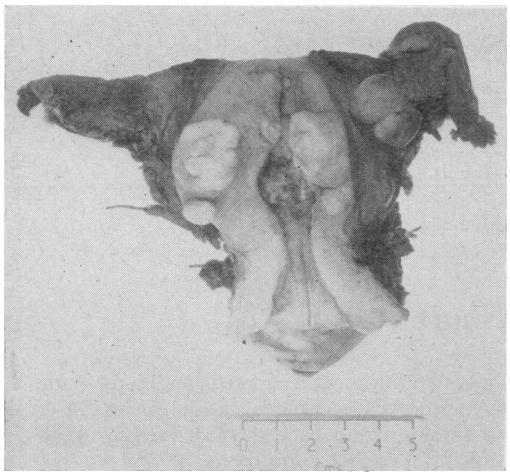

Fig 2 *Uterus showing site of adeno-acanthomatous lesion, after treatment*

Biopsies and photographs are taken at regular intervals, and a study made of effects on iliac and sternal bone marrow.

Of 23 cases treated, 20 were treated to 'optimal' toxicity. Treatment was incomplete in 3 for technical reasons. In 5 cases treatment was followed by Wertheim's hysterectomy, where there had been doubt as to the operability before infusion. All the remaining lesions showed some regression, but this stopped short of disappearance with the exception of 2 cases. There were 3 deaths early in the series, all in patients with advanced cancer.

One patient with Stage II carcinoma of cervix had refused Wertheim's hysterectomy; she had complete clinical regression of her tumour (Trussell & Mitford-Barberton 1961), and when last seen nine months after treatment showed no evidence of recurrence.

A second case, thought at first to be carcinoma of endocervix, proved to be an adeno-acanthoma of the lower part of the uterine body and was treated with methotrexate followed by Wertheim's hysterectomy. At operation, the site of the primary lesion in the body could be easily identified (Fig 2) but repeated histological section showed no trace of carcinoma. There were, however, adeno-acanthomatous deposits in glands on the pelvic wall.

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The paper was illustrated by a film prepared, in conjunction with the author, by the Department of Medical Illustration, Makerere College Medical School.

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Meeting March 9 1962

Blood Diseases in Obstetrics and Gynæcology [*Abridged*]

Dr D A G Galton
(*Chester Beatty Research Institute, London*)

The Management of Leukæmia in Pregnancy

The coincidence of pregnancy and leukæmia is fortunately extremely rare. Forkner (1938) found only 36 acceptable reports, and by 1960 there were still only about 150 (Hayhoe 1960). Leukæmia is a rare disease, and its age distribution and short fatal course account for the rarity with which it is found in association with pregnancy. Chronic lymphocytic leukæmia is a disease of later life; it hardly ever occurs during the child-bearing years, and is in any case less common in women. The mean survival of chronic granulocytic leukæmia is less than three years, and that of acute leukæmia about three months. The incidence of chronic granulocytic leukæmia rises with increasing age during the child-bearing years, but that of acute leukæmia is evenly distributed. Of the 150 cases of coincident leukæmia and pregnancy referred to by Hayhoe, 56% were of chronic granulocytic, 41% of acute, and only 3% of chronic lymphocytic leukæmia.

In chronic granulocytic leukæmia there is no evidence of impaired fertility, and in most reported cases of coexistent pregnancy conception occurred when the disease was already established although the diagnosis was sometimes made during or after pregnancy in symptomless cases. Acute leukæmia may lead to impaired fertility

and, since the course of the disease is usually stormy, it is rare for patients with established disease to become pregnant. In most cases the disease complicates the pregnancy.

