HAEMOGLOBIN LEVELS BEFORE AND AFTER LABOUR

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The Medical Research Council in 1943 carried out a survey of haemoglobin levels in Great Britain covering some 16,000 people of different ages and occupations (M.R.C., 1945). From the findings it was inferred that anaemia was probably less prevalent in Great Britain than before the war, but, although the incidence in children and pregnant women was almost certainly less than in the early days of the war, it was considered to be unduly frequent in these groups. The practice of prescribing iron prophylactically as well as therapeutically for expectant mothers was fairly common for some years before 1939, and there is reason to believe that it has increased since the Ministry of Health drew attention to the importance of giving suitable preparations of iron to guard against anaemia occurring in pregnant and nursing mothers (*Med. Offr*, 1943). It was, nevertheless, thought advisable to make, from time to time, occasional small-scale haemoglobin surveys on these vulnerable groups.

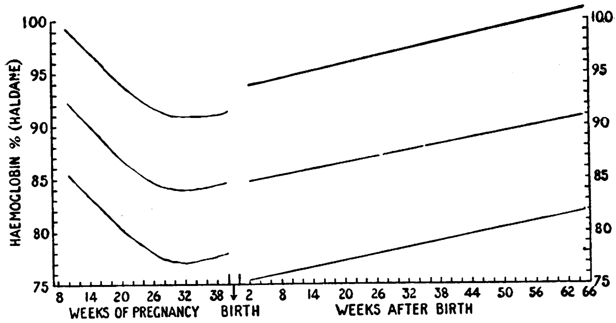
In this paper are reported the results of the statistical analysis of observations made in the Manchester area during the past three to four years on some 2,000 mothers during pregnancy or for a year or more after the birth of their babies. Surveys have also been carried out on schoolchildren, but these are not reported here.

A method for determining haemoglobin suitable for field conditions required some thought. The experience of the M.R.C. survey workers did not inspire confidence in the Haldane instrument, particularly in the hands of persons using it at irregular intervals, as was the case with our observations. Subsequent reports in which the Haldane instrument was compared with others have confirmed the earlier suspicions (Macfarlane, King, *et al.*, 1948). On the advice of Professor King we employed the M.R.C. grey-wedge photometer, using alkaline haematin. The procedure is described fully elsewhere (Adcock *et al.*, 1948). Preliminary accounts of the findings obtained in these surveys have already been published (Magee and Milligan, 1949, 1950). Further statistical analyses of the data obtained during and after pregnancy have brought to light a number of points of interest which we think worthy of more complete record.

Method

The survey was made on women attending the antenatal and child-welfare clinics in and around Manchester. They belonged, for the most part, to the working-class and were, of course, volunteers; there was no selection of any sort. Of all the 2,087 women whose blood was examined, 1,244 were sampled before and 843 after labour. All except 667 were examined clinically, and their nutritional state was assessed by the methods commonly employed by the Ministry's clinicians.

The observations were divided into weekly periods and averaged. From the means so obtained curves were fitted by the method of least squares. These curves are shown in the accompanying Chart. The equations were as follows:



Haemoglobin values of 2,087 women during and after pregnancy. Smooth curves with limits ± 1 S.D.

$$\text{Antenatal Hb} = 100.7 - 1.0x + 0.15x^2 \pm 6.7$$
$$\text{Post-natal Hb} = 84.4 + 0.104x \pm 9.4$$
Where x = time in weeks

The observations were classified into those of women who had been taking iron (1 gr. (65 mg.) t.d.s. of ferrous iron) for three weeks or more before sampling or who had not, and also according to parity.

In the past it has been customary to classify haemoglobin values during and after pregnancy according to where they fell in relation to certain empirically selected levels. The level most often selected was 80% (Haldane), and values falling below this were considered to be too low and were generally regarded as indicative of anaemia. The test was admittedly far from satisfactory, specially during and soon after pregnancy, for it is well known that the haemoglobin in healthy women falls steadily during pregnancy until shortly before labour and rises gradually again after labour. Therefore, in deciding whether a haemoglobin value taken during these periods is or is not satisfactory, account has to be taken of these physiological changes. This was done in the present series of observations, and two curves have been drawn, one standard deviation below and one above the curve of the means. It therefore seems that any values outside these limits are either abnormal or tend to be so.

