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Placental Oxygen Transfer in Pregnant Ewes During Hyperbaric Oxygenation

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Extract

Exposure of pregnant ewes to oxygen administration under three atmospheres of pressure produced large increases in maternal arterial blood pO_2, together with acidosis associated with an increase in pCO_2. Although maternal arterial blood pressure tended to increase and uterine arterial blood flow rate tended to fall, the changes had no statistical significance. Simultaneously, it was possible to increase umbilical venous blood pO_2 within the range 90–550 mm Hg, with corresponding changes in pCO_2 and pH as occurred in maternal blood. There was a significant decrease in umbilical venous flow rate, which failed to return to control levels after air-breathing was resumed at one atmosphere of pressure. Fetal arterial pressure was unchanged. In five animals studied, umbilical oxygen transfer was also unchanged during hyperbaric oxygenation.

Speculation

The lack of comparable increases in umbilical venous and maternal arterial blood pO_2 during oxygen administration to gravid ewes and the small reduction in umbilical oxygen transfer rates have been interpreted to be primarily the result of the nonlinearity of sheep oxyhemoglobin dissociation functions. Hyperbaric oxygenation allows umbilical oxygen transfer to occur independently of the function of maternal hemoglobin. The results of this study are consistent with, but do not prove, this hypothesis.

Introduction

Previously we have attempted to evaluate placental oxygen transfer at one atmosphere of pressure by combining direct measurements of flow rates and gas content in blood of pregnant sheep and fetal lambs [8, 12]. The results of those studies during air breathing and oxygen administration at one atmosphere have been reported [8] and an interpretation proposed [9]. It was concluded that the nonlinearity of the oxyhemoglobin dissociation curve was fundamentally important in determining results during oxygen administration [9]. The present study investigates the effects of hyperbaric oxygenation of pregnant ewes on placental gas transfer in order to determine whether the decrease in placental oxygen transfer that occurs during hyperoxia at one atmosphere of pressure was also present under hyperbaric conditions.

Materials and Methods

Experiments were carried out on 28 near-term pregnant ewes and their fetuses. Nineteen of the animals had been studied with respect to systemic and pulmonary vascular dynamics [1]. This study reports the results of experiments carried out in the other nine. Each animal was fasted for 24 hours prior to the experiment. Each acute experiment was carried out inside a hyperbaric chamber [18] and cables transmitting signals from pressure and flow transducers were passed through a seal to the flowmeters and Offner Dynograph outside.

Spinal anesthesia, using 8 mg of tetracaine hydrochloride and supplemented as necessary with 1 % lidocaine through an indwelling catheter, was induced in the ewes. Using local hexylcaine infiltration, one maternal carotid artery was cannulated for recording maternal arterial blood pressure and obtaining arterial blood samples. An endotracheal tube was inserted through a tracheostomy to assist respiration, when necessary, and to facilitate oxygen administration.

After laparotomy, the pregnant uterine horn was identified and marsupialized to the abdominal wall to prevent evisceration. The fetus was then delivered; marsupialization was carried out between the uterus and the fetal abdominal wall to protect the umbilical circulation. The fetal head was covered with a saline-filled glove to prevent air breathing. A catheter was inserted into a major umbilical vein through one of the intercotyledonary branches; another was inserted into the fetal descending aorta via the femoral artery. These were used for umbilical blood sampling and fetal arterial blood pressure recording. All but one experiment (No. 1) were carried out on single pregnancies.

Extraperitoneal groin dissection was performed in the ewe to allow exposure of the uterine vessels supplying the horn containing the marsupialized fetus. The uterine vessel adventitia were infiltrated with hexylcaine and phenoxybenzamine to prevent vascular spasm, and the artery was fitted with an electromagnetic flow transducer [2]. An accompanying tributary of a major uterine vein was catheterized for anaerobic sampling of uterine venous blood.

