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CHANGES IN O_2 DISTRIBUTION AND CONSUMPTION IN FOETAL LAMBS WITH VARIATIONS IN UMBILICAL BLOOD FLOW

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The oxygen saturation in the carotid blood is higher than that in the umbilical or femoral arteries in foetal goats (Huggett, 1927), lambs (Barcroft, Barron, Cowie & Forsham, 1938; Barcroft, 1946; Dawes, Mott, Widdicombe & Wyatt, 1953; Dawes, Mott & Widdicombe, 1954) and monkeys (Dawes, Jacobson, Mott & Shelley, 1960). The various streams of blood which enter the heart, one from the placenta which is relatively well oxygenated, and the others returning from the foetal tissues with less oxygen, do not completely mix. The oxygen content of blood in the pulmonary trunk is less than that in the ascending aorta (Dawes *et al.* 1954). Most of the output of the right ventricle passes through the ductus arteriosus to enter the descending aorta, and hence dilutes the blood derived from the left ventricle via the aortic arch.

Wide variations in the difference between the O_2 contents of carotid and umbilical (or femoral) arterial blood in foetal lambs have been reported (Barcroft *et al.* 1938; Dawes *et al.* 1953; Dawes *et al.* 1954). These variations suggested the possibility that the distribution of oxygenated blood within the foetal circulation might change under different physiological conditions. It seemed unlikely that the variation could be attributed entirely either to the differences in anaesthesia or handling, or to the fact that Barcroft's samples were not taken simultaneously. He took umbilical arterial samples directly from the cord, and mentioned the possibility of vascular spasm. Therefore umbilical blood flow has been reduced deliberately by various methods, a procedure which in certain circumstances, in immature lambs, has been found to increase the difference between the oxygen content of carotid and femoral arterial blood. A brief account of these investigations has been published elsewhere (Dawes, 1961).

In addition, in mature lambs, a reduction in umbilical blood flow by haemorrhage, but not by constriction of the umbilical vein, has been found to cause a rise in the O_2 saturation of umbilical venous blood.

METHODS

A preliminary series of experiments was carried out on eight lambs of 79–86 days gestation and eight lambs of 133–138 days gestation delivered by Caesarean section from Clun-Hampshire ewes under pentobarbitone (20–30 mg/kg I.V. initially) or chloralose (50–70 mg/kg) anaesthesia. The methods of delivery, handling and of measurement of blood pressure, heart rate and of the O_2 content and capacity of blood samples were similar to those described previously (Dawes & Mott, 1959). The foetal abdomen was opened to expose the abdominal portion of the umbilical vein, and a 6 mm wide tape was passed around it and tightened when it was desired to reduce umbilical blood flow.

Further experiments were carried out on twenty-two lambs of 87–95 days gestation and ten lambs of 137–141 days gestation, delivered by Caesarean section from Clun-Hampshire ewes anaesthetized with chloralose (30–40 mg/kg). The abdominal portion of the umbilical vein was exposed. Heparin (10 mg/kg) was injected intravenously into the foetus. The umbilical cord was occluded by compression with a tape against a soft plastic tube. The abdominal umbilical vein was divided and the cut ends were rejoined by cannulae and a short external circuit containing an electromagnetic flowmeter (Wyatt, 1961; Dawes, 1962) whose output was recorded, together with blood pressure and heart rate, on a Cambridge Instrument Co. Slow Recorder and Quick Response Recorders (Evershed & Vignoles, QU/CRD 19). The umbilical cord was released after a period of occlusion which usually did not exceed 2 min. Umbilical venous pressures and blood samples were taken from the external circuit. Haemorrhage was caused by withdrawal of blood from a femoral or carotid artery. The descending aorta was constricted with a tape below the origin of the renal arteries by a retroperitoneal approach. In all experiments the umbilical cord was intact, the foetus did not breathe and sets of blood samples were removed from the various vessels simultaneously.

RESULTS

Preliminary experiments were carried out on immature foetal lambs of 79–86 days gestational age delivered by Caesarean section under pentobarbitone anaesthesia. A pair of blood samples was withdrawn simultaneously from the carotid and femoral arteries and the difference between their O_2 contents (expressed as a proportion of O_2 carrying capacity) averaged $6{\cdot}7 \pm 0{\cdot}9\,\%$ (S.E.) and did not exceed 12 % (Fig. 1, ○). The umbilical vein was then constricted until the blood pressure fell and the heart rate began to rise. This degree of constriction was maintained for 4 min or more. During this period of constriction both carotid and femoral arterial O_2 saturations fell, but the latter more than the former, so that the carotid–femoral arterial O_2 difference increased (Fig. 1, ●). In 4 additional immature lambs, under local anaesthesia, the carotid–femoral arterial O_2 difference was $4{\cdot}4 \pm 2{\cdot}0\,\%$ (S.E., mean of 8 observations), a figure which is not significantly different from the observations under pentobarbitone before constriction of the umbilical vein.