Results

Mean Haemoglobin Level

The data show a steady decline from nearly 93% at the eighth week of pregnancy to a minimum of just under 81% from the 32nd to the 34th week approximately. Thereafter it rose consistently to nearly 85% at the 39th week. This rise gives the curve a slightly parabolic appearance.

The post-natal curve, on the other hand, is a straight line. It rises from about 85% at the fourth post-natal week to 90.5% at the 65th. The post-natal values are much more irregular than the antenatal, the standard deviation of the former series being 9.4 compared with 6.7 for the antenatal series. It is noteworthy that the level even at the 65th week after labour was still some 2–3% less than the value found at the eighth week of pregnancy. This finding suggests that an early effect of conception is to cause the haemoglobin to rise slightly —a notion which is strengthened by the fact that the mean obtained in 38 healthy nulliparous women of child-bearing age employed in the Manchester welfare centres was 88.5%. The M.R.C. Haemoglobin Committee regarded 98% as the desirable mean for non-pregnant women, but they actually quote means for different groups of between 87.3 and 96%.

Effect of Iron

Of the total of 1,249 women who were classified as taking iron, all but three began taking it before labour and 708 continued to take it for a variable time after labour. The average time for taking iron was 25 weeks; after a year only eight women continued to take it. All women who took iron for three weeks or more were put in the iron group irrespective of the length of time they continued to take it.

TABLE I.—*Effect of Ferrous Iron (1 gr. (65 mg.) t.d.s.) on Haemoglobin During and After Pregnancy*

	Antenatal			Post-natal				
Weeks:	0–13	14–26	27–39	0–13	14–26	27–39	40–52	53+
Iron: Hb %	95·1	88·3	84·1	86·3	87·8	87·7	91·0	89·6
S.E.	±1·33	±0·52	±0·35	±0·7	±0·77	±0·88	±1·1	±0·71
No.	17	215	479	189	169	126	86	130
No Iron: Hb %	91·5	86·6	80·9	80·5	83·3	84·5	88·2	85·8
S.E.	±0·79	±0·47	±0·64	±1·33	±1·44	—	—	±2·6
No.	92	267	174	44	46	17	9	27
Combined: Hb %	92·1	87·4	83·5	85·2	86·8	87·2	90·5	89·0
S.E.	±0·69	±0·37	±0·32	±0·66	±0·66	±0·87	±0·94	±0·58
No.	109	482	653	233	215	143	95	157
Total	1,244			843				
	2,087							

The figures (Table I) show that women having iron had haemoglobin values from 1.7 to 3.6 points higher before labour and from 2.8 to 5.8 higher after labour than women not having iron. It may be that the taking of iron during pregnancy lessened the amount of blood lost at parturition.

The effects of iron medication were more pronounced the longer the iron was taken, as the following figures show:

	No.	Weeks Taking Iron	Hb %
2nd trimester	18	15	90·0
2nd ,, ...	136	5	87·9
3rd ,, ...	42	26	88·5
3rd ,, ...	190	8	82·7

These differences are significant statistically.

The effects of iron taken during pregnancy continued into the post-natal period, but they were not quite so pronounced as when medication was continued into the post-natal period. The following figures demonstrate these differences:

No.	Group	Post-natal Weeks			
		0–13	14–26	27–52	53+
143	No iron (Table I)	80·5	83·3	85·8	85·8
251	Iron for 20·5 weeks before and 9·5 after labour on average	87·3	89·9	92·2	88·8
449	Iron for 22 weeks on average before labour only ..	85·9	86·8	88·0	90·1

The mean values for the three pregnancy trimesters compare very favourably with those obtained in the survey of 1943 (M.R.C., 1945, p. 29). Those for the combined group and especially for the iron group are consistently higher; the M.R.C. values (89, 86, and 82% in the respective trimesters) are almost identical with those for the non-iron group (92, 87, and 81%).