In some fetuses, blood samples were also obtained from the inferior vena cava, cephalad to the liver, via a catheter inserted into a femoral or external jugular vein. Positioning was established by demonstrating right atrial or ventricular pressure complexes and withdrawing the catheter until the complexes disappeared. Data from blood analysis through this catheter were discarded unless positioning was verified at autopsy. The common umbilical vein was isolated inside the fetal peritoneal cavity through a supra-umbilical midline incision and fitted with an electromagnetic flow probe. The procedure is similar in most details to that reported earlier [8, 12]. In other fetuses, thoracotomy was performed and a Rochester needle was inserted into the common pulmonary artery to allow blood sampling in that vessel.

Samples of maternal and fetal arterial and venous blood were collected anaerobically in syringes in which dead space was filled with heparin. Blood pO_2 was measured using the polarographic electrode and Instrumentation Laboratory model 125-A amplifier. Blood pCO_2 and pH was measured using the Instrumentation Laboratory Duo-matic model 123 electrode and amplifier. Temperature was maintained at $37.5 \pm 0.05°$ by means of a constant temperature water bath (Instrumentation Laboratory model 127). During compression and decompression, air temperature deviated from control values for seven to ten minutes, and water jacket temperature was sometimes altered for one to two minutes. No gas tension measurements were made until temperature stability had been regained. Oxygen and CO_2 electrodes were standardized against assayed gases (approximately 5 % CO_2, 95 % O_2 and 10 % CO_2, and 90 % N_2) inside the chamber.

Oxyhemoglobin saturation was measured by reflective photometry [8, 12]. Hemoglobin concentration was measured spectrophotometrically with standardization carried out against iron content measured by a modification of the method of WONG [16]. Except for hemoglobin concentration and saturation, gas measurements were made inside the chamber. With each change in chamber pressure, gas phase standardization was carried out and repeated if correspondence between pO_2 and saturation values was poor. Pressure stability within the chamber was maintained at ± 0.1 lb/in^2 during the hyperbaric phase. Multiple pressure gauges were employed; all agreed within ± 0.1 lb/in^2 over the range of operating pressure. The experimental protocol consisted of the following three periods:

1. A control period with the ewe breathing spontaneously or with respiration supported by compressed air administered with a Bird respirator. Measurements of blood gas content and pressure and flow rates were repeated to verify presence of a steady state. The average time elapsed was approximately 60 min, with a range of 36–100 min.

2. A hyperbaric oxygen period with the ewe breathing 100 % oxygen administered with the Bird respirator. Chamber pressure was increased to three atmospheres absolute, and blood gas instrumentation was standardized after water jacket temperature had returned to control levels. Time at elevated pressure with calibrated instrumentation averaged 50 min and ranged from 36–61 min. During this time, investigators inside

the chamber supervised data collection and oxygen administration. By adjusting the settings of the respirator and using a high pressure oxygen supply, an attempt was made to minimize the decrease in tidal volume that occurs with hyperbaric pressurization of the respirator. No measurements of tidal volume were made.

3. A recovery period during which oxygen to the ewe was replaced with compressed or ambient air and chamber pressure was reduced in accordance with modified U.S. Navy decompression tables. The period of time after return to one atmosphere absolute averaged 40 min and ranged from 21–62 min. The fetuses appeared viable at the conclusion of each experiment, but no attempt was made to determine survivability.

Throughout each experimental period, pulsatile and electronically averaged blood pressures and flow rates from mother and fetus were recorded at five-minute intervals. Blood samples were analyzed for blood gas tensions and pH to assure steady states of concentration. Prolonged pressure and flow readings were taken prior to and after blood sampling to assure that sampling was not done during a transient hemodynamic state. If possible, blood samples were withdrawn from ewe and fetus simultaneously; the sampling interval seldom exceeded one minute. In this regard, the technique was the same as that reported previously [8, 12]. The methods used for calculation of oxygen content and oxygen transfer rates have also been described [8, 12].