Similar experiments were carried out in five mature foetal lambs, and an increase in carotid–femoral arterial O_2 difference was observed in two; in the other three there was no change. These experiments were not wholly

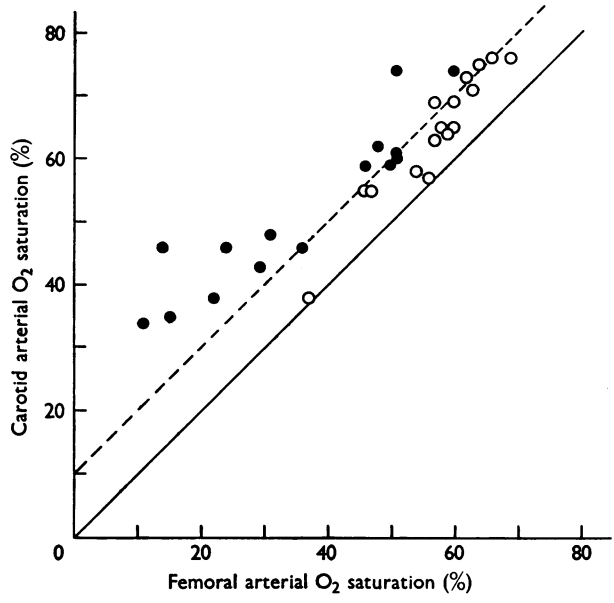

Fig. 1. Measurements of carotid and femoral arterial O_2 saturations in six foetal lambs of 79–86 days gestation before (○) and during (●) constriction of the umbilical vein. The solid line indicates equality and the interrupted line 10 % difference in O_2 saturations.

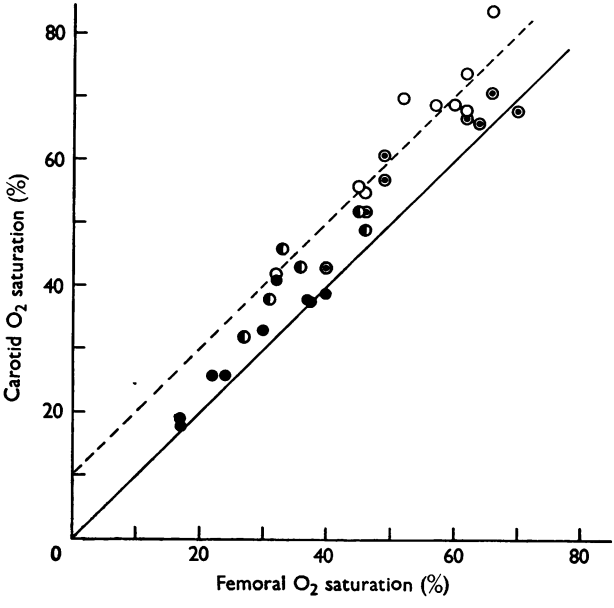

Fig. 2. Measurements of carotid and femoral arterial O_2 saturations in four immature (○) and three mature (⊙) foetal lambs whose mothers were breathing air, and in the same lambs (immature ◐, and mature ●) when the mothers were given 10 % or 7·5 % O_2 to breathe. The solid line indicates equality and the interrupted line 10 % difference in O_2 saturations.

satisfactory because there was no evidence that the rate of blood flow was reduced either in the same proportion as in premature lambs or indeed to a constant value.

The effect of hypoxaemia was also examined by giving the ewe 10 or 7·5% oxygen in nitrogen to breathe. In four lambs of 79–83 days gestation and in three lambs of 133–138 days gestation hypoxaemia almost always caused a small decrease in the carotid–femoral arterial O_2 difference, as is shown in Fig. 2. Reducing the oxygen content of the maternal inspired air decreases the oxygen saturation of umbilical vein blood (Acheson, Dawes & Mott, 1957) which has the highest oxygen content of any in the foetal circulation. Hence, irrespective of any redistribution of blood flow one would expect that hypoxaemia produced in this way would decrease the carotid–femoral arterial O_2 difference.

TABLE 1. Comparative measurements on immature and mature foetal lambs

	Immature	Mature
Gestation age (days)	87–95	137–141
Number of lambs	22	10
Weight (kg)	0·582 ± 0·017	4·22 ± 0·31
Blood pressure (mm Hg)	37 ± 3	66 ± 3
Umbilical blood flow (ml./kg.min)	217 ± 12	170 ± 14
O_2 carrying capacity of blood (ml./100 ml.)	10·5 ± 0·9	16·4 ± 0·5
O_2 saturation in umbilical vein (%)	83 ± 1·2	69 ± 3·8
O_2 saturation in carotid artery (%)	65 ± 1·8	55 ± 4·2
O_2 saturation in femoral artery (%)	59 ± 2·3	52 ± 3·2
O_2 consumption (ml./kg.min)	5·4 ± 0·5	4·6 ± 0·3
Blood lactate (mg/100 ml.)	19 ± 1·2†	25 ± 2·2*

* Six lambs only.

† Nine lambs only.

In all tables the figures indicate means ± S.E.; numbers in brackets show number of observations.

Quantitative reduction of umbilical blood flow

The development of a cannulated electromagnetic flowmeter of high accuracy and low resistance to blood flow made it possible to measure the effect of quantitative reduction in umbilical flow under good physiological conditions. Table 1 summarizes observations made when the preparation was complete and a steady rate of flow had been reached 15–20 min after the flowmeter had been placed in the abdominal umbilical vein. Mature foetal lambs weighed more than seven times as much as immature lambs of 87–95 days gestation and had a higher blood pressure and O_2 carrying capacity. The oxygen saturation of blood samples withdrawn from the principal vessels was less, and the rate of O_2 consumption expressed in terms of body weight was significantly less ($P < 0·02$).

Two sets of blood samples were withdrawn initially at an interval of 3–5 min. Umbilical blood flow was then decreased by partial constriction

of the umbilical venous flow circuit with a screw-clip, or of the descending aorta with a tape, or by haemorrhage. The rate of umbilical blood flow was held as constant as possible at its new value for 6 min or more, and two further sets of samples were then taken. Further changes in flow were then made, and finally umbilical flow was allowed to recover as far as it would on releasing the constriction or returning the blood to the lamb. The experiment usually lasted up to 1 hr from the first withdrawal of blood samples.