Parity

The figures (Table II) show that child-bearing apparently caused a progressive lowering of the haemoglobin level. The mean difference before labour between primiparae and women who had three or more children

TABLE II.—*Haemoglobin Levels According to Parity*

	Antenatal			Post-natal			
Trimester:	1st	2nd	3rd	1st	2nd	3rd	4th
Parity 1 Hb	93·0	88·0	85·5	87·5	87·0	90·0	91·0
Parity 1 No.	55	223	285	99	103	115	75
Parity 1 S.E.	±1·0	±0·5	±0·5	±0·99	±0·83	±0·9	±1·0
Parity 2 Hb	92·0	85·5	83·0	84·5	87·0	87·5	89·5
Parity 2 No.	32	130	195	79	56	73	45
Parity 2 S.E.	±1·7	±0·5	±0·57	±0·9	±0·87	±1·15	±1·5
Parity 3 Hb	90·5	86·5	81·5	82·0	87·0	86·5	85·0
Parity 3 No.	22	129	173	55	56	50	37
Parity 3 S.E.	±3·7	±0·74	±0·7	±1·5	±1·46	±1·7	±2·1
	109	482	653	233	215	238	157
	1,244			843			
	2,087						

TABLE III.—*Blood Pressure (Systolic) of Women with Low* and High† Hb Levels*

	Low Hb Levels	High Hb Levels
No.	35	38
Mean Hb	70·3% ± 0·55	102% ± 0·86
Mean B.P. (mm. Hg) ..	118 ± 1·7	116 ± 1·4

* Low = 86, 81, or 77% in the respective antenatal trimesters, or 79, 81, 81, or 84% in the respective post-natal trimesters.
† High = 98, 93, or 90% in the respective antenatal trimesters, or 91, 93, 93, 97, or 95% in the respective post-natal trimesters.

varied from 1.5 to 4%; after labour it varied from 0 to 6%. Iron therapy was not the cause of the higher values in the primiparae, for the proportions of women taking iron in the three parity groups were 88, 83, and 91% respectively.

Haemoglobin and Undernutrition

Of 825 women examined before labour 43 (5.2%) were graded as of fair or poor nutritional state. The mean Hb of the 43 was 82% ± 1.9, and of the 782 of good nutritional state 85 ± 0.3. The small difference of 3% is not significant. In the post-natal period 34 out of 843 women (4%) were graded fair or poor, with a mean Hb of 78 ± 6.7, compared with a mean of 88 ± 0.34 for 809 of good nutritional state. The difference of 10% is significant.

When the antenatal and post-natal periods are taken together, the total graded fair or poor was 77 out of 1,668 (4.6%). This incidence is only slightly above that found in 630 pregnant and nursing women (4%) in various places in England during 1946–7 by the Ministry of Health surveys (Adcock *et al.*, 1948). The incidence of fair or poor nutritional state was higher in women of three or more pregnancies (11%) than in women of the first or second pregnancy (3%).

Women with low Hb were not confined to those graded fair or poor. There were 138 women with low values during pregnancy (that is, below 86, 81, or 77%, or one standard deviation less than the means for the respective trimesters, Table I), but only 43 (31%) of these were graded fair or poor. After labour 104 women had low values (that is, below 79, 81, 81, or 84%, or one standard deviation less than the means for the respective post-natal trimesters, Table I), but only 34 of them (33%) were graded fair or poor. It is therefore clear from these analyses that low Hb and clinical undernutrition do not always go hand in hand, and there would have been no justification in excluding the values for the fair or poor women from the values on which the curves and Table I are based. The incidence of undernutrition also increased with parity: it was 2.4%, 3.8%, and 12.9% in the first, second, and third parity groups, respectively, in the antenatal period, and 2.8%, 1.9%, and 4% in the postnatal period.

Haemoglobin and Blood Pressure

The blood pressures were taken of women who had haemoglobin levels lower than or higher than the limits set out in Table III—that is, more than a standard deviation below or above the means in Table I. It is clear from the figures in Table III that there is no difference between the mean blood pressure of women with low and of those with high Hb.

Discussion

The general trend of the Hb level in pregnancy is well known; the fact that the lowest level reached is not immediately before labour but some eight weeks previous to this is not, however, so well known. This had been brought out previously by the work of Boycott (1936), Fullerton (1936), M.R.C. (1945, p. 30), and Mull and Bill (1945). The changes in Hb are in harmony with the increases in the blood and plasma volumes and with the declines in the concentration of other constituents, such as urea, calcium, and potassium, which have been observed by several authors—for example, Dieckmann and Wegner (1934), Mull and Bill (1945), and McLennan and Thouin (1948). Caton, Roby, Reid, and Gibson (1949) have shown that shortly before the onset of labour there is a diminution in plasma volume of about 25% of the volume during pregnancy. There can be no doubt that the changes in the concentration of the blood constituents are brought about mainly by the corresponding changes in blood volume, even though McLennan and Thouin found that the total Hb in the body actually increased by some 20% during pregnancy.

