PROPHYLAXIS OF ANAEMIA IN PREGNANCY

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DURING the past decade, there has been increasing interest in the recognition of folic acid deficiency in pregnancy and in the puerperium. The place and dosage of folic acid supplements, however, remain controversial. The definition of the normal range of haemoglobin levels, and thus of anaemia in pregnancy also remain controversial (Hytten and Leitch 1964). However, it has been clearly shown that low maternal haemoglobin levels are associated not only with an increased foetal mortality rate (Butler and Bonham 1963), but also with a number of 'avoidable' maternal deaths (H.M.S.O. 1963 and 1966).

The following study was undertaken to compare the effects of two different treatment regimes on haemoglobin levels in pregnancy.

Method

The patients studied comprised a selected group of 200 women who had booked at the hospital antenatal clinic before the twentieth week of pregnancy; whose antenatal care was undertaken wholly by the hospital antenatal clinic and who subsequently had a normal delivery in hospital. They had been referred to the antenatal clinic by their general practitioner and were then allocated randomly to either Group A or Group B, each group being under the care of a different consultant obstetrician.

Group A were treated with oral iron (Tabs. Ferrous Sulphate Co. N.F. 200 mg t.d.s.) throughout pregnancy. The obstetrician felt that folic acid therapy was indicated in nine patients who were therefore all given 5 mg t.d.s. during the last trimester.

Group B were treated with combined oral iron and folic acid tablets (ferrous sulphate 200 mg folic acid 1.7 mg t.d.s.) throughout pregnancy.

Blood was obtained by venepuncture and placed in sequestrene containers. The haemoglobin level was determined using an oxyhaemoglobin method in a photoelectric colorimeter (Dacie and

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Lewis 1963). The haemoglobin levels recorded are those obtained, (1) on the day of booking, and (2) on the third day after delivery. The haemoglobin estimations were performed by laboratory technicians who, at the time, were not aware that the blood samples were obtained from patients in different treatment groups.

Results

The distribution of the haemoglobin levels found at the time of booking and on the third day after delivery are given in tables I and II. For ease of comparison, the results are expressed as the percentage of patients in each group with haemoglobin levels above or below 12.0 grams per 100 ml. (82 per cent Haldane) respectively.

TABLE I
DISTRIBUTION OF HAEMOGLOBIN LEVELS AT TIME OF BOOKING

Haemoglobin level (Gm per cent)	*Group A*				*Group B*			
	Primigravida		*Multigravida*		*Primigravida*		*Multigravida*	
		Per cent		*Per cent*		*Per cent*		*Per cent*
Below 10.. ..	0	—	3	*5*	2	*4*	5	*9*
10–10.9	5	*12*	6	*10*	4	*9*	10	*18*
11–11.9	14	*33*	23	*40*	14	*31*	19	*35*
12–12.9	16	*38*	17	*29*	20	*45*	16	*29*
13–13.9	6	*14*	8	*14*	5	*11*	4	*7*
Above 14 ..	1	*2*	1	*2*	0	—	1	*2*
TOTAL.. ..	42		58		45		55	

At the time of booking there was little difference in the haemoglobin levels found in treatment groups A and B (tables I and II); it is, however, apparent that primigravidae tended to have higher haemoglobin levels than multigravidae (figure 1; $\chi^2=3.55$; P= <0.10> 0.05). The age distribution of primigravidae and multigravidae, and also the number of previous pregnancies in multigravidae was similar in each treatment group.

On the third day after delivery there was little difference between the haemoglobin levels found in primigravidae of either treatment group A or treatment group B, (figure 2; $\chi^2=1.45$; P= <0.30> 0.20); whereas it is apparent that the multigravidae in treatment group B (who had received combined iron and folic acid tablets) had significantly higher haemoglobin levels than those in treatment group A, who had received only iron tablets (figure 3; $\chi^2= 6.31$; P = <0.02 > 0.01). This difference does not appear to be related to variations in blood loss at the time of delivery (table III).

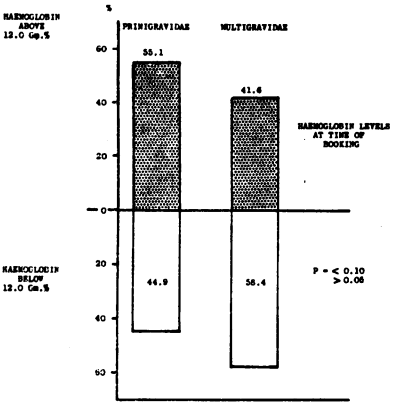

Figure 1
Percentage of patients with haemoglobin levels above or below 12.0 gm per cent at the time of booking

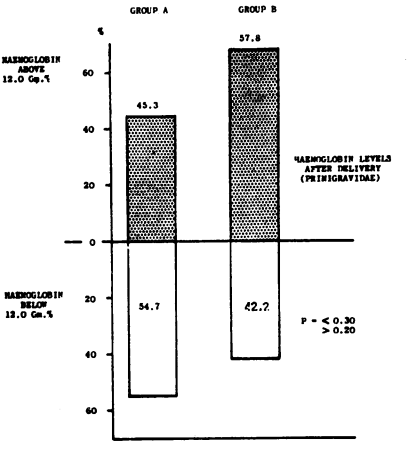

Figure 2
Percentage of primigravidae in each treatment group with haemoglobin levels above or below 12.0 gm per cent on third day after delivery

