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EXPLANATION OF PLATE

Typical 'hob-nail' liver from a malnourished anaemic African child who died aged 8. Histological examination revealed gross fatty change as well as fibrosis.

The anaemias of pregnancy in Dublin

By P. B. B. GATENBY, *Rotunda Hospital, Dublin*

Iron deficiency anaemia in pregnancy

Dublin, a city of over half a million, is served by three large maternity hospitals and over 80% of the pregnancies in the city are cared for by these hospitals. Each hospital has its own 'district' from which it draws most of its patients. These women usually return to the same hospital on each successive pregnancy, and each maternity centre over a chosen number of years has its own group of patients which is fairly constant. About 5000 deliveries are managed by the Rotunda Hospital each year, and about 25% of the attendance is made up of primigravidae but the remainder are multigravidae, almost all of which have attended the hospital on their previous pregnancies. Large families are common and the average parity of the total attendance at the hospital in 1953 was 3·8.

Though it had been realized for some time that anaemia in pregnancy was common and often severe, it was not until 1953 that actual figures of the incidence were obtained. From the beginning of 1953 the problem of anaemia has been specially investigated at the Rotunda. These investigations have been under the direction of Dr H. C. Moore, Pathologist to the Hospital. Every pregnant woman on her first

attendance, which is nearly always before 6 months' gestation, has had her blood examined for haemoglobin content and packed-cell volume. During 1953 and the early part of 1954, the haemoglobin estimations were made with the M. R. C. grey wedge photometer, and the method was standardized against a sample supplied by the Postgraduate Medical School, London. Since then a photoelectric colorimeter has been used and this method has also been repeatedly checked against similar standard samples. All cases with a haemoglobin content below 9 g/100 ml. are referred to special anaemia clinics. At the anaemia clinic particular care is taken of their treatment and the haematological response is checked monthly.

During 1953, 400 cases of severe iron-deficiency anaemia (i.e. Hb below 9 g/100 ml.) were specially studied (Gatenby & Lillie, 1955). It was confirmed that clinical recognition was highly unreliable unless the haemoglobin was below 6 g. Each of these patients was questioned about her diet. Approximately half of them appeared to have a defective diet. The most striking finding was the low consumption of meat, and 50% either never or very seldom ate meat. Most of them ate vegetables other than potatoes. Though protein deficiency may have been a factor in these cases, almost all the anaemias responded very well to iron. Clinical examination did not reveal any other important cause for anaemia, but it was noted that 25% of these patients knew that they were anaemic during a previous pregnancy. It was shown that the incidence of anaemia did increase with parity, particularly when there had been more than five pregnancies. Elsewhere other workers have not found this relation between anaemia and parity (Bethell, Gardiner & McKinnon, 1939; Scott & Govan, 1949; Lund, 1951) but Doyle & McGrath (1954), also working in Dublin, where high parity is common, have found it to be a factor.

The monthly incidence of anaemia amongst attendances over the past 3 years is shown in Fig. 1. It can be seen that when the investigation began the number of