Results

Table I summarizes changes in maternal arterial and uterine venous blood gas tensions and pH as grouped means ± one standard error. In general, two blood analyses were done during the control period, three or four during the period of hyperbaric oxygenation, and one or two during recovery. Electronically averaged blood pressures and flow rates of uterine arterial and umbilical venous blood corresponding to each sampling are shown in tables I–V. It was possible to produce a large increase in maternal arterial pO_2 throughout the hyperbaric interval. Simultaneously, there was an increase in maternal arterial pCO_2 and a decrease in arterial blood pH. The corresponding changes in uterine venous blood were comparable, but were slightly more variable.

Table II summarizes measurements of umbilical blood gas tensions and pH, fetal arterial pressure, and umbilical venous blood flow made during the experiments as grouped means ± one standard error. There was a striking increase in umbilical venous pO_2 with a smaller, but significant, increase in pCO_2 and a decrease in pH.

The relations between maternal arterial and fetal blood pO_2 during all 28 experiments have been reported [1]. It was possible to produce high values for umbilical venous blood pO_2 by administering hyperbaric oxygen, and there was considerable scatter in umbilical blood values. In fig. 1, the relation between uterine and umbilical venous blood pO_2 is depicted. Whenever uterine venous blood pO_2 was less than 100 mg Hg and

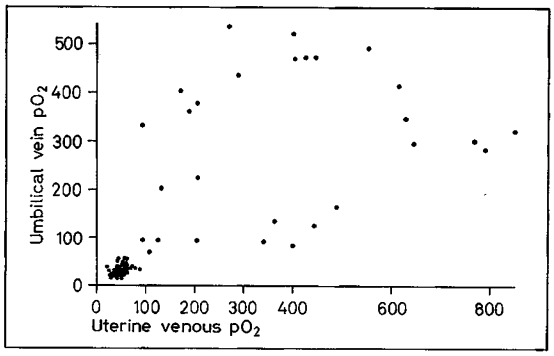

Fig. 1. Umbilical vein pO_2 as a function of uterine vein pO_2.

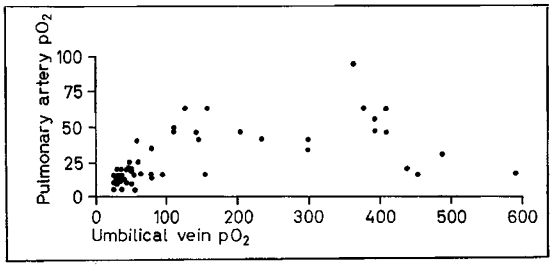

Fig. 2. Pulmonary artery pO_2 as a function of umbilical vein pO_2.

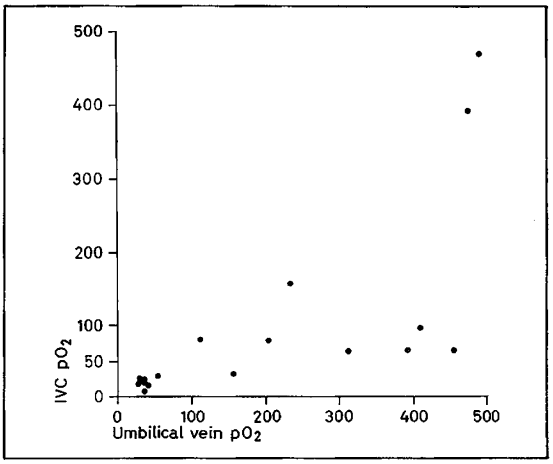

Fig. 3. Inferior vena caval blood pO_2 as a function of umbilical vein pO_2.