TABLE II
DISTRIBUTION OF HAEMOGLOBIN LEVELS ON THIRD DAY AFTER DELIVERY

Haemoglobin level (Gm per cent)	*Group A*				*Group B*			
	Primigravida		*Multigravida*		*Primigravida*		*Multigravida*	
		Per cent		*Per cent*		*Per cent*		*Per cent*
Below 10.. ..	1	*2*	6	*10*	2	*4*	2	*4*
10–10.9	10	*24*	14	*24*	7	*16*	10	*18*
11–11.9	12	*29*	20	*35*	10	*22*	13	*24*
12–12.9	15	*36*	13	*22*	14	*31*	18	*33*
13–13.9	4	*9*	4	*7*	9	*20*	10	*18*
Above 14 ..	0	—	1	*2*	3	*7*	2	*4*
TOTAL	42		58		45		55	

Discussion

The occurrence of physiological fall in haemoglobin concentration during pregnancy is generally accepted. This fall is greatest at about the thirtieth week of pregnancy and is associated with an increase in the total blood volume where the increase in the plasma volume is relatively greater than that in the red cell volume (Paintin 1962). This fall in haemoglobin concentration can be reduced or prevented by iron therapy and it is usually assumed that this implies iron

TABLE III
BLOOD LOSS AT DELIVERY

Blood loss (mls)		*1–124*	*125–249*	*250–374*	*375–499*
Primigravida:	Group A ..	11	20	8	3
	Group B ..	11	18	13	3
Multigravida:	Group A ..	19	24	11	4
	Group B ..	16	22	13	4

deficiency; however, Witts has shown that iron in therapeutic doses can cause haemoglobin concentration to rise even in the non-anaemic (Witts 1962). Nevertheless, iron deficiency in pregnancy is almost universal (Chanarin, Rothman and Berry 1965); indeed, the administration of oral iron supplements during pregnancy is now almost universal (Rhodes 1965), although controversial (W.H.O. 1965, Thomson, Hytten and Paintin 1967). However, it has been shown that haemoglobin levels of many women remain reduced for at least a year after delivery (Magee and Milligan 1952). In the present study the distribution of haemoglobin levels at the time of booking was found to be lower in the group of multigravidae than in the group of primigravidae; one explanation being that multigravidae have remained iron deficient from the time of a previous pregnancy.

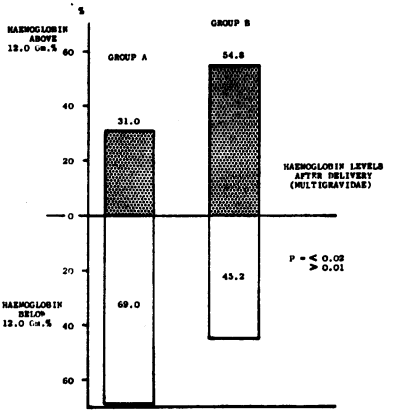

Figure 3
Percentage of multigravidae in each treatment group with haemoglobin levels above or below 12.0 gm per cent on third day after delivery

The place and dose of folic acid supplements in pregnancy is still controversial. The reported incidence of megaloblastic anaemia of pregnancy and the puerperium is variable but relatively small: less than 0.5 per cent (Gattenby and Lillie 1960), to more than 4 per cent (Hourihane, Coyle and Drury 1960). However, subclinical folic acid deficiency appears to be much more common and occurs in about 60 per cent of pregnant women (Chanarin *et al.* 1965). Following the introduction of folic acid prophylaxis during preg-

nancy the incidence of megaloblastic anaemia in pregnancy and the puerperium has fallen markedly in North Staffordshire (Giles 1966). In this same area it has been shown that women given prophylactic iron and folic acid have, in general, higher haemoglobin levels at term than those given prophylactic iron alone (Giles and Burton 1960).

In the present study it has also been shown that the group of women receiving supplementary iron and folic acid had a distribution of haemoglobin levels on the third day after delivery that was higher than that in the group receiving iron supplements only, in spite of the fact that nine per cent of this second group received therapeutic doses of folic acid. The differences were more marked in multigravidae than in primigravidae. Others have noted that megaloblastic changes in the bone marrow are more common in multigravidae and tend to recur in a subsequent pregnancy (Giles 1966, Varadi, Abbott and Elwis 1966). As noted earlier many multigravidae are iron deficient; their increased liability to become also folic acid deficient may be due to the accompanying deficiency of iron, persisting from the time of a previous pregnancy. The relationship between iron deficiency and folic acid deficiency is complex, but iron deficiency appears to be important in the genesis of overt folic acid deficiency (Chanarin *et al.* 1965). In theory, therefore, the difference between the treatment groups might well have been reduced by more energetic treatment with iron alone.

In practice, however, it appears that higher haemoglobin levels are obtained by the routine administration of supplementary iron and folic acid rather than by the routine administration of supplementary iron alone with added folic acid only if indicated haematologically. The risks of the widespread use of such a combined tablet are probably small when compared with the considerable advantages to the pregnant mother and her child. These disadvantages could be further reduced by ensuring (1) that such combined tablets are prescribed only during pregnancy, (2) that any untaken tablets are returned after delivery, and (3) that the smallest generally effective supplement of folic acid is used; at present this appears to be about 0.3 mg per day (Willoughby and Jewell 1966, Willoughby 1967).

Summary

The distribution of haemoglobin levels at the time of booking at a hospital antenatal clinic, and on the third day after delivery in hospital were studied in two selected groups of 100 women. One group was treated with oral iron (supplemental folic acid was also given to nine of these women) and the other group was treated with combined oral iron and folic acid during pregnancy.

At the *time of booking*, the distribution of haemoglobin levels in

both groups was comparable; it was noted, however, that primigravidae tended to have higher haemoglobin levels than multigravidae.

On the *third day after delivery* the distribution of haemoglobin levels of primigravidae was similar in each treatment group; but in multigravidae the group treated with combined oral iron and folic acid had significantly higher haemoglobin levels than those treated with oral iron alone.

The significance of these findings is discussed.

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