Archives of Disease in Childhood, 1974, **49**, 382.

Cord haemoglobin in low birthweight infants

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Burman, D., and Morris, A. F. (1974). *Archives of Disease in Childhood*, **49**, 382. **Cord haemoglobin in low birthweight infants.** Cord haemoglobin was measured in 349 low birthweight infants born after a pregnancy lasting 28 to 41 weeks inclusive. 82 babies were small-for-dates and were born after 36 weeks' gestation; their Hb was not related to sex or duration of pregnancy, but there was a negative correlation with placental weight and placental weight/birthweight ratios. The mean Hb of small-for-dates babies ($17\cdot09\pm2\cdot11$ g/100 ml) was higher than for comparable normal babies ($16\cdot24\pm2\cdot26$ g/100 ml).

In normal-for-dates females there was a linear relation between Hb and duration of pregnancy approximately expressed by: cord Hb (g/100 ml) = 7 + gestational age in lunar months. In males a plateau Hb of 16·22 g/100 ml was reached at 32 weeks.

Surprisingly, there are very few studies on cord Hb levels in low birthweight infants. Schulman (1959) reviewed the series published until 1957 and pointed out the paucity of information between 24 and 36 weeks' gestation. Corner (1960) showed a rising Hb with duration of pregnancy in 83 cases, but we know of no other large scale study of infants born after 28 weeks' pregnancy. To remedy this situation, this retrospective investigation was undertaken.

Methods

The records of 765 singletons weighing 2·5 kg or less, born alive in Bristol Maternity Hospital during 1965–71 were studied. One record could not be found but, of the remainder, 360 had cord Hb estimated by the standard cyanmethaemoglobin method using an EEL colorimeter and Acuglobin standards (Ortho Pharmaceuticals Ltd.). The blood was collected from the umbilical vein by a syringe and needle. The 360 with Hb measurements did not differ significantly from the remaining 404 in respect of maternal age, social class, legitimacy, number of previous pregnancies, sex, mode of delivery, placental weight/birthweight ratio, and mother's mean Hb taken within 28 days of delivery by the χ^2 test. There was, however, a significant excess of emergency admissions and mothers whose Hb was not known in the infants where the cord blood was not taken (Table I).

The period of gestation used was that assessed by the obstetrician and recorded at the time of delivery. It is expressed in completed weeks and was known for 758 of all the infants. If the distribution of gestational ages of these low birthweight infants are compared in 2-week groups with the national sample of Butler and Bonham (1963), there is a significant difference ($P < 0\cdot01$). Virtually one-half of the contributions to the χ^2 test was in infants over 42 weeks who were deficient in the Bristol series. If these are eliminated, the Bristol and national

Received 5 October 1973.

TABLE I

Significant differences between babies with a known cord Hb and those where it was not recorded

	No cord Hb	Cord Hb	P
	No.	No.	
Type of admission			
Emergency	162	112	0·05
Booked	242	248	
Mother's Hb			
Stated	204	225	0·01
Not known	200	135	
Duration of pregnancy (wk)*			
<28	20	3	
28–	26	14	
30–	32	16	
32–	42	31	0·001
34–	55	66	
36–	82	98	
38–	88	83	
40–	53	41	
Birthweight (kg) (2 not known)			
1 or less	25	4	
1·01–	44	26	0·001
1·51–	87	73	
2·01–	246	257	
Placental weight (g) (68 not known)			
<250	14	5	
250–	85	51	
350–	89	96	0·001
450–	98	149	
550–	39	36	
650+	19	15	

*Excluding 8 born after 42 weeks and 6 not known.

TABLE II

Mean cord Hb in 349 low birthweight infants

Completed weeks of gestation	Appropriate weight for dates						Small-for-dates males and females		
	Males			Females					
	No.	Hb (g/100 ml)		No.	Hb/g/100 ml		No.	Hb (g/100 ml)	
		Mean	SD		Mean	SD		Mean	SD
28,29	7	15·00	2·45	7	13·60	2·16	Nil	—	—
30,31	9	15·91	1·34	7	14·73	1·07	Nil	—	—
32,33	16	16·29	1·86	15	15·21	2·64	Nil	—	—
34,35	32	16·29	2·05	32	15·82	2·43	2	15·25	—
36,37	46	16·20	2·20	39	15·88	2·45	13	17·44	2·27
38,39	17	16·22	2·24	33	16·68	2·23	33	17·02	2·09
40,41	Nil	—	—	5	16·56	1·65	36	17·03	2·12

samples did not differ significantly. It was therefore decided that infants over 42 weeks should be excluded from the analysis.