Table I. Effects of hyperbaric oxygenation on maternal blood gas tensions, pH, arterial pressure, and uterine blood flow rate[1, 2]

Parameter	N[3]	Control	N[3]	Hyperbaric oxygen	N[3]	Recovery
Arterial blood						
pO_2, mm Hg	18	75±4	27	1160±60***	9	75±4***
pCO_2, mm Hg	18	25±1	25	32±2**	8	22±3***
pH	19	7.52±0.01	28	7.39±0.02***	9	7.56±0.02***
Uterine venous blood						
pO_2, mm Hg	11	44±4	15	335±60***	6	51±6***
pCO_2, mm Hg	11	29±2	12	41±5*	5	27±1*
pH	11	7.47±0.02	15	7.29±0.02***	6	7.46±0.02***
Arterial blood pressure, mm Hg	19	108±3	26	113±3	8	106±3
Uterine artery blood flow rate, ml/kg/min	13	204±26	18	177±17	7	248±37

[1] Values given are mean and S.D. of mean.
[2] Statistical significance of mean differences from the immediately preceding experimental period is denoted as follows: * $p<0.05$; ** $p<0.01$; *** $p<0.001$.
[3] Number of experiments.

Table II. Effects of hyperbaric oxygen on umbilical blood gas tensions, pH, arterial pressure and umbilical blood flow rate[1, 2]

Parameter	N[3]	Control	N[3]	Hyperbaric oxygen	N[3]	Recovery
Umbilical vein						
pO_2, mm Hg	19	28±3	27	302±28***	9	30±3***
pCO_2, mm Hg	16	30±2	22	37±3*	7	25±2*
pH	18	7.37±0.01	27	7.26±0.02***	9	7.42±0.02***
Umbilical artery						
pO_2	19	16±2	27	57±11***	9	17±2**
pCO_2	16	33±2	24	44±3**	7	28±2***
pH	19	7.35±0.01	27	7.23±0.01***	8	7.37±0.02***
Fetal arterial pressure, mm Hg	18	62±3	28	62±3	9	58±5
$\dot{Q}$ Umbilical vein, mm/kg/min	17	171±9	24	143±9*	9	140±7

[1] Values given are mean and S.D. of mean.
[2] Statistical significance of mean differences from the immediately preceding experimental period is denoted as follows:
follows: * $p<0.05$; ** $p<0.01$; *** $p<0.001$.
[3] Number of experiments.

hemoglobin saturation was less than 100 %, umbilical venous blood pO_2 was less than 60 mm Hg. Whenever uterine venous blood pO_2 exceeded 100 mm Hg and saturation was 100 %, umbilical venous blood pO_2 values were greater than 60 mm Hg and as high as 500 mm Hg.

In figs. 2 and 3, increases in oxygen tension in other parts of the fetal vasculature are shown in relation to umbilical venous pO_2. The relation between umbilical venous and arterial pO_2 for this series of experiments has been reported [1]. Increases were far less striking in umbilical and pulmonary arteries than in umbilical vein. Samples obtained from the inferior vena cava cephalad to the orifices of the hepatic veins showed the same trend, except for two aberrant samples (fig. 3). Perhaps these two are examples of lack of mixing of umbilical venous blood with iliac, hypogastric, hepatic portal, and renal venous blood.

In five experiments, it was possible to make satisfactory simultaneous measurements of flow rates of uterine arterial and umbilical venous blood and oxygen content of uterine and umbilical arterial and venous blood (tables III, IV, and V).

Uteroplacental Changes

Hyperbaric oxygenation produced irregular changes in the maternal parameters measured, and few significant changes were noted. Oxygen content of both uterine arterial and venous blood increased significantly. Although the mean arteriovenous content difference increased 25 %, the change was not statistically significant. In four of five experiments, flow rate of uterine arterial blood decreased during hyperbaric oxygenation. In all three of those four experiments in which recovery measurements were made, these rates tended to increase during recovery. Changes in individual values of the product of uterine arterial blood flow and the arteriovenous content difference, that is, partial uteroplacental oxygen transfer rates, were quite variable, but mean values for all five experiments showed little change.

Umbilical Changes

Hyperbaric oxygenation increased umbilical arterial and venous oxygen content and the arteriovenous oxygen content difference. Umbilical venous flow rate decreased significantly. The product of these latter two quantities, the umbilical oxygen transfer rate, did not change significantly. With return to air breathing at one atmosphere, there was no significant change in umbilical venous blood flow, but the arteriovenous oxygen content difference returned to control levels. The result was a significant decrease in net oxygen transfer through the umbilical circuit.

