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SOME CORRELATIONS BETWEEN RESPIRATORY MOVEMENTS AND BLOOD GASES IN CAT FOETUSES

By A. G. STEELE and W. F. WINDLE[1]

From the Anatomical Laboratory, Northwestern University Medical School, Chicago

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Foetal respiratory movements which occasionally can be palpated and observed visually in normal human subjects nearing term have excited interest for many years [Ahlfeld, 1891, 1905; Snyder & Rosenfeld, 1937], but the conditions under which they occur are not known. Attempts have been made to determine the relationship of carbon dioxide excess and oxygen want to their occurrence in experimental animals [Barcroft, 1935; Snyder & Rosenfeld, 1937; Windle, Monnier & Steele, 1938] by administering gas mixtures to the mother, but little has been done to correlate determinations of foetal blood gases with the presence or absence of these activities at the time of sampling. The present report concerns such correlations in the cat.

Methods

Pregnant cats were decerebrated by tying carotid and basilar arteries under ether and an hour or more was allowed for recovery before beginning experiments. The animals did not usually suffer lasting depression of respiration but, on the contrary, their breathing frequently became faster and deeper than normal. Blood pressure and body temperature were not greatly affected. In the instances in which breathing was slow, the cats were allowed to breathe a mixture of 5–8 % carbon dioxide in oxygen by tracheal canula. They were placed in a constant temperature bath of Locke's solution where the uterus was brought forth and foetuses delivered through small incisions in least vascular parts without disturbing the zonary placentae. Foetal respiratory movements were studied while the specimens were submerged and with placental circulation intact. Later, some were allowed to breathe air.

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The quantity of blood obtainable from cat foetuses without seriously disturbing the total volume is limited. Consequently 0·2 c.c. samples were drawn under oil into tuberculin syringes with no. 27 needles containing minute amounts of heparin. They were analysed by the Van Slyke-Neill [1924] micro-manometric technique. Oxygen capacity was estimated by the Van Slyke-Neill method for 1 c.c. samples of blood after the foetal blood had been shaken repeatedly with air at atmospheric pressure in the froth chamber of the gas pump to bring about saturation. The principal error seemed to be introduced in measuring the quantity of blood.

Results

Data on gas content of umbilical vein blood are presented in Table I. The carbon dioxide content of foetal blood was clearly an important factor in helping to determine the rate and depth of foetal respiratory movements. Thus, for example, foetus 4 of cat 15 managed to "breathe" at a rate of 28 per min. with only 3·7 vol. % oxygen, while other foetuses receiving as much or more oxygen were apnoeic. The difference lay in the carbon dioxide content which was high in the former and low in the others. In foetus 2 of cat 16, respiratory movements were weak and in foetus 4 of cat 15, strong and faster. More than 8 vol. % oxygen was present in both instances, but the former was poorer in carbon dioxide by 16·5 vol. %.

The presence or absence of respiratory movements could not be explained solely on the basis of carbon dioxide content. Foetuses receiving less than 3·7 vol. % oxygen in umbilical vein blood showed no respiratory movements or gasped infrequently, but most of those with greater amounts of oxygen did execute rhythmical respiratory movements. Relatively high concentration of carbon dioxide (40 % or more) in the absence of adequate oxygen in foetal blood did not lead to rhythmical respiratory movements but to arhythmical gasping. For example, the umbilical vein blood of foetuses 2 and 3 of cat 6 contained almost exactly the same carbon dioxide concentration, but only the specimen with higher oxygen executed rhythmical respirations. Similarly, foetus 3 of cat 17 lacked rhythmical activities when its blood was reduced (0·4 and 2·9 vol. % oxygen) but "breathed" at a rate of 14 per min. when the oxygen reached 5·1 vol. %, even though the concentration of carbon dioxide remained about 35 vol. %. It seemed that these differences in respiratory behaviour must have been related less to the carbon dioxide than to the increased oxygen content.