TABLE 2. The effect of haemorrhage or constriction of the umbilical vein on arterial pressure in immature and mature foetal lambs

Umbilical flow		Systemic arterial blood pressure	
		> 150 ml./kg.min	< 120 ml./kg.min
Immature lambs	Haemorrhage	37 ± 0·5 (15)	27 ± 0·8 (30)
	Constriction of umbilical vein	34 ± 2·9 (14)	28 ± 1·1 (19)
Mature lambs	Haemorrhage	75 ± 4 (14)	44 ± 4 (14)
	Constriction of umbilical vein	78 ± 4 (10)	76 ± 5 (10)

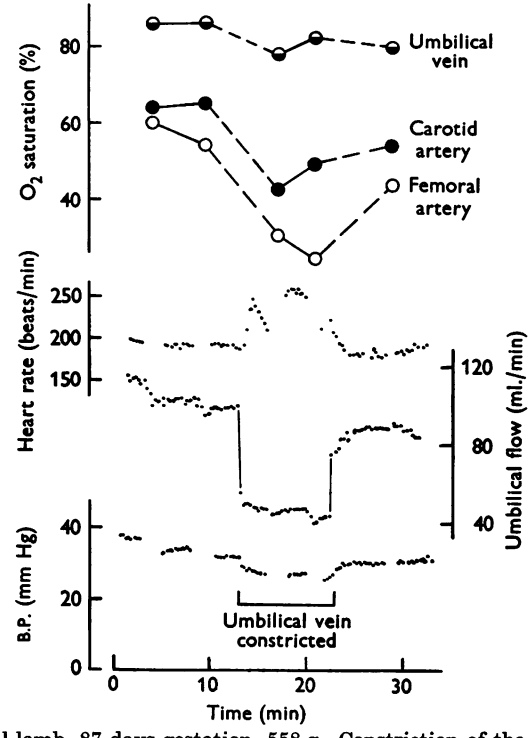

Fig. 3. Foetal lamb, 87 days gestation, 558 g. Constriction of the umbilical vein caused an increase in the difference between the O_2 contents of carotid and femoral arterial blood, a fall in femoral arterial pressure (B.P.) and a rise in heart rate.

Cardiovascular changes

Reduction of umbilical blood flow by umbilical venous constriction in immature foetal lambs always caused a large rise in umbilical venous pressure and a fall in femoral arterial pressure (Table 2), accompanied by a fall in vena caval pressure. There was also a rise in heart rate (Fig. 3). Four lambs were placed in a body plethysmograph, and when umbilical blood flow was decreased by this method the volume of the foetus fell by up to 15 ml./kg (Fig. 4). This demonstrated that there was a substantial transfer of blood from the immature foetus to the placenta, sufficient to

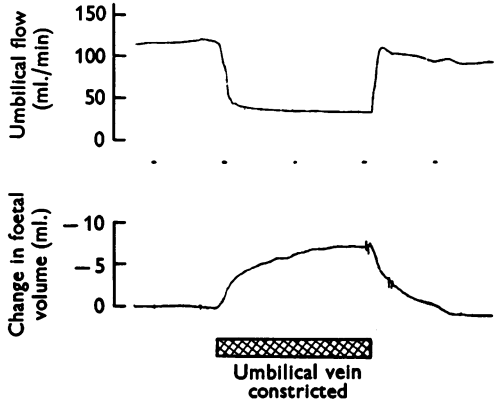

Fig. 4. Foetal lamb, 90 days gestation, 625 g. Constriction of the umbilical vein caused a decrease in foetal volume. Time marker, 0·5 min.

explain the fall in systemic arterial pressure. In mature foetal lambs constriction of the umbilical vein sufficient to cause comparable reductions in umbilical flow per kilogram caused no significant decrease in systemic arterial pressure (Table 2). Vena caval pressure fell and heart rate rose.

Reduction of umbilical flow by constriction of the abdominal aorta in immature foetal lambs caused a fall in femoral arterial and umbilical venous pressures, while carotid arterial and vena caval pressures rose. The heart rate almost always increased.

Withdrawal of blood samples for gas analysis in small immature lambs often caused a slight reduction in blood pressure and umbilical flow, sometimes accompanied by transient tachycardia. Nevertheless, over the course of those experiments in which flow was reduced by constriction of the umbilical vein or aorta, there was only a small, statistically insignificant, fall in O_2 carrying capacity, in spite of the redistribution of blood between foetus and placenta, and the withdrawal of numerous blood samples (Table 3).

When larger volumes of blood were removed from immature lambs, arterial pressure and umbilical flow fell precipitously and then began to recover; this was accompanied by sustained tachycardia. The mean fall in systemic arterial pressure after haemorrhage was similar to that observed when umbilical flow was reduced by constriction of the umbilical vein

TABLE 3. Effects of withdrawal of blood samples and reduction in umbilical flow either by constriction of the umbilical vein or aorta or by haemorrhage, on the O_2 carrying capacity of the blood in immature and mature foetal lambs

	O_2 carrying capacity (ml./100 ml.)	
	Immature lambs	Mature lambs
Initial	10·7 ± 0·3 (6)	—
At end of aortic constriction	10·4 ± 0·3	—
Initial	11·2 ± 0·5 (9)	16·6 ± 0·9 (5)
At end of umbilical vein constriction	10·4 ± 0·5	16·2 ± 1·3
Initial	9·7 ± 0·4 (7)	16·9 ± 0·8 (7)
At end of haemorrhage	7·3 ± 0·3	14·1 ± 0·6
Decrease (%)	25	17

