on the staff of the United Birmingham Hospitals for allowing me access to their cases. Dr. J. A. H. Waterhouse, of the department of medical statistics, also gave me helpful advice.

REFERENCES

- Cartwright, G. E., and Wintrobe, M. M. (1949). *J. clin. Invest.*, **28**, 86.
 — (1952). *Advanc. intern. Med.*, **5**, 165.
 Davidson, L. S. P., Davis, L. J., and Innes, J. (1942). *Quart. J. Med.*, **11**, 19.
 Hamilton, L. D., Gubler, C. J., Cartwright, G. E., and Wintrobe, M. M. (1950). *Proc. Soc. exp. Biol (N.Y.)*, **75**, 65.
 Hoyer, K. (1944). *Acta med. scand.*, **119**, 562.
 Laurell, C. B. (1947). *Acta physiol. scand.*, Suppl. **46**, **14**, 1.
 Moore, C. V., and Doan, C. A. (1937). *Arch. Path. (Chicago)*, **23**, 738.
 Powell, J. F. (1944). *Quart. J. Med.*, **13**, 19.
 Riecker, H. H. (1930). *Arch. intern. Med.*, **46**, 458.
 Ungley, C. C. (1949). *British Medical Journal*, **2**, 1370.
 Vahquist, C. S. (1941). *Acta paediat. (Stockh.)*, Suppl. **5**, 28.
 Vannotti, A., and Delachaux, A. (1949). *Iron Metabolism and its Clinical Significance* (Transl.). Muller, London.

IRON DEFICIENCY IN PREGNANCY

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Some fall in the level of haemoglobin during pregnancy is usual. This relative anaemia is often attributed to the rise in blood volume of 18–23% (Dieckmann and Wegner, 1934; Roscoe and Donaldson, 1946; Berlin *et al.*, 1953) which occurs towards the end of pregnancy. Since the haemoglobin levels of most non-pregnant women range from 80 to 95%, levels of haemoglobin of 70–85% at the end of pregnancy have come to be accepted as normal.

The fact that throws doubt on the "physiological" nature of the anaemia of pregnancy is that the anaemia can in most cases be prevented by the administration of iron (Corrigan and Strauss, 1936; Fullerton, 1936; Wills *et al.*, 1947; Kloppper and Ventura, 1951; Scott and Govan, 1949; Benstead and Theobald, 1952; Davis and Jennison, 1954).

The present investigation does little more than confirm this finding, but it was thought that our evidence should be added to that already available both because low haemoglobin levels in pregnancy are undesirable and because there is a continuing failure to recognize that they are unnecessary.

Plan of the Present Investigation

The investigation was carried out on patients booked for domiciliary delivery and attending two local health authority antenatal clinics between January, 1951, and April, 1953. All patients presenting themselves before the end of the fourth month of pregnancy were included. The haemoglobin levels were measured by the M.R.C. neutral grey photometer, taking 100% haemoglobin to be equivalent to 14.8 g.% of haemoglobin. Haemoglobin estimations were made at the first attendance, at 28 weeks, at 38 weeks, and six weeks after delivery. These dates are approximate, and occasionally the post-natal reading was at a rather later date.

Every patient was given an iron preparation by mouth from the time of first attendance until delivery. This was given in the form of one "fersolate" tablet (containing 3 gr. (0.2 g.) of ferrous sulphate) three times a day. The preparation was changed to "ferro-redoxon" (containing 2.04 gr. (132 mg.) ferrous sulphate and 50 mg. of ascorbic acid) if the patient complained of digestive disturbances or if the haemoglobin level had not risen. This change was made in about

half the cases, and it appeared that the preparation containing ascorbic acid was better tolerated. The main difficulty in satisfactory iron therapy during pregnancy is that patients who feel well cannot be relied on to take it regularly, partly because they see no necessity for it. We explained that taking iron regularly would make them feel "fighting fit" for their labour and also for their return to household duties after the lying-in period. In general this produced ready co-operation. At every attendance the patient was given the exact number of tablets to cover the period till she was due to come again and was asked to bring back the box with any that were left. These were counted and the number was recorded. It is clearly impossible to be certain that all the tablets not returned were consumed, but we felt that the record was as accurate as it could be, short of seeing the tablets swallowed.