Influence of Pregnancy on Leukæmia

In the past some authors believed that pregnancy exacerbated the leukæmic process (Kosmak 1921), and advocated the termination of pregnancy or even the sterilization of leukæmic patients of child-bearing age (Bower & Clark 1925, Neumann 1932, Hofstein 1931, Saidl 1931). There is now, however, general agreement that pregnancy has no adverse effect on the disease. Just over half the women with chronic granulocytic leukæmia who become pregnant may be expected to live one year or more after delivery. At least two cases are on record of patients who survived two normal pregnancies; in one case, the first was a twin pregnancy (Miles & Wheeler 1945, Erf 1947). Those patients who become pregnant late in the course of the disease cannot be expected to fare so well.

The course of acute leukæmia is usually so short that, for the most part, only those patients who succumb to the disease late in pregnancy can be expected to live on into the puerperium. In one series (McGoldrick & Lapp 1943) of 31 patients, 4 died during the pregnancy, 5 during parturition, and only 2 of the 22 who survived lived longer than two weeks after delivery.

Influence of Leukæmia on Pregnancy

In chronic granulocytic leukæmia, either untreated or in relapse, the main symptoms are commonly due to massive splenomegaly, to anæmia, and to the effects of a high metabolic rate. Pregnancy, as it advances, increases the discomfort to an extent which varies from case to case. The pregnancy itself is believed to be little affected by this disease, and about 75% of the offspring survive the neonatal period.

In acute leukæmia the symptoms arise from three main sources: (1) Neutropenia exposes the patient to infections which are all too frequently intractable. (2) Thrombocytopenia renders her liable to hæmorrhagic manifestations which may prove impossible to control. (3) Leukæmic infiltrations may occur at various sites, and may threaten life, as in the case reported by Bierman *et al.* (1956) in which a mediastinal mass was present. Abortion and premature onset of labour are common in acute leukæmia. Over half the offspring are stillborn or die in the neonatal period.

There is no good evidence that leukæmia is ever transmitted directly from mother to child. Hayhoe (1960), however, has pointed out that adequate follow-up studies of the children of leukæmic mothers have not been reported, though he thinks it likely that patients with leukæmia whose mothers were known to have had leukæmia at the time of their birth would have been reported.

Influence of Treatment on the Fœtus

The essential obstacle to the management of leukæmia by the usual methods, when the patient is pregnant, is that all the specific forms of treatment involve the use of agents which damage proliferating tissue of all kinds and are therefore potentially harmful to the embryo and the fœtus. The problem is one of helping the patient to live as comfortably as possible during her pregnancy, and at the same time to avoid harming her child. In practice the agents principally to be considered are X-rays, busulphan and 6-mercaptopurine.

There is much experimental evidence to show that each of these agents is harmful to developing embryos. The nature of the harmful effects and their severity depend on the dosage and on the stage of pregnancy at which the exposure occurs. Of the three agents X-rays appear to be the most damaging, 6-mercaptopurine the least. It is not known whether there are dose levels for these agents below which no damage is likely to occur, and it is this which makes it difficult to apply the results of experimental work, in which relatively large doses of the offending agents have been used, to clinical practice.

The effects in experimental animals, usually rats, have varied from stunting of growth (6-mercaptopurine; Thiersch 1954), to gross developmental defects not compatible with life (X-rays, busulphan; Murphy *et al.* 1958). Doses of busulphan large enough to cause marked depression of the neutrophil count may, however, be administered to rats without affecting the pregnancy. Dr M Till and I (unpublished observation) used a single dose of 8 mg/kg body weight administered on the ninth day of pregnancy. The number of offspring was normal, the animals appeared normal, and were mated amongst each other. The next generation was normal. Bollag (1954) used slightly larger doses rather later in pregnancy. The offspring appeared normal, but proved to be sterile and were found to have atrophic gonads. Murphy *et al.* (1958) found that larger doses of busulphan were definitely teratogenic for the rat, but this drug was less harmful than other alkylating agents (nitrogen mustard, triethylene melamine, triethylene thiophosphoramide, chlorambucil). It seems that the foetus is relatively less affected than the mother, as judged by the effect on the bone marrow. In the case reported by Bierman *et al.* (1956), the mother had received large doses of triethylene melamine for eleven weeks up to the time of Cæsarean

section. She had severe thrombocytopenia and anæmia at the time, but the child had only slight transient leucopenia.