TABLE I. Carbon dioxide and oxygen content of foetal blood

Gasping or no respiration at sampling							Rhythmical respiratory movements at sampling						
	Foetus				Umb. vein blood			Foetus				Umb. vein blood	
Cat no.	No.	Wt. g.	Age days	Time min.	CO_2 vol. %	O_2 vol. %	Cat no.	No.	Wt. g.	Age days	Time min.	CO_2 vol. %	O_2 vol. %
6	2	18	?	6	53·3	1·1	6	3	17	?	½	53·8	4·0
8	2*	19	46	0	39·7	1·4	11	3*	31	48	0	57·0	8·1
10	4	21	46	2	55·0	1·1	11	1	26	48	33	56·0	4·9
12	2	29	?	1	39·1	3·7	15	4	46	?	1	57·3	3·7
13	1	44	53	2	33·1	0·7	15	4	46	?	4	56·4	8·4
13	1	44	53	4	25·4	0·3	16	2	36	?	32	39·9	8·2
13	3*	28	53	0	31·5	4·8	17	2	42	?	4	25·1	6·9
17	3	38	?	¼	36·4	0·4	17	1	46	?	14	23·9	5·9
17	3	38	?	5	34·6	2·9	17	3	38	?	41	35·1	5·1
18	1	43	?	12	46·2	1·5	22	2	70	?	29	42·8	8·6
18	2	?	?	¼	51·6	1·6	28	1	99	?	4	49·6	7·7
22	1	73	?	5	36·4	4·5	28	2	106	?	¼	56·5	8·1
23	1	77	?	2	41·2	1·6	28	2	106	?	12	59·4	5·3
24	4	84	?	4	24·0	2·8	29	2	104	65	53	43·6	7·8
26	1	103	?	1	53·8	0·6	30	3	125	62	?	42·8	4·6
26	1	103	?	3	47·2	3·6						Carot. art.	
27	1	104	?	3	24·5	2·5							
27	1	104	?	5½	26·1	1·8	19	1	52	57	20	39·3	14·9
29	1	120	65	3	29·1	4·6	19	1	52	57	90	32·7	5·0
30	1	104	62	2½	33·3	1·3	19	2	46	57	30	36·1	6·9
31	1	118	?	1½	20·7	1·4	23	2	71	?	60	36·6	13·2
31	1	118	?	15	24·3	1·0	23	2	71	?	105	27·6	6·9
					Carot. art.		26	1	103	?	37	38·8	12·0
							26	1	103	?	65	54·3	6·5
32	3	84	?	1	33·0	2·4	28	1	99	?	165	57·7	6·6
Average, apnoeic unborn foetuses					36·7	2·1	29	3	115	65	19	43·3	9·7
Average, active unborn foetuses					46·6	6·5	30	3	125	—	1 day	43·4	13·0
							32	4	?	—	1 day	51·6	13·4

The cats bear the same numbers in this and a preceding article [Steele & Windle, 1939]. Under the heading "time" is indicated the number of minutes elapsing between exposing the foetus and drawing the blood sample. In three foetuses marked with an asterisk (*), blood was drawn without removing the foetus from the uterus. Placental circulation was intact in all experiments in which blood was taken from umbilical veins. In those under the heading "carot. art." (carotid artery), the umbilical cords had been tied and the foetuses removed from the bath; "time" in these instances refers to minutes elapsed after tying the umbilical cords.

TABLE II. Oxygen capacity of foetal blood

	Foetus		
Cat no.	No.	Wt. g.	O_2 capacity vol. %
6	1	18	11·0
12	2	29	15·5
18	1	43	11·6
23	1	77	16·9
23	2	71	14·8
26	2	90	15·6
27	2	100	14·8
28	2	106	15·9
32	3	84	11·5

A number of attempts were made to determine oxygen-carrying capacity of foetal blood, but the quantities of blood obtainable were so small that the figures in Table II may not be accurate and are probably too low. However, it becomes evident in comparing data in Tables I and II that rhythmical respiratory movements occurred in foetuses receiving blood no more than 40 or 50 % saturated with oxygen, and in others it could scarcely have been 30 %. Although it is yet to be proved what is the actual condition *in utero* for some cat foetuses in the last 2 weeks of gestation, 50 % saturation may not be a bad estimation, and for the following reason. In several experiments the umbilical vessels could be seen through small incisions in the uterus but without disturbing placenta and foetus. The veins were sometimes but not always brightly coloured. In one instance (foetus 3 of cat 11) a sample of blood was obtained without changing the scarlet colour of the vein. This blood contained 8·1 vol. % oxygen. Another time we were able to get blood with great dispatch at the moment of delivering foetus 2 from cat 28. It was brilliantly scarlet but began to darken as the last of the 0·2 c.c. sample entered the syringe. This contained 8·1 vol. % oxygen, about 50 % saturated. Both foetuses were executing rhythmical respiratory movements at rapid rates, due in part perhaps to the fact that the mother cats were breathing 5–8 % carbon dioxide in oxygen at the time and the foetal blood contained large amounts of carbon dioxide.