The babies with cord Hb measurements were compared with the rest of the Bristol sample and their distribution by gestational age was significantly different (Table I). The major contribution to the χ^2 test was infants born before 28 weeks, and if these were omitted then the difference between the two groups is only just significant ($P < 0·05$). If the remaining 349 infants with known cord Hb, born between 28 and 41 weeks inclusive, are compared with Butler and Bonham (1963) then the difference is just significant ($P < 0·05$) but the national sample contained 11·3% where the period of gestation was unknown compared with 1% in the present series.

By similar comparisons it was found that there was a conspicuous shortage of infants with a weight less than 1 kg and with a placental weight of less than 350 g in the cord Hb infants compared with those whose Hb was not measured (Table I). Omission of these low birthweight infants with a small placenta eliminates the statistical differences between the two groups.

From these data it is clear that there is a group of babies born to mothers, admitted to Bristol Maternity Hospital as emergencies with no maternal Hb measurement, who do not have their cord Hb taken. They are the very premature infants of low birthweight with a very low placental weight. If babies born between 28 and 41 weeks inclusive are considered, then the present sample is reasonably representative of low birthweight babies and it is these 349 infants whose results are recorded here.

Infants are considered small-for-dates if their birthweight for gestation was 2 SD below the mean using Gruenwald's (1969) data.

Results

Of the 349 infants discussed here, 84 were small-for-dates (Table II). All except 2 of these were born after 36 weeks' gestation and if the 82 remaining cases are analysed by the two-factor analysis of variance with proportional subclass numbers previously described (Burman, 1972), there is no relation of Hb to sex or period of gestation. From 34 to 38 weeks, there was no relation between cord Hb and sex or period of gestation in babies whose weight was appropriate for dates. It is therefore possible to compare the small-for-dates and normal-for-dates babies in later pregnancy ignoring sex and period of gestation. The significant difference between the Hb in these two groups is shown in Table III. Correlations between cord Hb and other parameters were sought in these two groups and the results are shown in Table IV.

TABLE III

Cord Hb in low birthweight infants of both sexes born between 36 and 42 weeks' gestation

	No.	Hb (g/100 ml)	
		Mean	SD
Normal-for-dates	140	16·24	2·26
Small-for-dates	82	17·09	2·11

$t = 2·783$; $P < 0·01$.

In the normal-for-dates infants the difference between the cord Hb of the two sexes is shown in Table II. At any single gestational age the difference between the sexes is not significant at the 5% level. Before 34 weeks, however, two-factor analysis of variance showed a significant difference between the sexes (Table V). This difference is not due to difference in birthweight, placental weight, or placental weight/birthweight ratios, for at each 2-week gestation period there is no significant difference between the sexes as far as these parameters are concerned, and there is no consistent

TABLE IV

Correlation coefficients (r) between cord Hb and other parameters in low birthweight infants born between 36 and 42 weeks' gestation

Correlation coefficients (r) between cord Hb and	Normal-for-dates			Small-for-dates		
	No.	r	P	No.	r	P
Birthweight	140	−0·073	NS	82	−0·034	NS
Placental weight	137	−0·037	NS	80	−0·250	0·05
Placental weight/birthweight	137	−0·024	NS	80	−0·227	0·05

TABLE V

Two-factor analysis of variance to show effect of sex upon cord Hb in infants born from 28 to 33 weeks' gestation inclusive

Variation	df	Sum of squares	Mean square	Variance ratio	P
Sex	1	2120	2120·000	4·949	<0·05
Gestation	2	2016	1008·000	2·353	NS
Sex and gestation	2	25	12·500	0·029	NS
Total between cells	5	4161	832·200		
Subjects within cells	55	23,561	428·382		

NS, not significant.

trend. The Fig. shows that the shape of the curve differs in the two sexes. Males whose weights are normal-for-dates reach a maximum cord Hb at 32 weeks, remaining constant with a mean of 16·22 g/100 ml until 38 weeks when the present data stop. Females, however, show a steady increase in Hb from 28 to 41 weeks and the regression line is expressed by the formula

Hb (g/100 ml) = 7·016+0·245 (gestational age in completed weeks).

There was a strong correlation between gestation and birthweight in both the small-for-dates and normal-for-dates babies. The Hb levels related to birthweight followed the same trend as Hb to gestation, but the relation was less clear cut. As the criterion for admission to the survey was based on birthweight, it was considered that gestation was the better parameter for these data as the primary measure of maturity.