These changes, however, merely describe but do not explain the phenomenon. For an explanation we should want to know the cause and the significance of the hydraemia, but the evidence available and theoretical considerations do not provide an answer. Nevertheless, the establishment of the facts about the changes in the blood constituents in pregnancy is useful in so far as it enables one to judge the normality of Hb determinations made during pregnancy. The curves shown in the Chart may be found useful in this way.

The post-natal curve, which is a straight line, has three noteworthy features: (*a*) a very slow rise; (*b*) the irregularity of the values (the S.D. is 9.4 compared with 6.7 for the antenatal values): and (*c*) the highest point reached, 90.5, is still, at 65 weeks after labour, two points less than the beginning of the pregnancy curve (see Chart). The reasons for (*a*) and (*b*) are not apparent from theoretical considerations or from our own or any other experimental evidence available. In regard to (*c*) it should be noted that the mean value for 38 non-parous women of child-bearing age in the Manchester clinics was 88.5%, or two points below the final value on the post-natal curve. We are therefore inclined to the view that 90.5% is substantially the normal value for non-parous and non-pregnant women and that an early effect of pregnancy is to cause a slight rise in Hb.

Hb levels after pregnancy seem to have been little studied. Fullerton's (1936) observations are the only attempt at systematic study we know of; his values are at a generally lower level than ours, rising gradually from 74% just after labour to 85% at 12 months. This is approximately at the same level as for our own non-iron group, but some 3–4% below the combined iron–non-iron groups. It is probable that the disappearance of hydraemia plays only a minor part in the recovery of the Hb in the post-natal period, because Caton *et al.* (1949) found that the plasma volume had returned to normal non-pregnant values 30 days after delivery.

The influence of parity is brought out clearly by the figures in Table II. The Hb was consistently lower with successive pregnancies both after and before labour. Iron can be dismissed as a factor, since the proportions taking iron in the three parity groups were 88, 83, and 91%. Age can also be ruled out; for, as Wintrobe (1946) points out from an extensive review of the literature, the Hb of non-parous women remains constant between about 20 and 65 years of age. The same effect of successive pregnancies was shown in the M.R.C. survey (M.R.C., 1945, p. 29), but the decline was less consistent.

The taking of iron consistently raised the Hb level, especially in the post-natal period, and the higher level was maintained for several months on the average after iron medication ceased. The return of the blood volume to the non-pregnant level shortly after the puerperium is not concerned, since the higher Hb was observed more than a year after labour in women who had taken no iron at all in the post-natal period.

The great bulk of the women, whether taking iron or not, were perfectly healthy and had no complaints, which raises the question whether a Hb level raised by iron therapy is in itself an advantage. To answer this question more precise clinical inquiries than we were able to make would be necessary.

Summary

The Hb levels of 2,087 unselected women attending welfare clinics were determined by the grey-wedge method at different times during pregnancy and after birth. The values were averaged in weekly periods, and curves were fitted by the method of least squares. It is suggested that these curves may be found useful to assess the normality of Hb values during and after pregnancy.

The antenatal curve agrees with previous observations and shows a rapid decline from 93% (Haldane) at the 8th week to a minimum of about 81% between the 32nd and 34th weeks, and then a rise to nearly 85% at the 39th week. Comparison of the curve with the levels found in healthy non-parous women of child-bearing age suggests that conception causes the Hb to rise in the early weeks of pregnancy.

The post-natal curve is a straight line, rising from 85% at the 4th to 90.5% at the 65th post-natal week. The values showed more variability than the antenatal ones.

The women who were taking or had recently taken iron (usually 1 gr. (65 mg.) of ferrous iron t.d.s.) had levels 1.7–3.6 points higher before labour and 2.8–5.8 points higher after labour than women who did not have iron. The longer iron was taken the more effective it was, and the effects persisted into the post-natal period even when nearly all women had ceased taking it.

Repeated pregnancies progressively lowered the Hb level.

