HYDROGEN CONCENTRATION, CARBON DIOXIDE TENSION AND ACID BASE BALANCE IN BLOOD OF HUMAN UMBILICAL CORD AND INTERVILLOUS SPACE OF PLACENTA

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In a previous paper (Sjöstedt, Rooth and Caligara, 1960) we reported on the oxygen tension (pO_2) in the blood of the human umbilical cord and the intervillous space of the placenta. It is the purpose of this paper to report on the pH and the carbon dioxide tension (pCO_2) in blood from the same sources in order to give a more complete picture of the gas exchange of the foetus and of its acid base balance.

Material and Methods

The cord blood was investigated in 222 cases after spontaneous delivery in vertex presentation; 154 of the infants were normal and without any signs of asphyxia before or after delivery; 46 had signs of asphyxia and 33 of these had slow or irregular heart beats during delivery but showed no signs of asphyxia after birth. The other 13 cases had signs of mild asphyxia after birth. In addition, 22 infants had meconium stained amniotic fluid without any other signs of asphyxia.

During labour the mothers were given 'trilene' (trichlorethylene) or nitrous oxide and in some cases a few drops of chloroform at the moment of delivery.

The blood in the intervillous space was investigated in 27 cases, 25 of which were normal and two of which had signs of mild toxæmia. The placenta was punctured through the abdominal wall before labour had started. Only local anaesthesia was used for the puncture and no complications occurred. The technique of the puncture has been described earlier by us (Sjöstedt *et al.*, 1960).

Great care was taken to obtain reliable information about the time of gestation. Any case in which the duration of pregnancy was doubtful was rejected from the series on the effect of gestation time upon the pH , pCO_2 or pO_2 of the blood.

The pO_2 was measured polarographically with the Clark electrode as described by us (Rooth, Sjöstedt and Caligara, 1959a).

The pH was measured with a radiometer type 22 pH

meter and an Astrup apparatus. The temperature was kept at $37.0^\circ C$.

The pCO_2 was measured by the Astrup method (1956). The principle is that the pH of the whole blood is first measured anaerobically. After centrifugation, the plasma is equilibrated with a gas of known pCO_2 (close to 40 mm. Hg) and the pH is again measured. The pCO_2 of the whole blood is then read off from the nomogram of Astrup (1956).

Standard bicarbonate buffer base (BB) and base excess (BE) are all terms which express the metabolic acid-base balance of the blood. In order to calculate those entities we used the nomogram of Siggaard Andersen and Engel (1960). Instead of measuring the haemoglobin in our cord blood we used a mean of 16.7 g./100 ml. blood, a figure which was established in a previous study on 414 cord samples in this laboratory (Rooth and Sjöstedt, 1957b). This introduces an error in the calculations which, if the haemoglobin varies ± 4 g./100 ml. blood from 16.7 g., will make about ± 1.3 mEq/litre in BB, but scarcely any error in BE and standard bicarbonate.

As the cord blood contains a considerable amount of reduced haemoglobin which is more alkaline than oxyhaemoglobin, this must be taken into account and we have used the correction given by Siggaard Andersen and Engel (1960) according to which 10 g. of reduced haemoglobin increases the BB 0.3 mEq. The oxygen saturation has been calculated from the pH and pO_2 measurements with the help of the dissociation curve for the foetal blood established by us (Rooth *et al.*, 1959b).

BB is the buffering protein of the blood + buffering bicarbonate. Henderson (1928) used this as an indicator of the metabolic acid base balance of the blood, but the term BB was introduced by Singer and Hastings (1948).

Standard bicarbonate is another indicator of the metabolic status introduced by Astrup (1956) and Jørgensen and Astrup (1957). Standard bicarbonate is the concentration of bicarbonate in plasma, when whole

FIG. 1.—Distribution of the pH in the umbilical vein in normal and asphyxiated infants and infants with meconium stained amniotic fluid.

FIG. 2.—Distribution of the pH in the umbilical arteries in normal and asphyxiated infants and infants with meconium stained amniotic fluid.

blood has been equilibrated with carbon dioxide at a pCO₂ of 40 mm. Hg at 38° C. and when the haemoglobin is fully oxygenated. The carbon dioxide-bicarbonate systems account for about 75% of the buffering action of the blood against fixed acid and bases.

