities of the foodstuffs which are particularly rich in the mineral. By so doing the intake of other important factors connected with haematopoiesis—e.g., protein and vitamins B and C—will be coincidentally improved. In this connexion we wish to draw attention to the value of national wheatmeal bread made of 85% extraction flour. Its content of iron is 0.7 mg. per oz., compared with 0.3 mg. per oz. for white bread made from 70% extraction flour. On an average intake of 6 oz. of bread daily an addition of more than 2 mg. of iron daily is consumed. Investigations which will be published shortly suggest that this increment during the past eighteen months has already made a significant contribution to the reduction of anaemia in school-children. Nevertheless, under wartime conditions it may on occasion be necessary to supplement the diet with medicinal iron.

The investigations reported in this paper clearly indicate that the administration of iron in doses of approximately one-third of that usually prescribed for curative treatment can significantly improve the haemoglobin levels of school-children. The increases shown in the Table are admittedly small. It might accordingly be asked whether any significant improvement in health could be expected to result therefrom. It should be pointed out, however, that the figures given represent mean

values. In the municipal-school children in Edinburgh the average haemoglobin figure was found to be 80%. Accordingly approximately half of the children had a haemoglobin level above this figure and half below it. It would be unreasonable to expect such small doses of iron to affect materially haemoglobin levels of normal or only slightly subnormal ranges. A study of individual cases showed this to be the case. It should be noted incidentally that when two tablets were given daily, as in School III, the mean haemoglobin was brought up to 93%. In the case of children whose haemoglobin was below 80%, and particularly when they were in the neighbourhood of 70%, a rise of 10 to 15% regularly followed the administration of one tablet of fersolate daily. It was due to these increments that the mean haemoglobin level was raised. Few would question the advantages to the health of school-children of such an increment.

It should be noted that the experiments recorded in this communication were essentially prophylactic in nature, and it must be clearly understood that in the treatment of individual cases of anaemia much larger doses of iron should be given.

Our knowledge of the aetiology, incidence, and treatment of iron-deficiency anaemia is now so complete that the medical profession must shoulder the responsibility if the necessary measures for its control are not widely adopted.

Summary

Experiments conducted over periods of three to six months indicate that a supplement of iron, even in such small amounts as 3 gr. of ferrous sulphate once daily for 5 days a week, can produce a significant rise in the haemoglobin levels of municipal-school children.

This suggests that the hypochromic anaemia of these children is mainly conditioned by an insufficiency of iron in the diet.

A supplement of 25 mg. of ascorbic acid daily had no effect in raising the haemoglobin levels.

We wish to express our thanks to Dr. Bradford Hill for his statistical help, and to Messrs. Glaxo Laboratories Ltd. and Roche Products Ltd. for their generosity in supplying free the supplements of iron and ascorbic acid respectively; and also to the Medical Officer of Health for Edinburgh and the staffs of the municipal schools, whose assistance was much appreciated.

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THE INFLUENCE OF SUPPLEMENTS OF VITAMINS A, B₁, B₂, C, AND D ON GROWTH, HEALTH, AND PHYSICAL FITNESS

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This is a summary of a vitamin feeding test carried out in 1941–2 on approximately 1,400 school-children and adults. A full report of the test has been prepared, but it is too lengthy for publication.

Towards the end of 1940 the Ministry of Health accepted a gift of multi-vitamin capsules from a group of United States physicians to carry out a feeding test on suitable groups of people. The time was opportune, and the capsules were employed as test material to ascertain whether a supplement of synthetic vitamins to the ordinary diet would improve growth, health, and physical efficiency. Each capsule contained:

Vitamin A ..	4,000 i.u.	Ascorbic acid ..	1,000 i.u.
Thiamin ..	333 i.u.	Nicotinamide ..	20 mg.
Riboflavin ..	2 mg.	Vitamin D ..	600 i.u.

Three of the five tests carried out were done on school-children and two on factory workers. Four times during the tests the vitamin content of the capsules was checked and found up to specification by the Medical Research Council. The school tests were performed on elementary-school children in Ipswich, Glossop, and London. The number of children who completed the test was 1,242: Ipswich, 425 boys and girls aged 5 to 13; Glossop, 370 boys aged 9 to 13; London, 447 boys