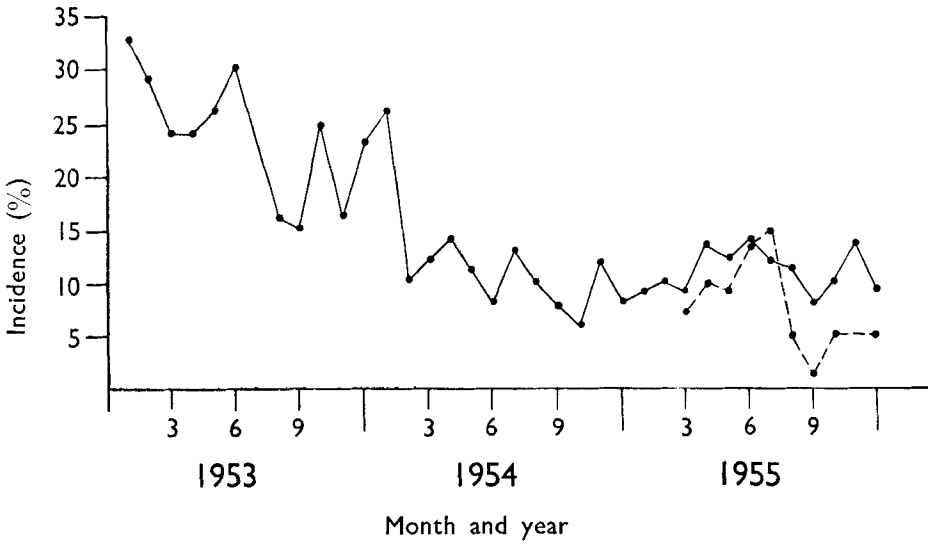

Fig. 1. Monthly incidence of anaemia (Hb below 10 g/100 ml.) amongst first attendances at Rotunda Hospital. — — — —, incidence in private patients.

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those with haemoglobin below 10 g was as high as 33% in the 1st month. The average incidence for 1953 was 24%. This figure is comparable to the figure of 31·4% found at the Coombe Maternity Hospital, Dublin, in the same year (Doyle & McGrath, 1954). There has been a surprising drop in the incidence in 1954 to an average for that year of 12%, and this level has remained unchanged during 1955 (11%). At first one might suspect that differences in the technique of haemoglobin estimation were responsible but it has already been pointed out that the techniques used were standardized. Furthermore, on clinical grounds there is no doubt that there have been far fewer severe cases of anaemia since the end of 1953. As there has been no major change in the diet of the population over this period, it is certainly possible that the change in the situation is due to the special intensive treatment of the severe anaemias. As has been pointed out most of the attendance consists of women who have been looked after at the hospital on a previous pregnancy. Apparently efficient iron therapy not only corrects the anaemia in one pregnancy but can prevent relapse to the iron-deficiency state before the next. It would seem here that the iron reserves have been built up in many women in one pregnancy, so that in the next they are no longer anaemic and thus the total incidence of anaemia has been reduced in subsequent years.

This reduction in incidence of anaemia by iron treatment might seem an obvious fact that hardly requires demonstration, but it shows how far this problem of iron deficiency, which is usually considered as reflecting a low standard of living, can be met by medical means. Fig. 1 also shows that in each year the incidence of anaemia falls towards September. This may be due to the fact that the diet contains more iron and ascorbic acid in the summer months. This seasonal drop has been noted by others (Lund & Kimble, 1943; Scott & Govan, 1949; Doyle & McGrath, 1954).

Since March 1955, all the private patients attending the hospital have also had routine haemoglobin estimations on first attendance. The average incidence of cases below 10 g is 8% which, as one might expect, is lower than in the ordinary patients (11%). Again there was a drop in the incidence towards the autumn (see Fig. 1).

Obviously the diet available to many of our patients who attend the Rotunda is inadequate to meet the increased haematopoietic requirements of pregnancy. This fact has been shown more clearly by Doyle & McGrath (1954) who studied a comparable group at the Coombe Hospital and found a definite relation between defective diet and anaemia. At the time of the National Nutrition Survey in Dublin about 7 years ago, the extraction rate of flour in the Irish Republic was 85–90% and had never been lower since 1941. This high extraction had ensured a reasonable content of iron in the diet (Jessop, 1950). This observation was supported by the findings of Bradshaw (1950) who investigated haemoglobin levels in Dublin at that time. In recent years the extraction rate has been down to 80%, which would favour a rise in the incidence of iron deficiency. The flour in the Irish Republic is not fortified with iron.

It is clear from basic physiological facts that every woman during reproductive life is on the brink of iron deficiency. When she is pregnant, even if her diet is good, it is not certain that she will obtain adequate iron from it alone. Some degree of

iron deficiency is probable in most pregnant women. Over the past few years it has been found by various workers that in many cases of pregnancy a rise in haemoglobin to 12–14 g late in pregnancy is possible with iron treatment (Benstead & Theobald, 1952; Davis & Jennison, 1954; Fisher & Biggs, 1955), which shows that the 'physiological' anaemia of pregnancy is not purely a matter of haemodilution. It would seem reasonable that every pregnant woman should receive efficient iron therapy to supplement her diet.