Several reports have now been published of patients with chronic granulocytic leukæmia who have received either busulphan (Izumi 1956, Sherman & Locke 1958, Reyes & Perez 1961) or mercaptopurine during and sometimes throughout pregnancy. In at least one case conception had occurred while the patient was receiving busulphan. The babies were apparently normal though occasionally underweight, but the longest follow-up is still only five years. In one case, alternating courses of busulphan and mercaptopurine were administered throughout the pregnancy (Diamond 1958). The infant weighed 3 lb and had multiple developmental defects including corneal opacities, cleft palate, microphthalmia and ovarian and thyroid hypoplasia. Sokal & Lessmann (1960) have reviewed all the reports on the effects of the administration of chemotherapeutic agents on the fœtus, and have pointed out that the abnormalities described by Diamond have not been recorded when either busulphan or mercaptopurine was the only drug administered. They believe that the drastic effect might have been due to a synergistic action of the two drugs, but they stress the fact that the mother received treatment during the first three months of pregnancy, and that fœtal damage did not occur when combinations of other drugs were administered later in the pregnancy.

Sokal & Lessmann have further drawn attention to the difficulty of applying the experimental results to the treatment of the human being. There are two major discrepancies: (1) Different species do not react in the same way to the same drug. Thus aminopterin produced relatively few fœtal abnormalities in rats, but has been shown to cause severe malformations in the human fœtus. (2) The most sensitive period for the induction of developmental defects was thought to be the middle third of pregnancy in laboratory animals, but in the human being no reports were found of malformations when the drugs were administered after the first three months of pregnancy.

Nevertheless, the experimental findings clearly cannot be ignored. Although apparently healthy infants have been born after a pregnancy during which they were exposed for long periods to the action of busulphan or mercaptopurine, it is impossible to conclude that these drugs are harmless to the fœtus, and, in planning treatment in each case, it would seem reasonable to assume that they are harmful.

In acute leukæmia, the remission rate for mercaptopurine therapy in adults is only about 7% in the common myeloid forms of the disease, and it would be possible to make out a case for omitting this drug from consideration, at any rate in the first four months of pregnancy. In the rare lymphoblastic form, steroid therapy is likely to be effective in about half the cases and so far as is known will not harm the fœtus. The problem is essentially to maintain the pregnancy as long as possible by symptomatic treatment to counteract anæmia, hæmorrhage and infection, and to employ such obstetric manœuvres as are judged most likely in each case to result in a live birth. Cæsarean section has sometimes been successfully employed (Fleischmann 1923, Hüssy 1934, Moloney *et al.* 1943, Erf 1947, Bierman *et al.* 1956, Dameshek & Gunz 1958).

In the case of chronic granulocytic leukæmia, there will be patients who can safely be left without treatment throughout the pregnancy. The difficult problems will be those of anæmia and of gross splenomegaly. Blood transfusion may be required. If the spleen gives rise to severe discomfort it may be necessary to resort to radiotherapy or busulphan. In either case treatment should be deferred as long as possible. Of the two forms of therapy busulphan is perhaps the less likely to harm the fœtus.

In the management of both forms of leukæmia, the changing hæmatological situation may be grasped most conveniently by plotting the hæmoglobin, leucocyte and platelet values on a chart which includes both a plain squared scale and a semilogarithmic scale (Galton 1959). Inspection of the past course of the disease makes it possible to predict, to some extent, its future behaviour.

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Dr J C White (*Department of Hæmatology, Hammersmith Hospital, London*) read a paper entitled **Pregnancy Anæmias in the Immigrant Population of London: Hæmatological Aspect.**

Dr Geoffrey Dixon
(*Institute of Obstetrics & Gynæcology, Hammersmith Hospital, London*)

Pregnancy Anæmias in the Immigrant Population of London: Clinical Aspects

The coloured immigrant is now part of the everyday pattern of life in this country. For both medical and social reasons the women must often be confined in hospital and many maternity units now find that a considerable percentage of their bookings are for immigrants.