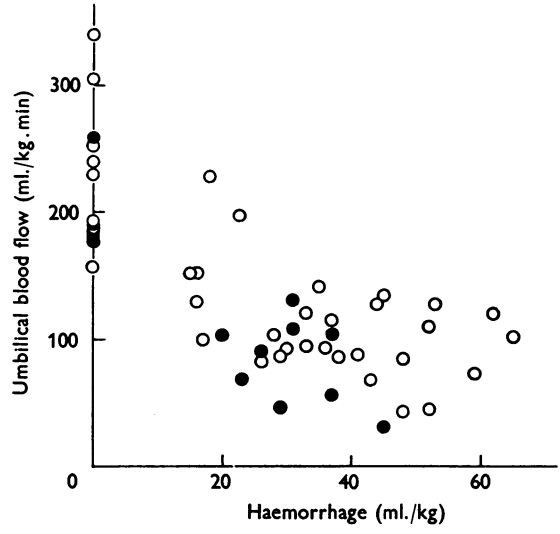

Fig. 5. The effect of haemorrhage on umbilical blood flow in seven lambs of 87–91 days gestation (○) and in five lambs of 136–143 days gestation (●).

(Table 2). After haemorrhage there was considerable and rapid haemodilution, as demonstrated by the fall in the O_2 carrying capacity of the blood (Table 3). In these immature lambs removal of about 30 ml. blood/kg reduced flow to 100 ml./kg.min (Fig. 5). In mature lambs a haemorrhage of similar proportion caused as much or more reduction of umbilical blood flow per kilogram, accompanied by a proportionally larger fall in systemic arterial pressure (Table 2), and haemodilution (Table 3).

Changes in the distribution and consumption of O_2

The lower part of Fig. 6 shows that as umbilical blood flow was reduced the difference between the O_2 content of carotid and femoral arterial

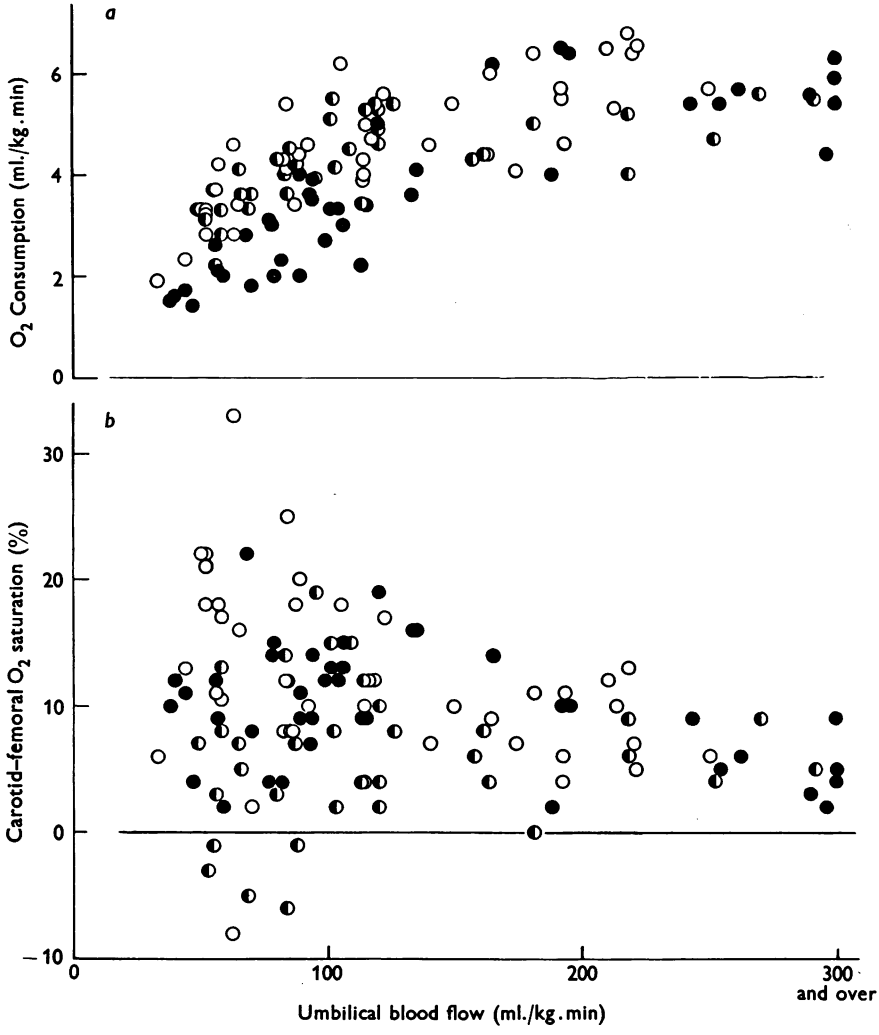

Fig. 6. (*a*) O_2 consumption and (*b*) carotid–femoral arterial O_2 difference in immature foetal lambs during constriction of the umbilical vein (○) or aorta (◐) or during haemorrhage (●).

blood tended to increase in immature foetal lambs. Table 4 shows the mean carotid–femoral arterial O_2 differences when umbilical blood flow was above 150 ml./kg.min or below 120 ml./kg.min. The carotid–femoral

O_2 difference increased significantly when flow was decreased by constriction of the umbilical vein ($P < 0.05$) or by haemorrhage ($P < 0.01$). When flow was reduced by constriction of the aorta there was no significant change in mean difference, but the scatter of individual observations greatly increased, and in five instances the O_2 content of femoral arterial blood exceeded that in the carotid. Table 4 also shows that in mature lambs

TABLE 4. Differences in O_2 content (expressed as a percentage of O_2 carrying capacity) in simultaneous carotid and femoral arterial blood samples under different experimental conditions in immature and mature foetal lambs