BE is the same as normal BB minus the actual BB. The term BE was introduced by Astrup, Jørgensen, Siggaard Andersen and Engel (1960). Consequently BE directly expresses the excess in mEq of strong base or acid for every litre of blood, when the normal mean is arbitrarily fixed at zero. For the discussion of the relative merits of these different entities the reader is referred to the work of Astrup *et al.* (1960).

Results

Cord Blood

HYDROGEN CONCENTRATION. The pH in the umbilical vein in 142 normal cases and in the arteries in 98 cases is given in Figs. 1 and 2. These figures also give the pH in the vein of 44 cases grouped as asphyxiated and 30 measurements from the arteries

in the same group. Finally they also show the pH of the cases with meconium stained amniotic fluid. In this group measurements have been done in 18 cases in the vein and in 11 cases in the umbilical artery.

It will be observed that the pH is lower in the asphyxiated and meconium groups than in the normal cases (see also Table 2). In the normal ones, 54% of the cases have a pH in the vein which is lower than 7.35. In the meconium group this percentage is 72 and in the asphyxiated group 75. In the arteries the pH is lower than 7.25 in 37% of the normal cases, in 73% of the meconium group and in 63% of the asphyxiated group.

Table 1 gives the pH and pO₂ in the normal cases for different gestation weeks. The material has been divided into primigravidae and multigravidae. It will be seen that the pH may decrease in the umbilical arteries and vein when the gestation time is 42 weeks or more, but pO₂ does not change with

TABLE 1
MEAN HYDROGEN CONCENTRATION, CARBON DIOXIDE AND OXYGEN TENSION IN THE UMBILICAL
CORD BLOOD AFTER NORMAL DELIVERY IN DIFFERENT GESTATION WEEKS

			Gestation Week								
			36	37	38	39	40	41	42	43	All
<i>Artery:</i>											
Primigravidae	pH	...	7.27		7.27	7.22	7.25	7.26	7.28	7.24	7.25
	No.	...	2		2	8	16	9	4	5	46
	pCO ₂	...	30			44	47	45	41	57	44
	No.	...	1			3	5	2	3	1	15
	pO ₂	...	24		19	21	19	19	23	19	20
	No.	...	2		2	9	15	6	8	7	49
Multigravidae	pH	...		7.34	7.30	7.26	7.29	7.29	7.21	7.19	7.27
	No.	...		1	2	3	16	13	7	3	45
	pCO ₂	...				38	45	51	57	49	47
	No.	...				2	6	3	1	1	13
	pO ₂	...		31	27	18	16	16	14	14	16
	No.	...		1	1	4	18	11	9	4	48
All	pH	...	7.27	7.34	7.29	7.23	7.26	7.28	7.23	7.22	7.26
	No.	...	2	1	4	11	32	22	11	8	91
	pCO ₂	...	30			41	46	49	45	53	45
	No.	...	1			5	11	5	4	2	28
	pO ₂	...	24	31	22	20	17	17	19	17	18
	No.	...	2	1	3	13	33	17	17	11	97
<i>Vein:</i>											
Primigravidae	pH	...	7.32		7.33	7.31	7.31	7.32	7.30	7.28	7.31
	No.	...	2		3	9	19	12	8	9	62
	pCO ₂	...	27		29	37	39	43	38	39	38
	No.	...	1		2	4	7	3	4	5	26
	pO ₂	...	34		31	30	29	29	33	30	30
	No.	...	2		2	11	18	7	9	8	57
Multigravidae	pH	...	7.38	7.40	7.34	7.33	7.35	7.36	7.31	7.27	7.34
	No.	...	1	1	3	6	23	20	9	4	67
	pCO ₂	...	33		38	37	36	34	43	48	37
	No.	...	1		2	3	8	6	2	2	24
	pO ₂	...	33	43	33	27	27	31	26	30	28
	No.	...	1	1	2	7	23	19	11	4	68
All	pH	...	7.34	7.40	7.34	7.32	7.33	7.35	7.31	7.27	7.32
	No.	...	3	1	6	15	42	32	17	13	129
	pCO ₂	...	30		33	37	38	37	40	41	38
	No.	...	2		4	7	15	9	6	7	50
	pO ₂	...	34	43	32	29	28	30	29	30	29
	No.	...	3	1	4	18	41	26	20	12	125