Some foetuses were allowed to be born, i.e. their umbilical cords were tied and they were brought out of the bath. Blood, obtained without anaesthesia from the carotid artery, was analysed after various periods of air breathing. In two 1-day-old kittens it contained quantities of carbon dioxide comparable with normal unexcited adult cats (Steele & Windle, 1939) and the oxygen was within normal range. Several, having breathed for shorter periods, gave similar oxygen values but the carbon dioxide was lower. The arterial blood of others was low in oxygen and some of the kittens showed less oxygen an hour or more after delivery than they had earlier. Perhaps they were not yet prepared to cope with air-breathing successfully. The data appear on the right side of Table I.

Apnoeic unborn foetuses receiving blood low in carbon dioxide were induced to gasp and start breathing air by pinching the umbilical cord. This was illustrated many times, and even in specimens whose umbilical vein blood proved to contain so little oxygen that further oxygen deficit could scarcely have been the only cause of the initial respiration. Umbilical vein blood was observed at the moment of natural delivery of cats 32 and 33. Its colour was dark and no different from blood of the

umbilical artery. A sample of carotid artery blood of one kitten (no. 3 of cat 32) taken at birth (several gasps had occurred) gave low values for both oxygen and carbon dioxide. During labour, the mother cat was breathing rapidly, a fact which could account for the reduction of carbon dioxide. A litter-mate (no. 4), allowed to live 1 day, had high blood values for both.

It has been shown that maternal blood fluctuated within wide limits in respect to its content of carbon dioxide under varying conditions of excitement and rapid breathing [Steele & Windle, 1939]. In the present experiments in which the mother cats were breathing normally, slowly or in which oxygen and carbon dioxide mixtures were being inhaled, the foetal blood contained 40 vol. % or more carbon dioxide. But in the instances in which the cats were breathing faster than normally and were active or showed marked rigidity at the time foetal blood samples were taken, the carbon dioxide was lower. These differences in maternal conditions were correlated with variations in foetal activity.

Under experimental conditions, foetal respiratory movements varied greatly. Some specimens had rather long periods of activity during which the respiratory rate was 14–32 a minute and often deep. Others, when the mother cats were breathing oxygen containing carbon dioxide, executed short sequences of respiratory movements at rates of 42–76 or even 135 per min. The highest rates were observed soon after the gas mixture had been withdrawn from the cats and may be interpreted as "rebound" phenomena after excessive dosing with carbon dioxide [Windle & Nelson, 1938]. Even in unanaesthetized, unoperated cats near term, continuous respiratory activity of the foetuses was not the rule. We were never able to palpate more than six or eight movements in sequence alternating with long periods of inactivity.

There appeared to be a relationship between pre-labour uterine contractions and the respiratory behaviour of the foetuses [Windle, Monnier & Steele, 1938]. In late foetal life, contractions of the uterus were accompanied by reddening of umbilical vein blood which imparted a better colour to the foetuses themselves. Such blood contained more oxygen than it had during uterine relaxation. In Table I, the two values for specimen 4 of cat 15 and for foetus 2 of cat 28 were obtained from blood taken at different stages of uterine activity. Other differences seen in Table I, such as that between the two foetuses of cat 6, were related to the same phenomenon. The differences in foetal respiratory activities were evidently correlated with these changes in oxygenation.

Comment

The present studies, together with those of Eastman [1930] and Haselhorst & Stromberger [1930] in the human and Barcroft [1936] and Barcroft, Elliott, Flexner, Hall, Herkel, McCarthy, McClurkin & Talaat [1934] in the goat and sheep, indicate that umbilical vein blood is poorly saturated with oxygen toward the end of gestation (last quarter in the cat). Although 50 % saturation or less may be the usual condition, not all investigators have obtained such low values and considerable variation has been the rule. Roos & Romijn [1938], who found the umbilical vein blood of one calf 90 % saturated at 8½ months, obtained lower figures (47–75 %) in four other 7–8 month foetuses. Barcroft & Mason [1938] have obtained a few high values in the sheep. Goldbloom & Gottlieb [1930] and Bidone [1931] reported high umbilical vein oxygen in human foetuses at birth.