At Hammersmith Hospital 20% of our bookings are for coloured women. They have brought their own obstetrical problems with them and one of the most frequent is anæmia. Thus, over 50% of patients attending the special antenatal 'anæmia' clinic are coloured. All women with a hæmoglobin level below 11·1 g% attend this clinic and 25% of our total bookings are seen there.

Anæmia in pregnancy is of profound concern to the obstetrician as it can influence unfavourably not only gestation but also labour and the puerperium. It is of such importance that in almost all centres routine oral iron therapy is given. If no response is obtained with oral iron, then frequent resort is had to intravenous iron.

There is a considerable danger in applying this routine type of therapy to patients with hæmoglobinopathy. The iron stores are usually high and, indeed, hæmochromatosis may occur terminally in the more severe varieties. The administration of parenteral iron to such patients is obviously not only useless but may be actively harmful. It should only be given to a patient with an abnormal hæmoglobin when there is clear-cut evidence of depleted iron stores; this rare coincidence is found when a hæmoglobinopathy exists with some other cause for iron deficiency anæmia.

The incidence of hæmoglobinopathy in our present series has been high: 38·5% of the 65 patients seen show traits for abnormal hæmoglobins or thalassæmia. A further 24·5% probably have thalassæmia trait but are as yet undelivered and incompletely investigated.

In all these chronic hæmolytic anæmias the bone marrow is extremely active and although the patient's hæmoglobin level may be low, she is well adjusted to it and transfusion, by depressing marrow activity, may provoke an aplastic episode. This was clearly shown for sickle cell disease (SS) by Anderson *et al.* (1960). The normal hæmoglobin level in this condition is about 8 g/100ml (Went & MacIver 1958). Transfusion at this level may be most dangerous. Henderson (1950) reported 17 reactions with 3 deaths in 44 transfusions in sickle cell anæmia. Our experience in Jamaica led us to the conclusion that transfusion simply to elevate the hæmoglobin level in SS anæmia was only justified if it fell below 6 g/100 ml. However, cross-matched blood should be available throughout labour in order that any blood loss may be restored.

The hæmoglobin levels given are for sickle cell anæmia itself. This is probably the most severe example of the group but all these conditions have an optimal level of hæmoglobin and in all of them transfusion except for active loss may worsen the condition.

Another severe complication that may arise in the pregnant woman with SS or SC hæmoglobin or sickle cell thalassæmia disease is the well-known sickle cell crisis. The most striking clinical manifestation is pain. This commonly occurs in bones and joints but may extend to or even be confined to abdomen or chest. It is usually associated with leucocytosis and fever. The possibility of such a crisis should always be borne in mind in the differential diagnosis of acute abdominal pain in the pregnant coloured woman. The painful crises appear to be associated with erythrostasis of sickled red cells (Golding *et al.* 1959) and not with any marked fall in hæmoglobin or rise in reticulocyte count.

Such crises may be precipitated by inadequate oxygenation, as in poor anæsthetic technique, by transfusion, and probably by infection (Anderson *et al.* 1960).

Duckett & Davis (1953) suggested that pregnancy itself may precipitate crises and our own observations in Jamaica support this suggestion as, of our 6 primigravidæ with sickle cell anæmia, 3 had been asymptomatic until pregnancy.

Whilst these severe reactions only occur in the more extreme hæmoglobinopathies, there is a well-recognized association between sickling and hæmaturia. This symptom seems particularly liable to develop in the sickle cell trait (AS) (Alleyne & Went 1959) but it has been observed with sickle cell anæmia (SS) and sickle cell hæmoglobin C disease (SC). We have not, however, observed it in the present series.