The mean Hb level of 43 out of 825 women clinically graded before labour as of fair or poor nutritional state was slightly but not significantly lower than the mean for 782 women of good nutritional state. The mean for 34 out of 843 women graded fair or poor after labour was significantly lower than that of the remaining 809 women graded good. Only about one-third of women with values more than one S.D. below the mean were found of fair or poor nutritional state; the remaining two-thirds appeared to be quite healthy.

The systolic blood pressure of women with low Hb did not differ from those with high Hb.

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Leprosy was widespread in Scotland from the eleventh to the fifteenth centuries, but in 1530 the magistrates of Edinburgh decreed that no leper might enter the city, and throughout the country they had to sound clappers when begging; this segregation undoubtedly did much to banish the disease (*Scientific Survey of South-eastern Scotland*, British Association for the Advancement of Science, 1951, p. 79). Until the fourteenth century Scotland was almost free of the plague, and it then appeared following a raid across the border, destroying one-third of the population. The first attempt at the control of the disease was the Rule of Pestilence, an Act passed over 100 years later. The measures adopted by local authorities were intended to prevent the spread of the disease rather than to care for those infected, and the main reason for the disappearance of the plague was not the advance of medicine but the fact that the vector, the black rat, was replaced by the brown or sewer rat in the seventeenth and eighteenth centuries. Early in the sixteenth century the town council of the City of Edinburgh began to make efforts to clean the streets, and one year the Provost had them cleaned at his own expense and used the refuse to manure his private estate. Smallpox was very prevalent, and until about 1750 accounted for 10% of all deaths in the city; the College of Physicians of Edinburgh pronounced the practice of inoculation to be highly salutary to the human race. It was not until the great outbreaks of cholera a century later that boards of health were set up in many towns and villages to protect the communities, and the streets were cleaned, hospitals equipped, and infected areas fumigated. But as soon as the state of emergency was over these measures were relaxed. The first medical officer of health was appointed in 1862 after public attention had forcibly been drawn to the problem of overcrowding and insanitary conditions by the collapse of a house in Edinburgh which killed 35 people.

DIFFUSE ARTERITIS OF UNKNOWN ORIGIN ACCOMPANIED BY EOSINOPHILIA

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There is a growing body of evidence that morphologically similar changes may occur in the arteries in a number of conditions presenting widely differing clinical characters. These arterial changes may be either acute or chronic, but are all of an inflammatory granulomatous type. The whole thickness of the vessel wall is involved and the inflammatory exudate often contains a proportion of eosinophil leucocytes. An eosinophilia of the peripheral blood may or may not form part of the clinical picture.

When the arteritis is the most prominent component of the disease, and especially when it is acute and confined mainly to the visceral vessels, the condition is usually labelled polyarteritis nodosa. When it is subacute or chronic and involving the arteries arising from the aorta proximal to their points of entry into the viscera, the generalized form of temporal or giant-cell arteritis (Harrison, 1948) is sometimes diagnosed. Occasionally the striking feature is the intensity of the eosinophilia, as a result of which the case is now and then initially misdiagnosed as eosinophilic leukaemia (Blackburn, 1950).

The histological similarity between the vascular and connective-tissue lesions of polyarteritis nodosa and those of lupus erythematosus disseminatus, the generalized form of scleroderma, dermatomyositis, rheumatic polyarthritis, and certain other ill-defined conditions associated with transient eosinophilic infiltration of the lungs, has been noted by many authors (e.g., Jaeger, 1932; Roessle, 1933; Banks, 1941; Bergstrand, 1946). This resemblance has occasioned much speculation about whether the lesions have a common aetiological origin in being hypersensitive or allergic reactions. Klemperer *et al.* (1942), while admitting that these conditions have a common basis in being diffuse collagen diseases with similar vascular changes, deplore, as an oversimplification, the attempt to ascribe to them all the same causal origin.

Apart from the clinical entities mentioned, there are cases like that described by Lumb (1950) with references to others in the literature which show similar vascular and collagenous lesions to those mentioned above, but which evade satisfactory classification. We have thought it might be of interest to report another such case of diffuse arteritis in which the clinical picture had features in common with polyarteritis nodosa, temporal arteritis, eosinophilic leukaemia, and the clinical syndrome described by Lewi (1949) and ascribed by him to hypersensitivity to chemotherapeutic drugs. Our case did not correspond entirely with any one of these conditions, and though we suspected on general grounds that it might be allergic in origin we were unable to obtain any direct proof of this.