BLOOD FORMATION IN INFANCY

PART III*. CORD BLOOD

BY

JOHN MARKS, DOUGLAS GAIRDNER and JANET D. ROSCOE

From the Department of Pathology, University of Cambridge, and the Cambridge Maternity Hospital

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Blood taken from the umbilical vein at birth is of particular interest from two aspects. On the one hand it represents foetal blood at the end of gestation and may thus give information about influences acting on the foetus before birth. For example, the cord blood picture is now an accepted guide to the prognosis in haemolytic disease of the newborn (Mollison, 1951). On the other hand, cord blood represents the blood with which the infant begins extra-uterine life, so that it becomes of interest to enquire whether the blood picture at birth in any way determines the subsequent course of the blood picture.

There are several reports in the literature giving normal values for the various constituents of cord blood, but many relate only to small series and there are many discordancies. We have examined the cord blood from a large series of infants so that the wide range of the normal values can be taken into account.

Material and Methods

The subjects investigated were healthy infants born in the Cambridge Maternity Hospital. Umbilical vein samples were collected from 221 infants with birth weights above 2,500 g. and from 11 infants with birth weights less than 2,500 g. In every case pregnancy had been uncomplicated by toxaemia and labour had not been prolonged. Nitrous oxide-and-air analgesia had been given to the mothers.

The cord was clamped as soon as conveniently possible but usually some 10 to 15 seconds elapsed before this was done. The sample of blood was taken with a large-bore needle from the maternal end of the umbilical cord immediately after clamping. The specimens were examined by the haematological methods already described (Part I).

Particular attention was paid throughout to the accuracy of haemoglobinometry. Haemoglobin was determined as oxyhaemoglobin in a photoelectric colorimeter, using a blood dilution of one part in 200 parts of 0·04% ammonia. The colorimeter was checked each week against the Medical Research Council type of grey wedge photometer. A further check was made each month of both machines with iron determinations on several blood samples.

Results

The 221 samples were analysed for haemoglobin, and on 106 of them a full haematological examination was made. The results are shown in Tables 1, 2 and 3.

Haemoglobin. The results for the haemoglobin estimations were found to be distributed about the mean in the form of a normal curve. Calculation of the 95% range of normal was therefore feasible from a determination of the standard deviation. The mean of the results was 16·9 g./100 ml. and the 95% range 13·7–20·1 g./100 ml.

The results of the present series are compared in

TABLE 1

RESULTS OF Hb CONCENTRATION IN CORD BLOOD IN THE PRESENT SERIES COMPARED WITH THOSE OF OTHER AUTHORS

Author	No. of Observations	Mean	S.D.	Range
Mugrage and Andresen (1936)	40	17·1		13-20
Guest, Brown and Wing (1938)	34	17·9		13-22
Waugh, Merchant and Maughan (1939)	52	15·7*		12·2-19·0
Vahlquist (1941)	32	16·6	0·32	
De Marsh, Alt and Windle (1948)	60	16·0*		
Mollison (1951)	134	16·6	1·5	
Dochain, Lemage and Lambrechts (1952)	40	17·9		14·4-21·6
Present series	221	16·9	1·62	12·3-22·0

* Corrected as suggested by Mollison (1951).

* Previous parts were published in this journal: Part I (The Normal Bone Marrow), 1952, 27, 128; Part II (Normal Erythropoiesis), 1952, 27, 214.

Table 1 with those of other recent workers. In these recent studies, based on modern methods of haemoglobinometry, the results agree well.

Red Cells. For the red cell count, haematocrit, mean corpuscular haemoglobin and mean corpuscular volume, the results were found to fit normal distribution curves. In these, therefore, theoretical 95% ranges of normal may be calculated (Table 2).