Whilst investigating these coloured patients at Hammersmith Hospital, we found an unexpectedly frequent association of reduced iron stores with hæmoglobinopathy, especially thalassæmia. As part of our search for possible causes of blood

loss we began to search the fæces for parasites. In the first patient so investigated we discovered hookworm ova. Impressed by this result we have added examination of fæcal specimens to our investigation of anæmic women coming from any locality where hookworm is endemic.

Almost all the areas from which immigrants come to this country are heavily infested with either *Necator americanus* or *Ankylostoma duodenale* and frequently with both. By virtue of the somewhat complicated and hazardous life cycle of these parasites it seems unlikely that reinfestation nowadays occurs in this country but we have found the ova in patients who have been in the United Kingdom for up to five years. There seems good evidence that the parasite may live in the gut for up to seven years (Manson-Bahr 1954).

We have so far examined fæcal specimens from 45 patients and found hookworm in 14, an incidence of about 30%.

In addition to causing anæmia, hookworm infestation appears to be associated with a higher incidence of abortion and stillbirth. Treatment is therefore urgent during pregnancy. The standard treatment of either tetrachloroethylene or oil of chenopodium is unpleasant and even, in the anæmic patient, dangerous. In Jamaica we formed the impression that it was frequently followed by an otherwise inexplicable intrauterine death. We have therefore treated our pregnant patients at Hammersmith Hospital with bephenium hydroxynaphthoate in the form of Alcopar granules.

We have not found it to be effective in the usually recommended dose of one sachet of 5 g and give one such dose daily for five days. Even in this dosage we have had three failures, but the drug appears to be so free of side-effects that on these occasions we have repeated the five-day course with success.

In addition to hookworm we have found other less pathogenic parasites, especially *Strongyloides stercoralis* and *Trichuris trichiuria.*

Eosinophilia in the blood count is, of course, a valuable indication of parasitic infestation and on one occasion in a patient from British Guiana, who had been in London for more than a year, we were led by the presence of a persistent eosinophilia in the absence of intestinal parasites to take blood smears at 2 a.m. In these the microfilariæ of *Filaria bancrofti* were easily identifiable. It thus seems that tropical diseases are no longer confined to the tropics.

On the basis of our experience with these patients and especially in the light of the therapeutic and obstetrical hazards of the hæmoglobinopathies we suggest that every anæmic coloured pregnant woman is investigated for the presence of sickling, abnormal hæmoglobin and abnormal red cell fragility. Whilst serum iron and iron binding capacity estimations are useful we suggest frequent resort to bone marrow biopsy for evidence not only of megaloblastic change but of the level of storage iron. Unless this is low, parenteral iron should not be given, but oral iron is unlikely to be harmful.

Because of the frequency of helminth infestation we also suggest that examination of fæcal specimens should become routine in such patients.

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Dr C Coyle and Dr F Geoghegan
(National Maternity Hospital, Dublin)

The Problem of Anæmia in a Dublin Maternity Hospital

The National Maternity Hospital is one of three large obstetrical hospitals catering for the urban population of Dublin and for the adjoining counties. It also serves as a regional centre for obstetrical emergencies arising within a radius of approximately seventy-five miles. There are over 5,000 deliveries in the hospital each year. Of the patients admitted to the hospital 15% are in the category of grand multiparity and severe accidental hæmorrhage is frequent. Approximately 27% of patients are over 35 years of age, and nearly two-thirds of patients fall into the least favourably circumstanced social groups (Registrar General's classification).