TABLE 2
MEAN OXYGEN TENSION, HYDROGEN CONCENTRATION, CARBON DIOXIDE TENSION, STANDARD BICARBONATE,
BUFFER BASE AND BASE EXCESS IN THE UMBILICAL CORD BLOOD AFTER NORMAL DELIVERY OR AFTER DELIVERY
WITH DIFFERENT SIGNS OF ASPHYXIA

	pO ₂ (mm. Hg)	No.	pH	No.	pCO ₂ (mm. Hg)	Standard Bicar- bonate	Buffer Base (mEq/ litre)	Base Excess	No.
<i>Artery:</i>									
Normal cases	18.3	104	7.26	98	45	14.8	34.7	-12.2	25
Slow or irregular heart beats before delivery	17.6	21	7.21	22	55	16.2	36.7	-10.2	12
Meconium stained amniotic fluid	16.4	14	7.20	11	51	10.8	27.6	-19.4	2
Asphyxiated after delivery	14.5	7	7.16	8	39	12.9	31.9	-15.1	2
<i>Vein:</i>									
Normal cases	29.2	137	7.33	142	38	17.6	39.2	-7.7	6
Slow or irregular heart beats before delivery	28.9	31	7.31	31	41	18.0	39.8	-7.1	20
Meconium stained amniotic fluid	28.4	18	7.30	18	44	15.8	36.3	-10.6	16
Asphyxiated after delivery	27.6	11	7.24	13	44	14.6	34.1	-13.9	5

FIG. 3.—Distribution of the pCO₂ in the umbilical vein and arteries of normal infants.

advancing gestation time, a fact which has been shown by us previously (Sjöstedt *et al.*, 1960). There is also a tendency for the pH to be lower in primigravidae than in multigravidae.

CARBON DIOXIDE TENSION. The distribution of the pCO₂ values in the cord blood of the normal cases is shown in Fig. 3. The mean values of pO₂, pH and pCO₂ are given in Table 2 for the normal cases and the groups with various signs of

asphyxia. The first group had slow or irregular heart beats before the delivery, but no signs of asphyxia after birth. The second group had meconium stained amniotic fluid, but no other signs of asphyxia before or after birth. The third group showed signs of asphyxia after the delivery, manifested by diminished muscular tonus and/or delayed onset of spontaneous respiration. No case of severe asphyxia was studied in this series.

It will be observed that pCO₂ in the umbilical arteries and vein is higher in the asphyxiated than in the normal cases. The asphyxiated cases also have reduced pO₂ and pH. The changes are of about the same magnitude in the arteries and the vein though perhaps a little more pronounced in the arteries.

Although the number of observations in the different gestation weeks is small there seems to be an increase of the pCO₂ in the umbilical vein blood with advancing gestation. No such increase can be observed in the arteries.

ACID BASE BALANCE. The distribution of the standard bicarbonate and BB in 56 normal cases from the vein and in 25 normal cases from the arteries is given in Fig. 4. The mean values for the metabolic acid base balance are shown in Table 2. The number of pathological cases is small especially in the arteries. There is a metabolic acidosis in the infants asphyxiated after birth and in those with meconium stained amniotic fluid.

FIG. 4.—Distribution of standard bicarbonate and buffer base in the vein and arteries of normal infants.

FIG. 5.—The relation between $p\text{CO}_2$ and $p\text{O}_2$ in the umbilical vein and arteries of normal infants.

The relation between the $p\text{O}_2$ and $p\text{CO}_2$ in the umbilical vein and arteries is given in Fig. 5. It will be seen that if the $p\text{O}_2$ decreases, the $p\text{CO}_2$ increases, as would be expected in any situation which obstructs the normal passage of gas from the mother and vice versa.

Intervillous Blood of the Placenta. The figures for the $p\text{O}_2$, $p\text{H}$, $p\text{CO}_2$ and the metabolic acid base balance in 27 samples from the intervillous blood of the placenta are given in Table 3. Compared with the umbilical blood, the intervillous blood has higher $p\text{O}_2$, $p\text{H}$, standard bicarbonate and BB. The $p\text{CO}_2$ is lower than in the umbilical artery and the same as in the umbilical vein.