Umbilical flow		Carotid–femoral arterial O_2 difference (%)	
		> 150 ml./kg.min	< 120 ml./kg.min
Immature lambs	Umbilical vein constriction	8·4 ± 0·86 (12)	13·8 ± 1·43 (29)
	Haemorrhage	6·1 ± 1·29 (12)	11·1 ± 0·87 (28)
	Aortic constriction	6·4 ± 0·73 (8)	6·1 ± 1·21 (27)
Mature lambs	Umbilical vein constriction	1·90 ± 0·88 (10)	3·68 ± 1·13 (22)
	Haemorrhage	2·33 ± 0·66 (15)	4·50 ± 1·90 (20)

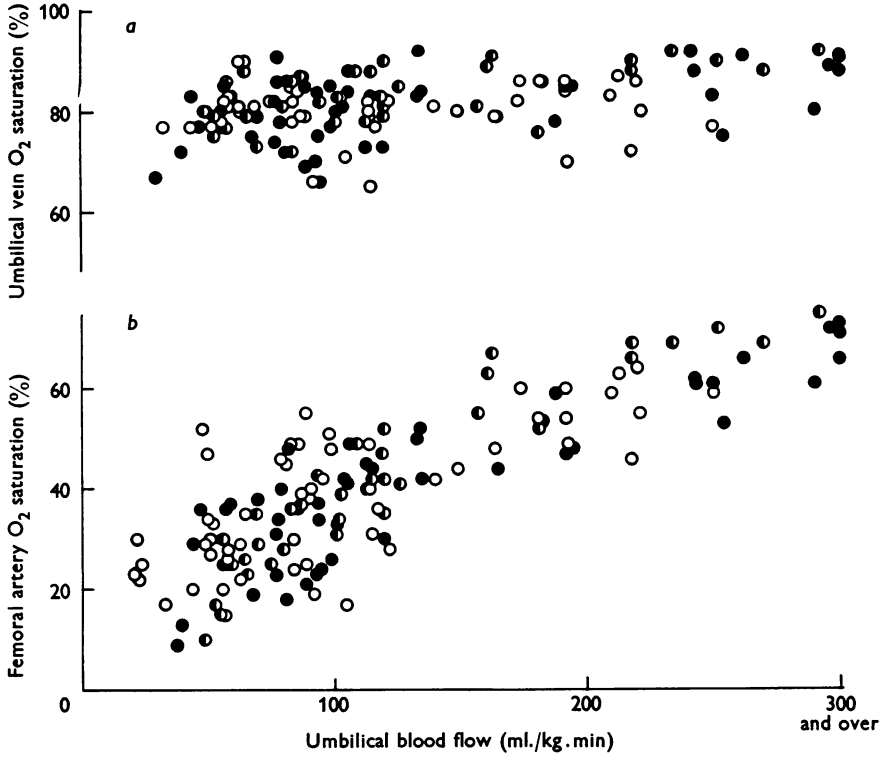

Fig. 7. (*a*) Umbilical venous and (*b*) femoral arterial O_2 saturations in immature foetal lambs during constriction of the umbilical vein (○) or aorta (◐) or during haemorrhage (●).

the carotid–femoral arterial O_2 difference was less ($P < 0{\cdot}001$) than in immature lambs. When umbilical flow was reduced by constriction of the umbilical vein or by haemorrhage there was an increase in the mean O_2 difference, but this increase was not significant. The scatter of observations about the mean increased after haemorrhage, to range from -6 to $+20\%$.

Oxygen consumption was calculated as the product of umbilical blood flow and the difference in arteriovenous O_2 content between femoral arterial and umbilical venous blood samples. In immature lambs O_2 consumption fell when umbilical flow was reduced below 120 ml./kg.min (Fig. 6). The fall in O_2 consumption was greater when flow was reduced

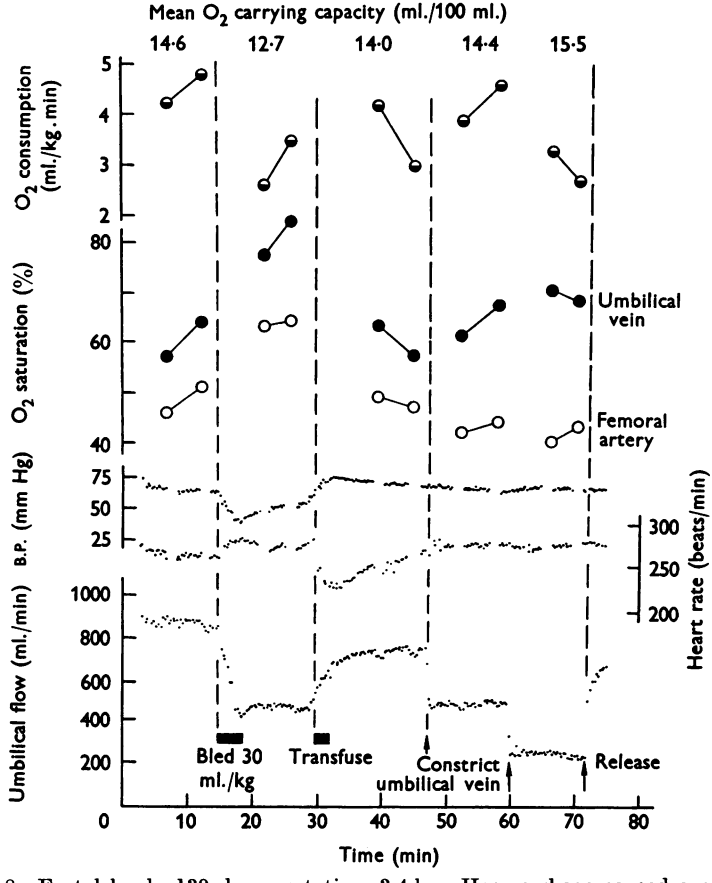

Fig. 8. Foetal lamb, 139 days gestation, 3·4 kg. Haemorrhage caused a rise in umbilical venous (●) and femoral arterial (○) O_2 saturations. Constriction of the umbilical vein to cause an equal fall in umbilical flow, or in O_2 consumption (◒), caused no rise in umbilical venous and a fall in femoral arterial O_2 saturation. Arterial pressure was measured from a femoral artery (B.P.).

by haemorrhage (●) than when it was reduced by constriction of the umbilical vein (○) or aorta (◐).