During the years 1959–60 a review of the anæmia problem existing in the hospital was carried out. Despite the frequency of high parity and the social and economic influences, already alluded to, initial hæmoglobin levels (measured at the first pre-natal visit) were not unsatisfactory, but in 44% of patients attending for ante-natal care the hæmoglobin level deteriorated significantly by the 32nd week of pregnancy. Oral iron was prescribed routinely at the first ante-natal visit. The hæmoglobin level was checked at the 32nd week. Patients who had failed to maintain their hæmoglobin level where it was initially satisfactory or who failed to improve where it was deficient were given parenteral iron. In cases which did not respond to parenteral iron, a

sternal marrow examination was carried out. A high incidence of megaloblastic erythropoiesis was detected. Among 6,017 patients investigated 195 showed hæmatological evidence of folic acid deficiency in greater or less degree. A significant association with multiple pregnancy was noted. Among the 195 patients who showed megaloblastic erythropoiesis there were 12 cases of multiple pregnancy, three times the incidence among the patients of the hospital as a whole. A peculiar frequency of megaloblastic erythropoiesis was noted among patients admitted in emergency with severe accidental hæmorrhage. Among 77 such cases there were 35 in which the bone marrow pattern showed some degree of megaloblastic change and it is believed that the unfavourable blood picture frequently presented in the puerperium by such patients is significantly influenced by this fact. High parity, antecedent untreated anæmia and advancing age are notoriously features of these cases.

A seasonal incidence of megaloblastic anæmia similar to that already noted in Dublin by Gatenby (1956) was observed. Cases were more frequent in the winter months. There was not invariably a close correlation between the severity of anæmia and the grade of megaloblastic change in the bone marrow. A particularly florid instance of megaloblastic erythropoiesis was detected in a woman whose hæmoglobin level at the time of diagnosis was 73% (10·6 g%). It was evident that the condition tends to recur in successive pregnancies. In 50% of cases the diagnosis was made in the puerperium, reflecting the frequency of the condition in unbooked cases, in patients whose attendance for antenatal care has been irregular, and in women admitted in emergency with accidental hæmorrhage. Because of the high proportion of patients of 35 years and over, the routine prophylactic administration of folic acid to patients attending the National Maternity Hospital for ante-natal care carries a certain risk, and cases in the age group referred to require special consideration.

[This paper will be published in full elsewhere.]

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Dr W G MacGregor (*London*) said he found the three months average duration of the acute forms of leukæmia helpful, because on at least two occasions where he had encountered pregnancy and acute leukæmia the problem had been to decide the fate of the unborn child. Should terminal or post-mortem Cæsarean section be contemplated, it would appear that the fœtus would almost certainly have died an anoxic death *in utero*. Fortunately, nature had solved both these problems.

Secondly, if the incidence of megaloblastic anæmia in Dublin practice was so high, it would seem wise, in an area so geographically placed, to give folic acid to all patients in the antenatal period; he presumed the reason for not doing so was that true B_{12} deficiency could be masked and subacute combined degeneration of the cord subsequently develop. This argument was more theoretical than true having due regard to the greatest good for the greatest number in Dublin. He asked whether anyone had any experience of the development of subacute combined degeneration of the cord following folic acid administration for macrocytic anæmia in pregnancy.

Miss W E Lewington (*London*) said she had looked after 5 cases of sickle cell disease recently. Four had the homozygous SS sickle cell anæmia, and one of these patients had an intra-uterine death at 34 weeks. This patient gave a history of two previous intra-uterine deaths and had no live child. The other patients all gave birth to live babies.

Mr Herbert E Reiss (*London*) said that at Hackney Hospital, London, the percentage of patients from the West Indies, West Africa, and Cyprus had risen from about 20% in 1959 to about 37% in 1961. There had been no overall increase in the incidence of anæmia during that time; in 1961, out of 2,665 patients delivered, 39% had one or more readings below 70% Hb during pregnancy, and 6·9% below 60%. The majority of anæmias in the immigrants were of the iron deficiency type. However, in 1961, 46 cases of hookworm infestation had been found, and stool examination of anæmic patients from abroad was now performed routinely.

During the last four years there had been 39 pregnancies in 34 patients with abnormal hæmoglobins (Table 1).

In this series there had been no maternal mortality, although serious crises had occurred in patients with sickle cell anæmia, Hb SC disease and sickle cell thalassæmia.