Concentrations of maternal and fetal blood hemoglobin and fetal weights are listed in table VI.

Table III. Maternal values—uterine artery flow, arterial and uterine venous oxygen contents[1]

Exp. No.	Control				Hyperbaric oxygenation				Recovery			
	$\dot{Q}_M$	A_M	V_M	$\dot{V}$	$\dot{Q}_M$	A_M	V_M	$\dot{V}$	$\dot{Q}_M$	A_M	V_M	$\dot{V}$
2	605	13.30	11.35	11.80	616	18.23	16.78	8.93				
	562	13.36	11.58	10.00	473	19.31	16.70	12.34				
					462	18.93	16.91	9.33				
3	878	10.31	8.46	16.24	693	14.84	10.62	29.24	1010	10.84	10.32	5.25
	878	10.63	9.26	12.03	740	15.52	12.30	23.83	972	10.62	9.71	8.85
					786	14.52	12.36	16.98				
4	1138	14.07	13.00	12.18	890	17.78	17.19	5.25	857	14.37	13.27	4.43
	998	14.08	13.00	10.78	847	17.95	17.78	1.44	872	13.76	12.70	4.24
					783	18.86	18.00	6.73				
5	453	10.63	8.29	10.60	368	13.40	10.99	8.87	812	10.67	8.73	15.75
	506	10.76	8.52	11.36	317	14.25	12.23	6.40				
20	180	12.91	10.01	5.22	198	17.51	13.72	7.70	165	12.74	9.01	6.15
	189	12.91	10.21	5.10	180	17.39	13.72	6.61				
					180	18.25	13.60	8.37				

[1] Uterine artery flow rate ($\dot{Q}_M$) is expressed as milliliters per minute, arterial (A_M) and venous (V_M) oxygen contents as milliliters O_2 at one atmosphere, 37.5 °C per 100 ml whole blood. Partial uteroplacental O_2 transfer ($\dot{V}$) is the product $\dot{Q}_M$ (A_M–V_M) and has units ml O_2/min.

Table IV. Fetal values—umbilical vein flow, umbilical arterial and venous oxygen contents

Exp. No.	$\dot{Q}_F$	V_F	A_F	$\dot{V}$	$\dot{Q}_F$	V_F	A_F	$\dot{V}$	$\dot{Q}_F$	V_F	A_F	$\dot{V}$
2	188	11.94	10.06	3.53	82	14.53	9.80	3.88				
	151	11.64	9.35	3.46	72	13.61	9.27	3.12				
					68	13.01	7.87	3.50				
3	183	11.23	9.06	3.97	122	14.38	10.59	4.62	134	11.88	9.07	3.71
	190	11.62	9.46	4.10	124	15.06	11.29	4.67	139	11.68	9.00	3.73
					131	14.72	11.09	4.76				
4	141	11.75	7.86	5.48	131	17.40	14.34	4.01	135	13.61	10.85	3.73
	148	11.07	7.86	4.75	149	16.95	13.85	4.62	116	13.05	10.44	3.03
					145	17.08	14.15	4.25				
5	187	10.29	8.17	3.96	164	13.49	11.35	3.51	118	8.98	5.67	3.91
	187	10.82	8.74	3.89	161	13.49	9.98	5.65				
20	145	7.06	2.83	6.13	171	15.34	11.38	6.77	177	10.19	7.63	4.53
	171	10.87	7.34	6.04	163	14.82	11.68	5.12				
					163	15.43	10.86	7.45				

Umbilical vein flow rate ($\dot{Q}_F$) is expressed as milliliters per minute per kilo fetal weight, umbilical vein (V_F) and artery (A_F) oxygen content as milliliters O_2 at one atmosphere, 37.5° per 100 ml whole blood. Umbilical oxygen transfer rates ($\dot{V}$) are the products of $\dot{Q}_F$ (V_F–A_F) and have units ml O_2/min/kg.