The investigation included 138 patients. Of these, five could not be persuaded to persevere with iron and were excluded. In 26 instances the complete set of haemoglobin estimations was not obtained, either because the baby arrived before the calculated date, so that the 38-week reading was not made, or because the patient removed from the district or was transferred to the care of a hospital or general practitioner. Three further patients were excluded because they were given blood transfusions after post-partum haemorrhage. The 104 remaining cases are listed according to age and parity in Table I. There were no complications of pregnancy or labour in these patients apart from three forceps deliveries.

TABLE I.—Age and Parity of 104 Women who Took Iron Regularly During Pregnancy

Age	Parity					
	0	1	2	3	4	5
Under 20 ..	3	—	—	—	—	—
20–29 ..	14	18	11	6	1	—
30–39 ..	1	9	12	17	6	1
40 or over ..	—	—	3	1	1	—
Totals ..	18	27	26	24	8	1

Results

A difficulty in the analysis of the results of this survey is that a few patients failed to respond to iron therapy. We have isolated as a separate group all those in whom the haemoglobin level was still below 85% at 38 weeks and have termed them "non-responders." Table II shows the distribution of haemoglobin levels before the end of the fourth

TABLE II.—Haemoglobin Levels Before the End of the Fourth Month of Pregnancy in 104 Patients who Took Iron Regularly

	Hb Levels				Total
	80% or Less	81–89%	90–99%	100%+	
Responders ..	15	33	33	11	92
Non-responders	4	3	5	0	12

Note.—Statistical examination of the age and parity of the responders does not show any significant difference between the four groups.

month of pregnancy in both "responders" and "non-responders" and indicates that there is no systematic difference in this respect between the two groups.

The effect of iron on the haemoglobin level is illustrated in the chart, where the "responders" have been subdivided according to their initial haemoglobin. This shows that when the initial haemoglobin is below 90% the administration of iron leads to a marked rise during pregnancy. When the initial haemoglobin is above 90% there is little systematic change in the level. In all the "responding" groups the haemoglobin level is around 98% at 38 weeks and remains at much the same level for six or more weeks after delivery. The "non-responders," who show a general downward trend

in haemoglobin levels from 16 to 38 weeks, show a sharp post-partum rise to the same level as all the "responding" groups.

It is to be noted that very little effect on the form of the curves would be produced if the "non-responding" cases were included in the appropriate subclasses of "responders." In general the curves would be not more than 2% lower at 28 weeks, not more than 4% lower at 38 weeks, and unaltered post partum.

Change in mean haemoglobin level in pregnant women receiving iron. The line marked 75 gives mean values for 15 patients whose haemoglobins were initially 80% or under. That marked 85 refers to 33 patients starting between 81 and 89%. Similarly, 95 denotes the range 90-99% (33 patients) and 105 denotes initial levels from 100% upwards (11 patients). The interrupted line refers to the 12 patients classified as "non-responders."

Discussion

The results of this investigation suggest that patients whose haemoglobin levels are below 90% at the beginning of pregnancy are iron-deficient, since the level rises steeply when they are treated with iron. The patients whose haemoglobin level is over 90% at the beginning of pregnancy maintain their high level at 38 weeks when treated with iron. Thus the steady fall in haemoglobin repeatedly reported to be characteristic of pregnancy—for example, M.R.C. (1945)—does not occur if iron is administered, except in the small group of "non-responders." Moreover, the level of haemoglobin at 38 weeks is almost the same as that observed six weeks or more after delivery—again with the exception of the few "non-responders." This finding appears to dispose of the idea that a fall in haemoglobin as pregnancy proceeds is due to haemodilution and is therefore "physiological." It is possible that this process may occur in the "non-responders," in view of the sharp rise that they show in their haemoglobin level after delivery; alternatively, they may have been unable to utilize iron during pregnancy but able to do so after delivery. These 12 patients were clinically well at all stages. Full haematological investigations were carried out in six of them, but no cause for their failure to respond was found.