Table 1
Pregnancies in patients with hæmoglobinopathy

Type of Hb	*No. of patients*	*No. of pregnancies*	*Perinatal loss*
Hb SA	20	22	Nil
Hb SC	3	4	Nil
Hb SS	1	3 (Twins / Triplets / Single)	4
Thalassæmia minor	8	8	1
Sickle cell thalassæmia	2	2	1

Dr O A N Husain (*London*) mentioned the use of the FIGLU (formiminoglutamic acid) test in pregnancy. He had carried out a small pilot survey at the Lambeth Hospital over the winter 1960–61 on about 170 consecutive pregnancies. Using a screening FIGLU test each month in the last trimester he had found about 20% of positive tests around term and early puerperium.

Amongst these there had been 4 true megaloblastic anæmias of pregnancy and 6 other cases with some other collateral evidence of folic acid deficiency though usually without anæmia. Moreover, the test had been positive at the 28th week in all the true megaloblastic anæmias and in most of the other 6 cases, which suggested that the FIGLU test provided a very early method of detection of folic acid deficiency. Of the negroes who constituted 20% of the series, nearly half gave a positive FIGLU test and included two of the megaloblastic anæmias.

Certainly the 20% of positive results supported the policy of routine folic acid therapy in the last trimester, though he stressed that the majority of these FIGLU-positive cases were not anæmic or otherwise clinically abnormal.

Professor J H M Pinkerton (*London*) said that the apparent increase in megaloblastic anæmia of pregnancy over the past decade was very striking. It might be explained in part by more thorough investigation of anæmic patients during pregnancy, but, having searched during the past 15 years for this form of anæmia in Belfast, Jamaica and London, and having found it only very occasionally, certainly not in 3% or 4% of antenatal patients, he was forced to the conclusion that the workers reporting these cases in such large numbers must be making the diagnosis on criteria other than the presence of classical megaloblasts in the bone marrow. There was bound to be much greater difficulty in getting agreement among hæmatologists if the diagnosis were to depend upon the presence of abnormal normoblasts intermediate in type between classical megaloblasts and classical normoblasts. Some would and apparently did make the diagnosis of megaloblastic anæmia more readily than others. The picture was further complicated by the co-existence in many of these patients of an undoubted iron deficiency which certainly needed correction before folic acid would cure the anæmia.

He agreed that patients with hæmoglobinopathies associated with hæmolysis must not be over-treated with parenteral iron. However, he could see no logical reason why a woman with sickling hæmoglobin who grew up on a grossly iron-deficient diet and had had several pregnancies to deplete her iron stores still further should be much less iron deficient that her neighbour whose blood contained normal hæmoglobin. And if she was deficient in iron she should be given iron.

The most common and important form of anæmia, especially in pregnant women, the world over, was iron-deficiency anæmia; the proper treatment for this was the administration of iron and protein in a form that the patient would take and could assimilate; if necessary the iron should be given parenterally.

Dr B M Hibbard (*Liverpool*) said that as Hammersmith was to Jamaica, so Liverpool was to Dublin. The population was similar and 10% of hospital bookings were grand multiparæ. The findings in these patients confirmed those of Dr Coyle and Dr Geoghegan–a high incidence of megaloblastic anæmia and of abruptio placentæ with a marked correlation between the two conditions. Abruptio placentæ occurred in 2·3% of the grand multiparæ, which was three times the rate in primigravidæ and twice the overall rate. Over two-thirds of recent patients with abruptio placentæ showed evidence of folic acid deficiency.

In reply to Dr McGregor, for the last five years it had been the practice in the majority of antenatal clinics in Liverpool to prescribe folic acid for all anæmic patients in a combined iron, folic acid and ascorbic acid tablet. Approximately 12,000 new patients attended these clinics annually and no case of subacute combined degeneration of the cord had been reported to date. There had only been two cases of Addisonian anæmia, both of which were diagnosed and treated prior to pregnancy. Both these patients were infertile prior to treatment. This was a common finding and might in part account for the low incidence of Addisonian anæmia in association with pregnancy.