Discussion

Hydrogen Concentration. The present investigation corroborates and extends knowledge about the $p\text{H}$ of the cord blood. A detailed discussion of earlier works has recently been published by Kaiser (1959). Table 4 shows the $p\text{H}$ values available in the literature after 1932.

These studies have established that the $p\text{H}$ of the umbilical arteries is lower than that of the umbilical vein. The $p\text{H}$ of the umbilical vein in its turn is lower than that of the maternal vein and artery. In this respect it is perhaps better to make a comparison with the $p\text{H}$ of the intervillous blood, which we have found to be 7.41 against 7.33 for the

TABLE 3
OXYGEN TENSION, HYDROGEN CONCENTRATION, CARBON DIOXIDE TENSION, STANDARD BICARBONATE, BUFFER BASE AND BASE EXCESS IN THE INTERVILLOUS BLOOD OF THE PLACENTA

Case	$p\text{O}_2$ (mm. Hg)	$p\text{H}$	$p\text{CO}_2$ (mm. Hg)	Standard Bicarbonate	Buffer Base (mEq/litre)	Base Excess
1	36					
2	30	7.37				
3	30	7.32				
4	43	7.35				
5	54	7.45				
6	36	7.42				
7	48	7.41				
8	34	7.40				
9		7.33				
10	33	7.39				
11		7.44				
12	36	7.36	43	22	44	-1
13	51	7.43	38	24	47	+2
14	38	7.41	38	23	45	0
15	48	7.39	27	18	38	-7
16	46	7.43	29	20	41	-4
17	35	7.42	48	28	51	+7
18	48	7.40	43	25	47	+3
19	28	7.39	48	25	49	+3
20	48	7.40	36	22	45	-1
21	50	7.40	38	23	45	0
22	35	7.39	34	20	42	-4
23	40	7.43	38	23	45	-1
24	41	7.44	34	23	46	0
25	37	7.45	38	25	49	+3
26	45	7.47	37	26	52	+4
27	37	7.44	38	25	47	+2
Mean	40	7.41	38	23.2	45.8	+0.3
Mean umbilical artery . . .	18	7.26	45	14.8	34.7	-12.2
Mean umbilical vein . . .	29	7.33	38	17.6	39.2	-7.7

TABLE 4
SURVEY OF UMBILICAL CORD BLOOD pH STUDIES

Author	Artery		Vein	
	pH	No.	pH	No.
<i>Normal cases:</i>				
Eastman (1932)	7.33	3	7.36	8
Noguchi (1937)	7.32	14	7.36	14
Kaiser (1953)	7.26	12	7.32	12
Goodlin and Kaiser (1957)	7.28	28	7.32	28
James <i>et al.</i> (1958)			7.26	30
Kaiser and Goodlin (1958)			7.34	25
MacKinney <i>et al.</i> (1958)			7.29	200
Wulf (1959a)			7.35	40
Wulf (1959b)	7.30	36	7.41	36
Present series	7.26	98	7.33	142
<i>Asphyxiated cases:</i>				
Eastman (1932)			7.04	6
Noguchi (1937)			7.24	7
James <i>et al.</i> (1958)	7.04	10		
Wulf (1959)	7.18	20	7.23	20
Present series	7.20	41	7.29	62

umbilical vein. It will be seen from Fig. 1 that there are more cases with a pH between 7.35 and 7.40 than in any other group. Thus the pH difference between the intervillous maternal blood and the umbilical vein is small in normal cases. The pH of foetal blood increases during its passage through the placenta, indicating that this blood is giving up carbon dioxide and/or fixed acids. This will be discussed later.

The highest mean pH values in the umbilical vein given in the literature are those of Wulf (1959b), Eastman (1932) and Noguchi (1937). Wulf gives the high value of 7.41 and the others give 7.36. Noguchi also has the highest value in the umbilical artery, i.e. 7.32. The largest series (MacKinney, Goldberg, Ehrlich and Freymann, 1958) consisting of 200 cases before respiration has a mean of only 7.29. Most of the investigators have a mean of about 7.32. These variations are probably due, in the main, to differences in technique, particularly in the pH standard, and in material. If the pH is high and the technique sound, this indicates that the cases are normal and the pH values represent the true intrauterine figures.