Table V. Placental oxygen transfer. Mean values from tables III and IV

	Control	Hyperbaric oxygenation	Recovery
Utero-placental			
Uterine artery flow	639±98	538±67	781±116
Uterine flow per kg	217±33	179±22	266±39
Arteriovenous O_2 content difference	1.9±0.2	2.4±0.4	1.5±0.4
Fractional uteroplacental O_2 transfer	3.6±3	3.7±0.5	3.3±0.7
Arterial O_2 content	12.3±0.5	16.9±0.5***	12.3±0.6***
Venous O_2 content	10.4±0.5	14.5±0.7***	10.6±0.7**
Umbilical			
Umbilical vein flow per kg	169±6	132±9**	137±8
Umbilical O_2 transfer	4.5±0.3	4.7±0.3	3.8±0.2*
Arteriovenous O_2 content difference	2.8±0.3	3.7±0.2**	2.8±0.1**
Venous O_2 content	10.8±0.4	15.0±0.4***	11.6±0.6***
Arterial O_2 content	8.1±0.6	11.3±0.5***	8.8±0.7**
Number of observations	10	14	6

Units are the same as in tables III and IV, O_2 transfer rates are expressed as ml O_2 at one atmosphere per kg fetal weight per minute. Statistical significance of mean differences from the immediately preceding experimental period is denoted as follows:

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

Table VI

Experiment No.	Fetal weight (kg)	Hemoglobin concentration(g/100 ml)	
		Maternal	Fetal
1	–	9.0	10.0
2	3.2	10.5	9.5
3	3.4	7.7	8.9
4	2.8	10.2	10.8
5	2.3	7.8	8.9
6	2.1	7.8	7.1
18	3.4	9.6	8.3
19	4.7	9.0	7.7
20	2.9	8.8	9.5

Discussion

Control observations of blood gas and gas transfer measurements in this series of experiments agree generally with those obtained using the same techniques during a study of oxygen transfer at one atmosphere [8]. In the present study, however, maternal arterial pressures were somewhat higher than those obtained previously. In addition, there was a higher mean value for uterine arterial flow per kg of fetal weight and a lower mean value for utero-placental arteriovenous oxygen content difference. The good correlation between maternal arterial pressure and uterine arterial flow has been noted previously [12]. There was no difference between fractional uterine placental oxygen consumption per kg of fetal weight reported in this study and that reported in the earlier study. In the present study, values for gas content were higher in maternal and lower in fetal blood, compared with values previously reported. Since there was no significant difference in pO_2 values, these differences reflect differences in hemoglobin concentrations in the two series (table VI). Fetal measurements otherwise agreed well.

As before, there was a significant alveolar gas-arterial blood pO_2 gradient in the ewe, both at one and three atmospheres. This would appear to stem from a combination of hypoventilation, uneven ventilation, and impaired diffusion resulting from immobilization of the ewe in the lateral recumbent position.

It has been demonstrated that umbilical venous pO_2 is below 60 mm Hg, despite oxygen breathing at one atmosphere [8]. This finding led us to believe that the nonlinearity of the hemoglobin-oxygen dissociation curve was the responsible mechanism [9] and that the blood-shunting, variable diffusibility and the O_2 consumption of the placenta were less important factors. The data in fig. 1 offer some support to this hypothesis. When uterine venous blood is fully saturated, the utero-placental oxygen requirement is met by the physically dissolved portion of blood oxygen content. With respect to oxygen transport, hemoglobin is not directly participating; that is, hemoglobin-bound oxygen passes through the utero-placental circuit without dissociation. Data shown in fig. 2 may be summarized as follows: Whenever uterine vein pO_2 is less than 100 mg Hg, umbilical venous pO_2 is less than 60 mm Hg, assuming a normal umbilical venous flow rate. Whenever uterine venous blood is fully saturated, umbilical venous pO_2 is greater than 60 mm Hg.