Discussion

This series of low birthweight infants emphasizes the importance of separating those who are small-for-dates from those whose weight is appropriate for dates. The criterion used here (2 SD below the mean using the data of Gruenwald, 1969) is very stringent. The high Hb level in these infants confirms earlier observations of Walker and Turnbull (1953) and MacKay (1957) who produced evidence suggesting a relation between Hb and the degree of neonatal anoxia. This could not be

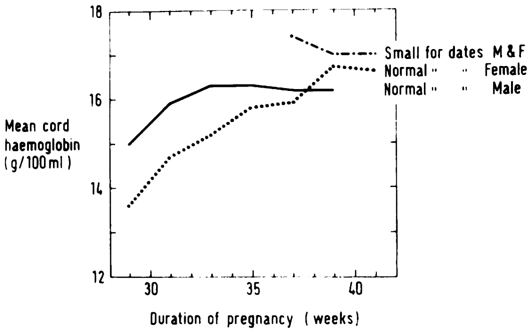

FIG.—*The mean cord Hb of low birthweight babies born between 28 and 42 weeks of pregnancy.*

confirmed by Rooth and Sjöstedt (1957), but Zachau-Christiansen, Hoff-Jørgensen, and Østergäard Kristensen (1962) and Haworth, Dilling, and Younoszai (1967) confirmed higher Hb levels in severely growth-retarded infants. Humbert *et al.* (1969) also confirmed Walker and Turnbull's work and described symptoms produced by neonatal polycythaemia in a few of these infants. Lugo and Cassady (1971) showed that polycythaemia was twice as common in the growth-retarded infants as in the mature normal birthweight or immature low birthweight infants.

The mechanism by which this high Hb is produced seems to be due to an increased production of red cells by the bone marrow, for Finne (1966) found higher erythropoietin levels in cord blood in the postmature and in infants born to mothers suffering from toxaemia of pregnancy. Seip (1955) found higher reticulocyte levels in asphyxiated babies, but Cook, Brodie, and Allen (1957) and Lochridge, Pass, and Cassady (1971) thought that reticulocytes in growth-retarded infants were commensurate with their gestational peers rather than their weight peers. The high Hb can also be explained if the suggestion of Cook *et al.* (1957), that it is due to haemoconcentration, is true, and Flod and Ackerman (1971) found that perinatal asphyxia results in the transfer of blood *in utero* from placenta to fetus.

In the small-for-dates infants there was no correlation between the cord Hb and birthweight, but there was a negative correlation with placental weight and placental weight/birthweight ratios, correlations which were absent in the normal for dates (Table IV). The functional significance of placental weight and its relation to fetal weight has been considered to be very limited by Thomson, Billewicz, and Hytten (1969), but they also point out that it depends upon the margin of placental reserve which for oxygen is low. Factors related to oxygen tension, such as Hb, would be a sensitive indication of placental function and this would account for the relations between cord Hb and placental weight and placental weight/birthweight ratio shown here. Aherne (1966) thought that placental weight was related to chorionic villous surface area and fetal oxygen uptake and thus was of functional significance, but one must agree with Little (1960) that only marked deviations are of clinical importance. Gruenwald (1963) stated that the 'weight of the placenta is by no means a good measure of size in the functional sense, but no better parameter is available for routine determinations'. He found that if the placental weight for gestation or for birthweight was 2 SD below the mean, the perinatal mortality was increased sixfold.

Aherne (1966) suggested that total fetal metabolism varies as the 2/3 power of fetal weight and that this was directly related to placental weight. We therefore recalculated the correlation coefficients between cord Hb and placental weight/birthweight ratios using placental weight/$\text{birthweight}^{2/3}$ instead. This increased the correlation coefficient in the small-for-dates from 36 to 41 weeks insignificantly from $-0 \cdot 227$ to $-0 \cdot 243$.

The lower Hb in the low birthweight babies whose weight is appropriate for duration of pregnancy has been suggested before by Schulman (1959), but he admitted that the data were incomplete. The difference between the two sexes reported here has not been found before and certainly needs confirming. We have no explanation for this difference, but attempts to explain it in terms of birthweight, placental weight, and placental weight/birthweight ratio were unsuccessful in the present series.

The linear relation between Hb and duration of pregnancy in the female fetus can be approximately expressed by the formula

cord Hb (g/100 ml) $= 7 +$ gestational age in lunar months.

This gives a term Hb of $17 \cdot 0$ g/100 ml, which is the figure observed in many series (Burman, 1959).

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