TABLE 2

RED CELL VALUES IN CORD BLOOD

	Mean	S.D.	Calculated 95% Range
Haemoglobin (g./100 ml.) ..	16·9	1·62	13·7–20·1
Red cells (m./c.mm.)	5·09	0·78	3·5– 6·7
Haematocrit (%)	53·1	2·9	47·3–58·9
Mean corpuscular Hb (γγ) ..	33·5	1·48	30·5–36·5
Mean corpuscular vol. (c.μ) ..	104·2	7·0	90–118
Mean corpuscular Hb concentration (%)	32·3	—	30·9–36·5*
Reticulocytes (per 100 R.B.C.)	2·94	—	0– 8·3*
Normoblasts (per c.mm.) ..	590	—	0–5,400*

* Figues not represented by normal curve and extreme range of results given.

The macrocytosis previously noted by other workers has been confirmed, but the results show that the mean cell volume in about 25% of cord bloods will fall within the accepted range of normal for adult cells. These are, however, all on the upper side of normal as judged by adult standards. Only one determination was below 90 c.μ.

The values for mean corpuscular haemoglobin concentration were found not to follow a normal curve. The mean of the observations was 32·3% and the majority of the results lie above 32%. A small proportion of the results fall into the range 31-32%, but the stained film showed no hypochromia.

Reticulocytes. In the majority of infants the reticulocyte counts were above the normal adult values—in only 6% of the cases were the reticulocytes below 1%. The mean of the observations was 2·94% and although only a few of the infants showed values exceeding 5%, one showed a reticulocyte count of 8·3%.

Normoblasts were present in the majority of the specimens with a mean count of 590/c.mm. An occasional high value was found, the cord blood of three infants having normoblasts over 4,000/c.mm. None of the infants showing high normoblast counts showed other evidence of blood abnormality, nor was there any relationship between the normoblast count and the cord haemoglobin value.

Leucocytes. The values for the mean and the range of the leucocyte counts are shown in Table 3.

TABLE 3

LEUCOCYTE VALUES IN CORD BLOOD

	Mean	Range	95% Range
Leucocytes/c.mm.	12,900	5,900–26,000	6,000–22,000
Neutrophils juvenile % ..	0·7	0–4·0	0–3·0
juvenile/c.mm.	104	0–500	0–300
bands % ..	3·7	0–14	0–6
bands/c.mm. ..	464	0–2,100	0–1,200
segmented % ..	59·2	32–81	40–76
segmented/c.mm. ..	7,395	4,000–18,000	4,500–12,000
Eosinophils %	1·6	0–9	0–4·5
Eosinophils/c.mm.	230	0–1,100	0–800
Basophils %	0·25	0–2·5	0–1·5
Basophils/c.mm.	38	0–350	0–200
Lymphocytes %	26·2	9–47	13–40
Lymphocytes/c.mm. ..	3,245	900–9,500	1,000–6,000
Monocytes %	6·08	0·5–16·0	2–12
Monocytes/c.mm.	731	150–2,800	200–1,600

The results do not follow normal curves, so that theoretical ranges cannot be calculated. In the majority of the estimations, however, it has been possible to give a range which would cover about 95% of normal subjects.

In cord blood all the cell types are present in increased numbers, but in proportions similar to those of adult blood. The leucocytosis is thus a general rise and not the neutrophil leucocytosis which is quoted in many textbooks. The error appears to have arisen because it has usually been assumed that cord blood and blood sampled a few hours after birth are equivalent. In Part I it was shown that during the first few hours there was a rise in neutrophils while the lymphocytes remained unchanged.

Discussion

Relationship of Cord Haemoglobin Level and Foetal Maturity. The wide spread of the haemoglobin values, from 12 to 22 g./100 ml., raises the question whether the more extreme values are still to be accepted as normal. According to Walker and Turnbull (1953) the normal cord blood haemoglobin level varies relatively little. These authors found the haemoglobin level of the foetal blood tended to rise throughout pregnancy, and at 40 weeks' gestation averaged 16·5 g. (agreeing with our mean value of 16·9) with a range of 15·0 to 18·6. They considered higher values as implying that some degree of more or less prolonged hypoxia had been

suffered by the foetus, and stressed that post-maturity was associated with abnormally high haemoglobin values: at 43 weeks' gestation, for instance, the range was 16·8-20·5 g. From their findings Walker and Turnbull concluded that post-maturity leads to placental insufficiency, a conclusion which would be in accord with what is known about post-maturity in experimental animals.