Kaiser (1959), in his review, states that no information is available about alkalosis in the umbilical cord blood. It is true that the figures so far discussed are those of a mild acidosis. It must be remembered, however, that this expression is used solely because the pH is lower than the conventionally given figure for adult arterial blood and that the term acidosis in this sense has no pathological significance. As seen from Fig. 1, in 24 venous samples we have found a pH of 7.40 and above. In comparison with the mean pH of the umbilical vein this may be called alkalosis. In 40 normal cases Wulf (1959a) found eight with a pH

higher than 7.40, i.e. about 20% of the total cases, as in the present series. The foetus cannot decrease its pCO₂ and thereby increase the pH as the respiring individual does. The only way for the foetus to achieve this is if the pCO₂ of the intervillous blood decreases, i.e. by hyperventilation of the mother. This also occurs during labour and values of arterial maternal pCO₂ of less than 30 mm. Hg have been found by Boutourline-Young and Boutourline-Young (1956) and Weisbrot, James, Prince, Holaday and Apgar (1958).

If the infant is asphyxiated the pH is reduced in the umbilical arteries and vein. This decrease in pH is first seen in the arteries (Table 2). In the umbilical vein the pH is reduced particularly in those cases showing definite signs of asphyxia after birth. The pH is then about 0.1 units lower than the normal mean. As seen in Table 4, Eastman (1932) and James, Weisbrot, Prince, Holaday and Apgar (1958) report much lower values. The reason is that these authors analysed cases with severe asphyxia, whereas our cases were only mild. A few of our asphyxiated infants as well as a few of our normal infants have shown very low pH values (Figs. 1 and 2). Very low values even in vigorous infants have also been found in cord blood oxygen saturation studies and have been discussed earlier by us (Rooth and Sjöstedt, 1957a).

As seen in Table 1, there is a tendency for the pH to be lower in the cord blood of the primigravidae than in that of the multigravidae. As the pCO₂ is the same, this could be explained by more difficult labour during which the mother and/or the foetus has increased production of lactic acid and other fixed acids.

Carbon Dioxide Tension. Tables 5 and 6 give a survey of some pCO₂ and oxygen saturation values available in the literature. A survey of pO₂ values has earlier been given by us (Sjöstedt *et al.*, 1960). It can be seen from these Tables that our material, whether earlier or from the present series, shows high pO₂ or oxygen saturation values and low pCO₂ values. Our pH values are of the same magnitude as those established by others, suggesting that our cases are perhaps nearer to normal than those studied by others. This has a special interest in view of the fact that many authors are very cautious about figures obtained from cord blood drawn after delivery. The higher the pO₂ and oxygen saturation and the lower the pCO₂ the higher the probability that the figures represent the original intrauterine conditions. It seems reasonable to assume that the true intrauterine level for the pCO₂ is about 40 mm. Hg for the umbilical artery.

TABLE 5
SURVEY OF UMBILICAL CORD BLOOD $p\text{CO}_2$ STUDIES

Author	Artery		Vein	
	$p\text{CO}_2$ (mm. Hg)	No.	$p\text{CO}_2$ (mm. Hg)	No.
Haselhorst and Stromberger (1931)	50	4		
Eastman (1932)	42	3	36	8
Beer <i>et al.</i> (1955)	60	20	45	20
Goodlin and Kaiser (1957)	53	11	42	11
James <i>et al.</i> (1958)	55	27		
MacKinney <i>et al.</i> (1958)			48.5	189
Wulf (1959a)			44	40
Wulf (1959b)	49	36	44	36
Present series	45	27	38	58

TABLE 6
SURVEY OF UMBILICAL CORD BLOOD OXYGEN SATURATION STUDIES

Author	Artery		Vein	
	Oxygen Saturation	No.	Oxygen Saturation	No.
Eastman (1932)	16	15	50	15
Clemetson and Churchman (1953)	31	10	63	12
Walker (1954)	20	9	48	10
MacKinney <i>et al.</i> (1958)	24	234	48	286
MacKay (1957)	30	112	64	112
Rooth and Sjöstedt (1957a)	34	172	62	225
James <i>et al.</i> (1958)	22	43	49	55