Figure 7 shows the changes in umbilical venous and femoral arterial O_2 saturations during restriction of umbilical blood flow in immature foetal

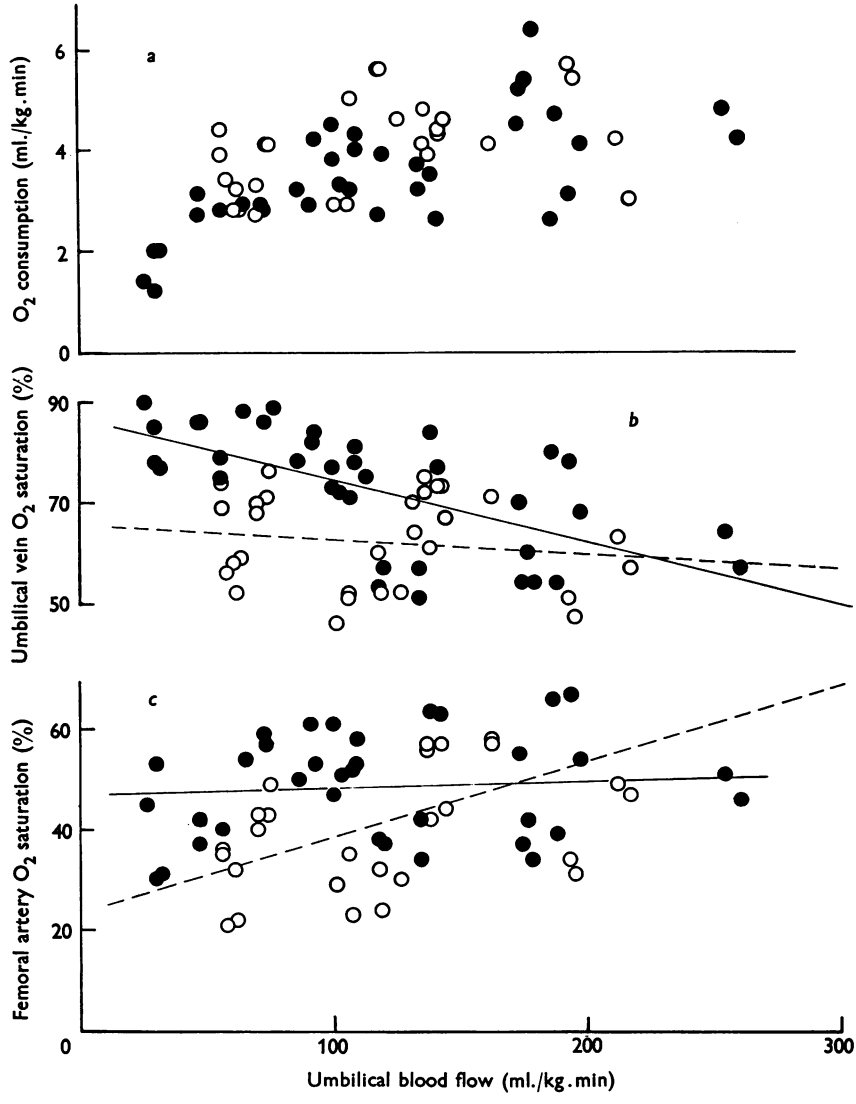

Fig. 9. (*a*) O_2 consumption, (*b*) umbilical venous and (*c*) femoral arterial O_2 saturations in eight mature foetal lambs during constriction of the umbilical vein (○) or haemorrhage (●). The regression lines are drawn for O_2 saturation on umbilical flow during constriction of the umbilical vein (-----) and haemorrhage (——).

lambs. When blood flow was reduced by haemorrhage or constriction of the aorta there was a small but significant ($P < 0{\cdot}001$) fall in umbilical venous O_2 saturation; when flow was reduced by constriction of the umbilical vein, there was no significant change in umbilical venous O_2 saturation. In all instances reduction of umbilical flow caused a fall in femoral arterial O_2 saturation but the magnitude of the fall did not vary systematically with the method used to reduce flow.

The effect of haemorrhage in mature lambs

In mature foetal lambs the O_2 saturation of umbilical venous blood was both lower and more variable than that of immature lambs (Table 1). Haemorrhage sufficient to cause a substantial decrease in umbilical blood flow always caused an increase in umbilical venous O_2 saturation (Fig. 8). The effect was greater in lambs with lower initial umbilical venous O_2 saturations. It was usually accompanied by increases in the O_2 saturation of femoral (and carotid) arterial blood, provided that flow was not reduced excessively. As Fig. 8 shows, the return of the blood which had been removed caused a fall in both umbilical venous and femoral arterial O_2 saturations to their initial values. Haemorrhage of a magnitude sufficient to produce this phenomenon caused a decrease in O_2 consumption, but umbilical venous constriction sufficient to cause the same decrease in umbilical blood flow or in O_2 consumption caused little change in umbilical venous O_2 saturation and a fall in femoral arterial O_2 saturation.