These findings support the proposition that persistently low umbilical blood pO_2 is a function of the contribution of maternal hemoglobin to net placental transfer. Abolition of the functional role of maternal hemoglobin by hyperbaric oxygenation is associated with abolition of persistently low umbilical vein pO_2.

Possibly, fully oxygenated maternal hemoglobin still participates in oxygen transport by means of its continuing role in CO_2 transport, even though no reduction of oxyhemoglobin occurs. This seems unlikely in view of two overriding relations:

1. Maternal arterial pCO_2 increases during exposure to high alveolar gas pO_2. This finding has been noted in dogs exposed to hyperbaric oxygen [3, 4, 6, 13]. In studies of human responses to oxygen at 3.5 atmospheres, LAMBERTSEN *et al.* [10] found a decrease in arterial pCO_2, the result of an increase in the tidal volume of respiration [11]. The relative importance of changes in respiratory center stimulation and sensitivity, pulmonary diffusion capacity, pulmonary capillary hematocrit, lung volume, and vascular shunting in determining this change in humans remains to be investigated. At present, no interpretation can be made of the differences in these changes in man, dogs, or sheep. In the present study, the increased maternal pCO_2 may have been the result of hypoventilation induced by the effects of hyperbaric pressure on the tidal volume of gas delivered by the respirator.

2. Failure of reduction of hemoglobin in transit through an organ interferes with the transfer, from tissue to blood, of CO_2 by abolishing the Bohr-Haldane effect [10]. This mechanism might be expected to influence CO_2 transfer from fetal blood to fully oxygenated maternal blood in the areas of contact in the placenta. Whether the increase in fetal blood pCO_2 arises from altered placental transfer of CO_2 or simply passively reflects changes in maternal blood is uncertain. In view of the findings of MOYA *et al.* [14] the former seems somewhat more likely.

At first encounter, the small increases in umbilical arterial [1] and in pulmonary arterial and inferior vena cava pO_2 demonstrated during hyperbaric oxygenation might be attributable to increases in oxygen

consumption in some fetal regional circulations. This does not appear to be the case; rather, the findings appear to stem from the increase in size of the oxygen transfer rate, relative to fetal hemoglobin concentration, and the fetal oxyhemoglobin dissociation curve. The averaged data of table V may be used to illustrate this point.

In the transition from control to hyperbaric oxygen, umbilical arterial content increased from an average of 8.1 to 11.3 vol. % with an insignificant increase in net oxygen transfer. Assuming an average fetal hemoglobin concentration of 10 g/100 ml, blood oxygen capacity would be 13.4 vol. %. We may ignore dissolved oxygen for purposes of this calculation, except to note that umbilical vein O_2 content during hyperbaric oxygenation reflected its presence at a mean pO_2 of about 300 mm Hg. It now appears that umbilical artery saturation must increase approximately from 60 to 85 % in the transition from maternal air to hyperbaric O_2 breathing. Using published sheep oxyhemoglobin dissociation curves [7], this corresponds to an umbilical artery pO_2 increase from 15 to 40 mm Hg at average fetal blood pH. The mean values for control and hyperoxic umbilical arterial pO_2 are 14.2 and 42.3, respectively (table V).

A similar calculation can be used to show that the relation between umbilical venous and inferior vena cava pO_2 (fig. 3) was the result of admixture with blood returning from iliac, hypogastric, renal, and hepatic portal veins. It was unnecessary to assume exceptionally high rates of hepatic oxygen consumption to explain the low pO_2 in inferior vena caval blood noted in most of our samples obtained during hyperbaric oxygenation.