The arteriovenous difference in $p\text{CO}_2$ of about 7 mm. Hg is a measure of the carbon dioxide given up to the maternal circulation in the placenta. In 26 cases we have found the $p\text{CO}_2$ of the intervillous blood of the placenta to be on an average 40 mm. Hg or identical with that of the foetal $p\text{CO}_2$ of the umbilical vein. These figures indicate an almost complete exchange of CO_2 across the placenta as opposed to the oxygen transport. The difference in $p\text{O}_2$ is about 10 mm. Hg (Sjöstedt *et al.*, 1960). These differences between oxygen and carbon dioxide are to be expected from the higher diffusion coefficient for carbon dioxide.

No previous comparison seems to have been made between the intervillous $p\text{CO}_2$ and the $p\text{CO}_2$ of the foetal circulation in man. Beer, Bartels and Raczowski (1955) assume for their calculations a complete equilibration. In animals with a syndesmochorial placenta five layers thick such as cows and sheep, pressure differences of about 20 mm. Hg have been found (Roos and Romijn, 1940). In rabbits with a haemoendothelial placenta, Young (1952) has observed values between 14 and -2 mm. Hg.

Darling, Smith, Asmussen and Cohen (1941) calculated the relation between $p\text{H}$ and $p\text{O}_2$ if the $p\text{H}$ of the foetal blood is changed by varying

the $p\text{CO}_2$. Consequently there is a relation between $p\text{CO}_2$ and $p\text{O}_2$ and this is evident also from Fig. 5. There is a large scatter in these figures as might be expected because we are dealing with individual blood samples and not systematic $p\text{CO}_2$ or $p\text{O}_2$ changes in one and the same blood. It will be observed, however, that even when $p\text{CO}_2$ rises to high levels, the $p\text{O}_2$ is usually maintained, although at a relatively low level. As a rule these cases have a metabolic acidosis and they demonstrate how the $p\text{O}_2$ is kept up at all costs.

Acid Base Balance. Compared with the mother the foetus has a metabolic acidosis (Table 3) and it can be seen that in comparison with the umbilical vein, the umbilical artery has a metabolic acidosis (Table 3 and Fig. 4). Expressed in BB the mean difference between the arteries and the vein is about 4.5 mEq/litre. This difference is a measure of the fixed acids which pass from the foetal to the maternal circulation. Once pulmonary ventilation starts after birth the BB of the arteries and the veins is similar to that in adult blood. Because of the error inherent in our way of estimating the metabolic acid base balance, the present series cannot be used for an exact determination of the normal values in cord blood, but the values are of the same order as those of James *et al.* (1958).

As already shown by Eastman (1932) the slightly asphyxiated foetus compared with the normal foetus has no metabolic acidosis, whereas those with more pronounced asphyxia have low bicarbonate content as a sign of metabolic acidosis. These findings are confirmed and expressed in the more exact form of BB by James *et al.* (1958). Our material is small but the same tendency is present.

Summary

The cord blood of 222 infants has been analysed for $p\text{H}$, $p\text{CO}_2$, $p\text{O}_2$ and metabolic acid base balance expressed as standard bicarbonate, BB and BE.

From the placenta 26 samples of intervillous blood have been analysed in the same way and the results are compared with the cord blood in order to show the gas exchange of the foetus.

The mean $p\text{H}$ after normal delivery is 7.26 in the umbilical artery and 7.33 in the umbilical vein.

The mean $p\text{CO}_2$ after normal delivery is 45 mm. Hg in the umbilical artery and 38 mm. Hg in the vein.

The mean BB after normal delivery is 35 mEq/litre in the umbilical artery and 39 mEq/litre in the vein, indicating that during the passage through the placenta the foetal blood gives up fixed acids to the maternal circulation.

In the intervillous blood of the placenta the mean pH is 7.41, the mean pCO₂ 38 mm. Hg and the mean BB 46 mEq/litre.

The pCO₂ in the umbilical vein and the intervillous space of the placenta are the same, 38 mm. Hg, indicating an almost complete exchange of carbon dioxide between the foetal and maternal circulation.

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