Figure 9 illustrates the results of haemorrhage and umbilical venous constriction in eight mature lambs which weighed 3·2–6·0 kg. The slopes of the regression lines for the O_2 saturation of umbilical venous and femoral arterial blood on umbilical flow per kilogram during haemorrhage (——) were significantly different from those during umbilical vein constriction (– – – –; $P < 0{\cdot}001$).

DISCUSSION

Carotid–femoral arterial O_2 differences

The results demonstrate that in immature foetal lambs reduction of umbilical blood flow by constriction of the umbilical vein or by haemorrhage results in an increase in the difference between the O_2 contents of carotid and femoral arterial blood. The maximum difference observed was 33% (expressed in terms of O_2 carrying capacity), but this was exceptional (Fig. 6). Even this is not as large a difference as that sometimes observed by Barcroft (1946) in a smaller number of lambs, in which umbilical flow was not knowingly reduced. Barcroft's lambs were delivered under spinal anaesthesia, whereas our observations were made

under pentobarbitone, chloralose or local anaesthesia; it is unlikely that the anaesthetic is responsible for the discrepancy.

In the experiments on immature and mature lambs in which umbilical flow was reduced by constriction of the umbilical vein or aorta, and in the mature lambs subjected to haemorrhage, the statistical variation of carotid–femoral O_2 difference about the mean was increased, irrespective of whether the mean difference was significantly increased (Table 4). In some groups of experiments the range of individual observations varied from -6 to $+20\%$ (expressed as a proportion of O_2 carrying capacity). These observations suggest that the lambs were then in an unstable condition so far as the distribution of O_2 was concerned, in spite of the fact that *at least* 6 min had elapsed since flow was last altered, and although umbilical flow and arterial pressure were steady. The minimum period of 6 min had been chosen because previous experience had shown that equilibrium was attained by this time after altering the O_2 content of the gas breathed by the mother (Born, Dawes & Mott, 1956). The fact that such large variations can exist under some experimental conditions may be a partial explanation of Barcroft's results. It also follows that observations which are known to be made under unstable conditions, as on delivery, should be interpreted with caution. The O_2 saturations of blood in the carotid and umbilical arteries might then be very different.

In immature lambs a reduction in umbilical blood flow by constriction of the abdominal umbilical vein caused an increase in the carotid–femoral arterial O_2 difference, whether the constriction was caused by tightening a tape round the vessel, or by a more elaborate quantitative procedure which involved heparinizing the foetus and inserting a flowmeter between the cut ends of the vessel. Although reduction in umbilical blood flow by constriction of the umbilical vein or haemorrhage caused an increase in carotid–femoral arterial O_2 difference, the change on aortic constriction was not significant (Table 4). Hence the reduction in umbilical flow is not in itself the determinant cause of the phenomenon. We must suppose that the phenomenon is due to a change in the proportions in which the various blood streams mix as they pass through the heart. The distribution of these streams of blood must depend on variations in pressure in the great veins and atria, and it may be pertinent that whereas either constriction of the umbilical vein or haemorrhage causes a fall in vena caval pressure, constriction of the aorta causes a rise. No attempt has yet been made to measure the relative changes in pressure in the great veins and atria simultaneously. Other considerations may affect the issue. First, when umbilical flow is reduced (below 120 ml./kg.min) sufficiently to cause an increase in the carotid–femoral arterial O_2 difference, the O_2 consumption of the whole foetus falls (Fig. 6). It is probable that the rate of O_2

consumption may decrease more in some tissues than in others (as in new-born lambs; Cross, Dawes & Mott, 1959), and this may alter the proportion of less well oxygenated blood returning to the heart by the superior and inferior venae cavae, the coronary sinus and the pulmonary veins. Secondly, a reduction in umbilical flow causes hypoxaemia (Fig. 7). It is likely that this will lead to a redistribution of cardiac output. For example, asphyxia causes pulmonary vasoconstriction and a reduction in pulmonary flow in both mature and immature foetal lambs (Cassin, Dawes, Mott, Ross & Strang, 1964; Cassin, Dawes & Ross, 1964), while there is usually a rise of arterial pressure and an increase in carotid flow (Dawes & Mott, unpublished).

In mature lambs neither haemorrhage nor umbilical vein constriction caused a significant increase in carotid–femoral arterial O_2 difference (Table 4). In previous experiments in mature lambs more deeply anaesthetized with chloralose, in which umbilical flow was measured by a velodyne flowmeter, umbilical vein constriction gave similar results (Dawes & Mott, 1959). The reason for this difference between immature and mature lambs is not known.

Cardiovascular changes

In immature foetal lambs reduction of umbilical blood flow, whether by constriction of the umbilical vein or of the aorta or by haemorrhage, caused hypoxaemia (Fig. 7) and tachycardia. This tachycardia was usually very striking, and was always seen unless the heart rate was already very high. Presumably it is attributable to the same mechanisms which caused tachycardia during hypoxaemia induced by giving the mother low O_2 mixtures to breathe (Born *et al.* 1956). Similar increases of heart rate during hypoxaemia caused by reduction of umbilical blood flow were seen in mature foetal lambs unless either the heart rate was high ($\sim$280 beats/min) or/and umbilical flow was low, in the present as in previous experiments (Dawes & Mott, 1959). In both immature and mature foetal lambs the heart began to slow when the hypoxaemia became very severe as described and illustrated previously (Born *et al.* 1956). Assali, Holm & Sehgal (1962) state that they never observed foetal tachycardia during hypoxaemia in lambs delivered under spinal anaesthesia, but the flow which they measured in one umbilical artery alone was only 28–55 ml./kg.min, judging from their illustrations.