It has been suggested that even if the fall in haemoglobin which occurs in pregnancy is not prevented by iron therapy the patients are none the worse clinically (Samuel, 1952). It

is probable that this belief is widely held. In spite of repeated demonstrations that iron raises the haemoglobin in pregnancy, it is not administered routinely to pregnant women. It is, of course, difficult to prove that patients with haemoglobin levels above 90% are in better health than those with levels between 70 and 80%. One gains the impression that at the higher level they are more energetic and tire less easily; and there can be no doubt that they are in a better position to withstand haemorrhage or infection. Apart from the benefit to the patients, the confidence of both doctor and midwife, particularly in domiciliary practice, is greatly increased by the knowledge that the haemoglobin level is high at term.

Throughout this communication the figures quoted are averages, and averages are in some ways misleading. In this small series, 15 of the "responding" patients had initial haemoglobin levels of 80% or less. Some of these, if untreated, might have had terminal levels of 60% or less and would have been in a dangerous condition if not transfused during pregnancy. Considered on a national scale, it is probable that these dangerously low levels (sometimes but not always detected and treated by transfusion) could be avoided in the vast majority of cases by iron therapy.

It is customary to give iron to pregnant women who are "really" anaemic, the critical level at which treatment is considered necessary varying from one centre to another. When facilities for haemoglobin estimations are not readily available the presence or absence of "anaemia" is sometimes judged clinically. This is highly fallacious, as one of us (M. F.) proved some years ago by comparing the haemoglobin levels in pregnant women as judged clinically and estimated in the laboratory. Comparisons were made on 173 occasions and an error of 10% or more was observed on 87 of them. The limits of error were a clinical overestimation of 34% and an underestimation of 46%. In view of the findings in our series of patients, it would seem advisable to prescribe iron for all pregnant women and to see that it is really taken. If this is done it is doubtful whether routine haemoglobin estimations are necessary, though any patient with symptoms indicating anaemia should be fully investigated in case she is suffering from the rare macrocytic anaemia of pregnancy.

Conclusions

The administration of iron in pregnancy ensures a high level of haemoglobin at term in about 90% of cases.

It is suggested that giving iron as a routine to all pregnant women is a valuable and inexpensive preventive measure worthy of general application. The safety of domiciliary midwifery—which is questioned at times—would undoubtedly be increased by this means.

We are indebted to Dr. R. G. Macfarlane for helpful criticism, to Dr. Sheila Callender for the haematological investigation of "non-responders," to Dr. R. B. Fisher for statistical advice, and to Glaxo Laboratories and Roche Products Limited for generously supplying fersolate and ferro-redoxon respectively for this trial.

REFERENCES

- Benstead, N., and Theobald, G. W. (1952). *British Medical Journal*, **1**, 407.
- Berlin, N. I., Goetsch, C., Hyde, G. M., and Parsons, R. J. (1953). *Surg. Gynec. Obstet.*, **97**, 173.
- Corrigan, J. C., and Strauss, M. B. (1936). *J. Amer. med. Ass.*, **106**, 1088.
- Davis, L. R., and Jennison, R. F. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 103.
- Dieckmann, W. J., and Wegner, C. R. (1934). *Arch. intern. Med.*, **53**, 71.
- Fullerton, H. W. (1936). *British Medical Journal*, **2**, 577.
- Klopper, A., and Ventura, S. (1951). *Ibid.*, **2**, 1251.
- Medical Research Council (1945). *Spec. Rep. Ser. No. 252*. H.M.S.O., London.
- Roscoe, M. H., and Donaldson, G. M. M. (1946). *J. Obstet. Gynaec. Brit. Emp.*, **53**, 430.
- Samuel, H. S. (1952). *British Medical Journal*, **1**, 817.
- Scott, J. M., and Govan, A. D. T. (1949). *Ibid.*, **2**, 1083.
- Wills, L., Hill, G., Bingham, K., Miall, M., and Wrigley, J. (1947). *Brit. J. Nutr.*, **1**, 126.