Megaloblastic anaemia of pregnancy

In the 3 years under review (1953–5) thirty-seven cases of megaloblastic anaemia of pregnancy have been detected at the Rotunda Hospital. This figure represents an incidence of 1 in 365 pregnancies, which is considerably higher than that reported from other centres. Davidson (1951) saw forty-two cases in 11 years at Edinburgh, Thompson & Ungley (1951) found only forty-five cases over 17 years at Newcastle, Lund (1951) estimated the incidence at New Orleans as 2 in 4000 deliveries, but Israëls & Da Cunha (1952) at Manchester diagnosed five cases over a period of 6 months when a special effort was made to find them. There is no doubt that the condition is often missed unless a special watch is kept for such cases, and our large number is partly due to our particular interest in the problem. Many cases present as anaemia refractory to iron therapy during pregnancy but most of them are found in the puerperium. Twenty-six of the thirty-seven cases were diagnosed after delivery, and as noted elsewhere confusing signs such as pyrexia, diarrhoea, and oedema are frequently present at this stage (Callender, 1944; Thompson & Ungley, 1951). This anaemia is more common in multigravidae and only five of the thirty-seven were in their first pregnancy. All cases were confirmed by sternal marrow examination.

In twenty-eight patients a particular note was taken of the diet. It was apparently normal in eight, but twelve were on a diet definitely very low in meat and eggs. The remaining eight had a fair diet, but many of them lacked protein foods. These findings are similar to those of Ungley (1952). Only eleven of twenty-seven of his patients had deficient diets. He doubted whether megaloblastic anaemia in temperate climates was nutritional at all. Indeed it is difficult to believe it is purely a matter of deficiency. Apart from the fact that a fair proportion of patients have had a normal diet, many patients with a grossly inadequate one fail to develop the disease.

The true role of folic acid and vitamin B_{12} in the aetiology of megaloblastic anaemia of pregnancy is obscure. All the cases, or almost all cases, respond to folic acid but this fact does not necessarily mean that the diet is deficient in folic acid. This substance occurs in a wide variety of foods and to postulate an exogenous folic-acid deficiency does not appear to be reasonable. Some cases will also respond to vitamin B_{12} if it be given in massive doses (Moore, Lillie & Gatenby, 1955; Badenoch, Callender, Evans, Turnbull & Witts, 1955), but again there is no clear-cut relationship between the dietary intake of protein, which supplies most of the vitamin B_{12}, and megaloblastic anaemia. Badenoch *et al.* (1955) found no reduction in the secretion of the intrinsic factor, and the serum levels of vitamin B_{12} were also normal. Moore *et al.* (1955) found no evidence of malabsorption of fat, and this finding is confirmed

by Badenoch *et al.* (1955). As they suggest, the cause of megaloblastic anaemia of pregnancy seems to be a resistance to the action of haematopoietic factors rather than a deficiency state.

Conclusion

1. Inadequate diet is an important cause of iron-deficiency anaemia in pregnancy. Nevertheless iron therapy itself is effective in the individual case and there is some suggestion that iron therapy in one pregnancy will prevent or ameliorate iron deficiency in the subsequent pregnancy; presumably by replenishing depleted stores.
2. Inadequate diet is not likely to be the cause of megaloblastic anaemia of pregnancy, at least in European climates. Temporary failure to utilize certain haematopoietic factors is a more probable explanation of this disease.

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The role of pteroylglutamic acid and related compounds in macrocytic anaemia

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As dietary aspects in the narrow sense form such a small part of this subject and will be partly covered by other speakers, I have made this paper rather more general in its scope. It is impossible in a limited space to survey all the literature, and more details can be found in the reviews of Jukes & Stokstad (1948), Welch & Heinle (1951), Girdwood (1952*a*), Stokstad, Harris & Bethell (1954), and others.