Constriction of the umbilical vein in immature lambs caused a fall of arterial blood pressure (Table 2). At this age more than half the total blood volume is in the placenta (Barcroft, 1946, p. 74) and constriction of the umbilical vein caused the transfer of as much as 15 ml. blood/kg from the foetus to the placenta (Fig. 4). In mature foetuses, in which the

blood in the placenta only comprises about 15% of the total volume, constriction of the umbilical vein would be expected to cause the transfer of a much smaller proportion of the whole. The fall in arterial pressure after the withdrawal of a fixed quantity of blood per kilogram was *proportionately* the same in immature as in mature lambs, or less. So far as these observations go there was no evidence that immature lambs are less well able than the mature to control their arterial blood pressure. Haemodilution was rapid and considerable in both groups (Table 3).

O_2 *consumption*

The results confirm the conclusion already reached elsewhere by different methods, that progressive hypoxaemia causes a progressive fall in O_2 consumption in foetal lambs (Acheson *et al.* 1957; Dawes & Mott, 1959). There are two differences in the results. First, the mean rate of O_2 consumption in mature foetal lambs under chloralose anaesthesia was greater ($4{\cdot}64 \pm 0{\cdot}26$) than in the previous experiments ($4{\cdot}16 \pm 0{\cdot}18$, Dawes & Mott, 1959) in which the dose of chloralose used was larger; the difference between the means is not significant. Secondly, whereas in the previous experiments there were insufficient observations to demonstrate a significant decrease in the rate of O_2 consumption per kilogram body weight during the last half of gestation, the present experiments show that there is a significant fall ($P < 0{\cdot}02$) from $5{\cdot}40 \pm 0{\cdot}50$ ml./kg.min at 87–95 days gestation to $4{\cdot}64 \pm 0{\cdot}26$ at 137–141 days.

In immature lambs subjected to haemorrhage, O_2 consumption per kilogram body weight fell more at a given umbilical blood flow than when hypoxaemia was produced by constriction of the umbilical vein or aorta (Fig. 6). This could not be attributed to more severe arterial hypoxaemia (Fig. 7), nor to a greater fall in arterial pressure during haemorrhage (Table 2), as compared with umbilical vein constriction. It seems likely to be due to a decrease in blood flow through foetal tissues combined with haemodilution (Table 3). In mature lambs there was no systematic difference in the decrease of O_2 consumption when umbilical flow was reduced by haemorrhage or by umbilical vein constriction. But in mature lambs haemorrhage caused no significant change in femoral arterial O_2 saturation (Fig. 9), whereas in immature lambs this fell (Fig. 7).

Haemorrhage and umbilical venous O_2 *saturation*

In mature lambs the O_2 saturation of umbilical venous blood was less than that in immature lambs. In mature lambs it rose when umbilical flow was reduced by haemorrhage, and carotid and femoral arterial O_2 saturation rose correspondingly (Fig. 8). The simplest explanations of this observation are that in large mature lambs either the rate of blood flow

through the foetal villi in the placenta is too great for equilibrium to be reached, or that the absolute rate of O_2 uptake is so large that maternal mean placental pO_2 falls excessively. If either of these hypotheses is correct, we then have to explain how it is that when umbilical flow is reduced by constriction of the umbilical vein, umbilical venous O_2 saturation does not increase (Figs. 8 and 9). The only obvious difference between the two situations is that whereas during haemorrhage the foetal villi are filled with less and diluted blood, during constriction of the umbilical vein they are distended at unusually high vascular pressures; in both instances the rate of flow is reduced. The effect of distending the foetal villi may be either to reduce blood flow through the maternal side of the placenta, or to reduce the diffusion capacity of the intervening layers, or to decrease the ratio of villous surface area to vascular volume to such an extent that O_2 transfer is hindered, or to distend vascular shunts across the foetal villi (Bøe, 1954). Although the experimental situations are complicated, their comparison would suggest that distension of the foetal villi by a high umbilical venous pressure is disadvantageous.

In the mature foetus O_2 consumption falls with progressive reduction in umbilical blood flow. When flow is decreased by haemorrhage there is a large fall in systemic arterial pressure (Table 2) and hence in the pressure available to perfuse the foetal tissues, even though femoral arterial O_2 saturation is maintained (Fig. 9). When flow is decreased by umbilical venous constriction, arterial pressure is maintained but O_2 saturation is reduced.

Finally, these experiments demonstrate the wide variation in arterial O_2 saturation compatible with maintenance of normal foetal O_2 consumption, always provided that umbilical blood flow is adequate. It would be unwise to conclude that a foetus is in good physiological condition solely as a result of measurements of the O_2 content of arterial blood.

SUMMARY

1. The effect of reducing umbilical blood flow by various methods on the O_2 content of blood in the principal vessels was examined in mature and immature foetal lambs.

2. The mean carotid–femoral arterial O_2 difference was increased by constriction of the umbilical vein or haemorrhage in immature foetal lambs of 79–95 days gestation. It was not altered by constriction of the aorta sufficient to cause a similar decrease in umbilical blood flow.

3. The mean carotid–femoral arterial O_2 difference in mature foetal lambs of 137–141 days gestation was less than in immature lambs and was not significantly altered by constriction of the umbilical vein or by haemorrhage, although the range was increased.

4. The effects of these procedures upon foetal O_2 consumption and the cardiovascular system are described. Hypoxaemia and haemorrhage almost always caused tachycardia; haemorrhage caused rapid haemodilution even in immature lambs.

5. In large mature foetal lambs haemorrhage, but not constriction of the umbilical vein, caused a rise in umbilical venous O_2 saturation and, if umbilical flow was not reduced excessively, a rise in carotid and femoral arterial O_2 saturations also. The reasons for this phenomenon are discussed in relation to O_2 transfer across the placenta.

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