In view of the obvious importance of this theory, should it be confirmed, we have checked our data on menstrual age and birth details carefully, but without finding the least suggestion of correlation between maturity and cord blood level (Fig. 1). Cord blood haemoglobin was also plotted against crown-heel length and against birth weight, two other possible yardsticks of foetal maturity, but in neither instance was any correlation found.

In addition we have scrutinized the nine cases of our series in which the cord blood haemoglobin was 20 g. or higher, values which, according to Walker and Turnbull, are to be found only in circumstances where post-maturity or other abnormalities causing foetal hypoxia are present. Details of the cases are set out in Table 4. In addition to the details recorded in Table 4, the existence of abnormalities of pregnancy or labour was sought, such as clinical signs of post-maturity, maternal diabetes, toxaemia, prolonged or difficult labour, Caesarean section, foetal distress or previous history of miscarriages. None of these abnormalities was found.

TABLE 4

BIRTH WEIGHT, MENSTRUAL AGE, AND LENGTH OF NINE INFANTS WITH CORD HAEMOGLOBIN VALUES OF 20 g./100 ml. AND HIGHER

	Haemoglobin (g./100 ml.)	Birth Weight (lb. oz.)	Birth Weight (g.)	Menstrual Age ± 280 Days	Length in.	Length (cm.)
1	20·0	8 0	3,630	− 2	—	—
2	20·0	7 4	3,290	− 2	—	—
3	20·0	9 6	4,226	− 4	22	56
4	20·1	6 8	2,952	?	19	48
5	20·2	6 5	2,860	? + 18	18½	47
6	21·0	5 12	2,620	− 5	19	48
7	21·2	7 2	3,234	+ 4	—	—
8	22·0	8 1	3,650	− 7	22	56
9	22·0	7 9	3,430	+ 4	21	53