We do not know whether foetal respiratory movements would manifest themselves in the absence of some degree of foetal anoxaemia (lowered oxygen and increased carbon dioxide) or not. Foetal anoxaemia was encountered in every experiment in the late foetal life of the cat. Earlier in gestation, the foetuses of decerebrated cats were apnoeic [Windle *et al.* 1938], and carbon dioxide inhaled by the mothers caused respiratory movements to start in these foetuses. No blood gas analyses could be obtained in these small specimens but perhaps, like the goat and sheep [Barcroft, 1936; Barcroft *et al.* 1934], the umbilical vein blood would have been found more nearly saturated with oxygen throughout the middle of the gestation period than towards its end. In view of the present experiments, in which it was observed that the faster respiratory movements were associated with the higher oxygen estimations, it is doubtful if the apnoea of younger foetuses was due entirely to high oxygen saturation. The part played by carbon dioxide must be taken into account.

A deficit of carbon dioxide seems to lead to apnoea in rabbit foetuses [Snyder & Rosenfeld, 1937], but what constitutes a normal level of this gas in foetal blood? The arterial blood of non-pregnant, unoperated, unanaesthetized female cats fluctuated widely (25–50 vol. %) in carbon dioxide content [Steele & Windle, 1939] depending in part upon the degree of excitement and rapidity of breathing while samples were being drawn. The average value was 36 vol. % carbon dioxide. Under our experimental conditions, blood of the foetuses showed similar fluctuations. The average carbon dioxide content of foetuses lacking respiratory movements

or showing only occasional gasps was 36·7 vol. % and for those executing rhythmical respiratory movements, 46·6 vol. %. Others [Eastman, Geiling & De Lawder, 1933] observed that the carbon dioxide tension of human umbilical vein blood varied within wide limits. Keys [1934] reported that foetal goat blood had a higher carbon dioxide capacity than the maternal blood due to a greater alkali reserve. The data in these and other articles [Roos & Romijn, 1938; Bidone, 1931; Haselhorst & Stromberger, 1930; Kellogg, 1930] dealing with carbon dioxide content of umbilical vein blood in late pregnancy indicate that this gas is not unusually low according to adult standards but only relatively so, perhaps in respect to the foetal carrying capacity.

In some of the present experiments it would seem that conditions simulated asphyxia neonatorum. This is suggested by the very low content for both oxygen and carbon dioxide sometimes encountered in umbilical vein blood of the cat foetuses lacking respiratory efforts. Very rapid breathing of some of the mother cats together with probable excessive lactic acid formation during the activity and rigidity of the decerebrate state may have brought about the reduction of the carbon dioxide level. The blood gas analyses resemble those obtained in the human foetus in a state of asphyxia at birth [Eastman, 1932; Wilson, Torrey & Johnson, 1937].

The part played by the uterus itself in regulating the oxygen content of umbilical vein blood has received little attention previously. In the experiments in cat foetuses, alternate lightening and darkening of umbilical vein blood with uterine contractions was a very striking phenomenon. Here is a mechanism which, if operating under normal as well as experimental conditions, can well serve to alleviate periodically a normally existing state of partial anoxaemia in the foetus as birth approaches. The intermittent character of intra-uterine respiratory and other somatic foetal movements seen in normal unanaesthetized subjects may be correlated with this uterine activity.

Conclusions

1. The occurrence during the last quarter of foetal life of rhythmical respiratory movements in cat foetuses whose placental circulation was intact was related both to the oxygen and carbon dioxide content of umbilical vein blood.

2. The umbilical vein blood was at best little more than 50% saturated with oxygen in the last foetal quarter.

3. When the oxygen and carbon dioxide were very low (average 2·1 and 36·7 vol. %) no respiratory movements occurred.

4. Rhythmical respiratory movements were observed in foetuses receiving blood containing greater amounts of these gases (average 6·5 and 46·6 vol. %).

5. Arhythmical deep gasps like those initiating air breathing at birth were encountered in foetuses receiving blood very poor in oxygen but high in carbon dioxide.

6. The fluctuation of foetal blood within wide limits in respect to both oxygen and carbon dioxide content was apparently due to such factors as maternal respiratory rate and depth, muscular work done by the maternal animals and the contraction and relaxation of the uterine muscle. The uterine contractions were accompanied by intermittent improvement in oxygen content of umbilical vein blood.

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