Using the following symbols and subscripts
C: blood oxygen content (ml STP O_2/ml blood)
$\dot{Q}$: blood flow rate (ml/kg fetal weight/min)
$\varnothing$: rate of hepatic oxygen consumption (ml STP O_2/kg fetal weight/min)
a: umbilical vein
b: iliac, hypogastric, hepatic portal and renal veins
c: inferior vena cava
it is possible to write equation 1:

$$(1)\quad \dot{Q}_a C_a + \dot{Q}_b C_b - \varnothing = \dot{Q}_c C_c = (\dot{Q}_a + \dot{Q}_b) C_c$$

and by rearranging, to write equation 2, which defines the rate of blood flow from pelvis, hindlimbs, mesentery and kidneys in terms of the other variables:

$$(2)\quad \dot{Q}_b = \frac{\dot{Q}_a (C_a - C_c) - \varnothing}{(C_c - C_b)}$$

Let us estimate $\dot{Q}_b$ sufficient to decrease the average umbilical venous pO_2 from 300 mm Hg (table II) to 100 mm Hg, an approximate value noted in the inferior vena cava (fig. 3). From table V, $\dot{Q}_a$ equals 132 and C_a equals 0.15. Using the oxygen solubility coefficient for blood calculated by SENDROY *et al.* [15] $(C_a - C_c) = 0.0068$, and, therefore, $C_c = 0.1432$. Assuming CARLYLE's [5] value for fetal lambs at a gestational age of 130 days, $\varnothing = 0.63$. Substituting into equation 2 gives equation 3:

$$(3)\quad \dot{Q}_b = \frac{0.2676}{0.1432 - C_b}$$

The value of C_b is unknown, but it must be less than the oxygen content of umbilical artery blood which, from table V, is 0.113. This enables calculation of a maximum value for $\dot{Q}_b$ of 8.8 ml/kg/min. Since C_b is actually smaller than 0.113, the blood flow returning from iliac, hypogastric, renal, and hepatic portal veins necessary to reduce umbilical vein pO_2 from 300 to 100 mm Hg by admixture is less than 8.8 ml/kg/min.

As in previous work [12], technical difficulties limited measurement of uterine arterial blood flow through a single uterine artery. The relation between measured and total uterine flow varied with the sizes and numbers of fetuses in other horns, with fetal well being, and with the effects of the surgical preparation. Statements with respect to changes in uterine blood flow and utero-placental oxygen transfer are valid only if it is assumed that the fraction of total uterine blood flow measured remains constant throughout the experiment. This assumption is strengthened by the agreement in values of fractional utero-placental oxygen transfer calculated in the control periods of this and the earlier study [8], even though in the present study there was a greater increase in uterine arterial flow per kg of fetal weight, both in unselected observations (table I) and in oxygen transfer studies (table V).

Maternal values during hyperbaric oxygenation were similar to values obtained at one atmosphere of oxygen. Oxygen content increased strikingly, but changes in uterine artery flow and the arteriovenous oxygen content difference were so correlated that no change in net utero-placental oxygen uptake occurred. Changes noted in fractional uterine artery flow and uterine arteriovenous oxygen content differences were not statistically significant.

Umbilical blood flow was reduced significantly by hyperbaric oxygenation of the ewe; the same finding was noted at one atmosphere in an earlier study [8]. Oxygen content in both umbilical arterial and venous blood increased during hyperbaric oxygenation, but the increase in oxygen content in arterial blood permitted net umbilical oxygen transfer to remain unchanged.

The reduction in net umbilical transfer seen with maternal oxygenation at one atmosphere [8] was not seen under hyperbaric conditions. Our interpretation of the earlier data suggested that the reduced transfer

rate was dependent on the nonlinear dissociation properties of hemoglobin [9]. Since hyperbaric oxygenation of the ewe abrogates that functional property of maternal hemoglobin, we believe that the finding of unaltered hyperbaric umbilical oxygen transport tends to support our earlier interpretation.

Net umbilical oxygen transfer decreased after the transition from hyperbaric oxygen to air breathing in the ewe. The reasons for this change are obscure. The grouped data of tables II and III show only that values for umbilical blood pCO_2 are lower, and those of pH are higher than normal. It seems likely that some change in tissue metabolism might be the responsible factor since the major determinants of placental diffusion were altered little. Although the decrease could be attributable to deterioration of the preparation with time, this seems unlikely, since most of the fetuses were viable at the conclusion of the experiment. Within the time span of the experiment, umbilical venous blood flow did not return to control levels.

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