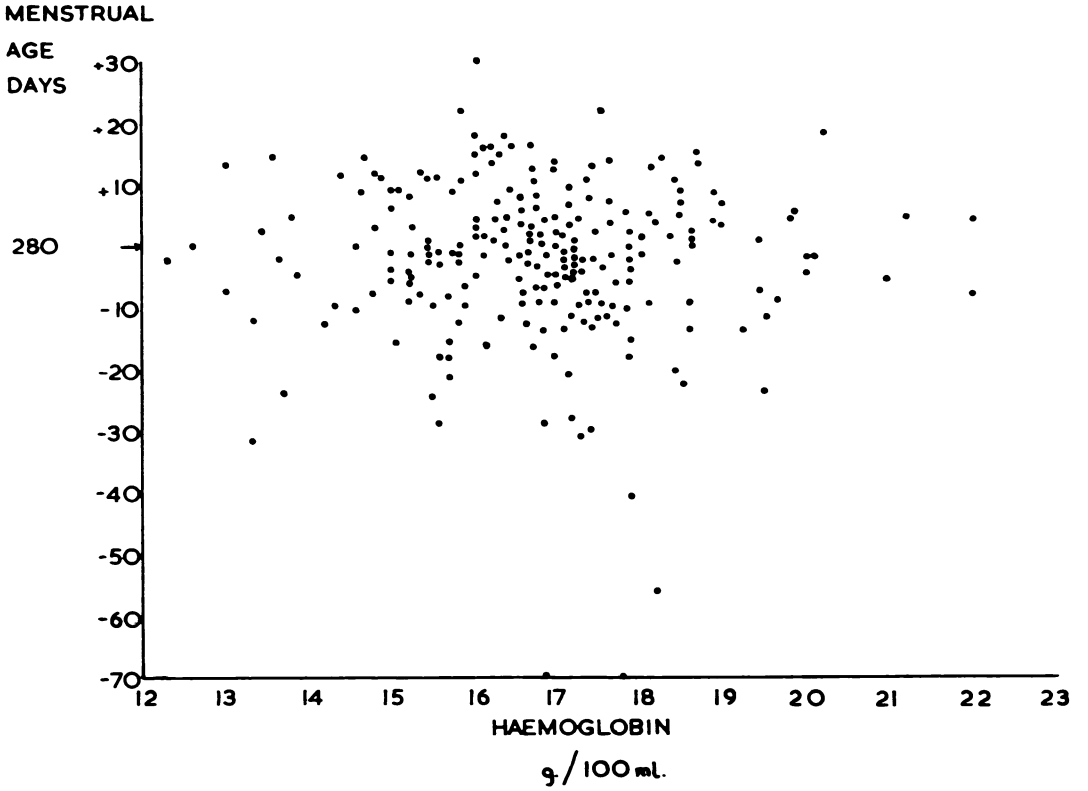

FIG. 1.—Scattergram of haemoglobin values of cord blood from 232 infants (11 with birth weights below 2,500 g.) against menstrual age expressed as days greater or less than 280 days to show absence of any correlation between cord blood haemoglobin level and foetal maturity.

Our results thus argue against the view that post-maturity or other abnormality or pregnancy is common in cases with high cord haemoglobin. The menstrual age of our 232 infants varied from 70 days premature to 30 days post-mature, with quite as wide a variation as in the smaller series of Walker and Turnbull. At present we can offer no explanation of the divergence between our results and theirs.

Relationship between Haemoglobin Concentration at Birth and at 7 and 9 Weeks. The wide spread in the normal concentration of the haemoglobin at birth prompted a second question: Does the extent to which the haemoglobin level falls during the first three months depend upon the haemoglobin level at birth?

During the first eight weeks of life the haemoglobin concentration of the infant falls to an average value of about 11 g./100 ml., due to a physiological hypoplasia of the bone marrow (see Part II). The precise level at which the haemoglobin level stabilizes at this time does show some variation: this might be due to variations in the initial count at birth. To test this possibility 19 infants were examined at 7 weeks and 9 weeks after birth: 11 of these had low normal cord haemoglobin values (13·0–15·0 g.) and eight had high normal cord haemoglobin values (18·4–20·1 g.). The results are shown in Table 5. There is no significant difference between these two groups of infants 7 and 9 weeks after birth. Both in the low and high cord haemoglobin groups an occasional infant showed a drop in haemoglobin value to below 10 g. at the seventh week after birth.

These results show that whether an infant is born with a cord blood haemoglobin as low as 13 g. or as high as 20 g. the haemoglobin will have stabilized at a level of about 11 g. at 2 months of age.

TABLE 5

HAEMOGLOBIN VALUES AT 7 WEEKS AND 9 WEEKS OF INFANTS BORN WITH HIGH OR LOW CORD HAEMOGLOBIN VALUES

Cord Blood Haemoglobin (g. %)	No. of Cases	Mean Hb (g. %) (and Range) at 7 Weeks	Mean Hb (g. %) (and Range) at 9 Weeks
'High' (18·4-20·1)	8	11·5 (9·1-12·8)	11·5 (10·6-14·0)
'Low' (13·0-15·0)	11	11·6 (9·1-13·9)	11·8 (10·9-12·9)

Summary

From analyses of cord blood from a large series of infants normal haematological values have been derived.

The normal cord blood haemoglobin level ranges from 12 to 22 g. No relationship between cord blood haemoglobin and foetal maturity was found.

The haemoglobin level at 7 weeks and 9 weeks of age was determined in two groups of infants, (*a*) those born with a high normal cord haemoglobin and (*b*) those born with a low normal cord haemoglobin. At 2 months of age each group had a similar haemoglobin level of about 11 g./100 ml.

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