

**THE TRANSPORT OF OXYGEN IN THE SHEEP'S PLACENTA:
THE DIFFUSION CONSTANT OF THE PLACENTA***

The problem of how oxygen is transferred from lung alveoli to blood was considered in 1909 by Christian Bohr,³ who used the calculus to develop the appropriate equation for the diffusion of oxygen from alveoli into blood and presented a graphical solution. In this way, the integrated mean oxygen pressure gradient causing oxygen transfer across the alveolar membrane[†] was obtainable and, in addition, the diffusion constant of the lungs. While the theoretical basis was then at hand, refinements in experimental techniques were needed to yield further knowledge of the transfer of oxygen in the lungs. Lilienthal, Riley, *et al.*⁶ have contributed substantially to the understanding of this process and their paper refers to other notable contributions since Bohr's.

The pulmonary methods of Bohr do not seem to have been applied to the more complex transport of oxygen from maternal to fetal blood, although the data for such an application, in the case of the sheep, are now at hand.^{1,2‡} We shall develop the theory of diffusion across the placental membrane separating maternal and fetal blood in the sheep and then apply it to a sample set of the data available.

ANALYSIS OF DIFFUSION OF OXYGEN IN SHEEP'S PLACENTA

Inherent in the development of a theory is the choice of simplifying abstractions to condense the actual complex situation into an analogous one more easily handled. Our basic assumption for the purpose of studying gas transport in the placenta of sheep is that the complex network of two sets of contiguous vessels can be adequately represented by two single vessels, each of uniform (though not the same) bore, equal in length, and separated by intervening tissue such that the rate of gas diffusion from any point of one vessel to the other is proportional to the pressure gradient of the gas

* An abstract of this paper has been published elsewhere.⁵

† The integrated mean oxygen pressure gradient across the alveolar membrane is that oxygen pressure difference which, if maintained along the entire length of alveolar capillaries, would cause the same rate of oxygen transfer as actually diffuses under biological conditions.

‡ Barron and Alexander analyzed their data by an inexact graphical method.

Received for publication May 12, 1954.

$$(1) = a\Delta x/100; (2) = \Delta x/L; (3) = P_x - p_x; (4) = \Delta x/v.$$

Since $i = av$,

$$\Delta q = (P_x - p_x) \frac{100k}{iL} \Delta x,$$

and, when $\Delta x \rightarrow 0$, $\frac{dq}{dx} = \frac{100k}{iL} (P_x - p_x)$.

Correspondingly, for the maternal circulation, which is opposite in direction to that of the fetal circulation,

$$\frac{dQ}{dx} = \frac{100k}{iL} (P_x - p_x)$$

When these two equations are combined to eliminate dx and then integrated to obtain the relationship of q_x to Q_x , one obtains:

$$Q_x - Q_0 = (q_x - q_0) \frac{Q_L - Q_0}{q_L - q_0},$$

or

$$Q_x = Q_0 + (q_x - q_0) i/L.$$

Returning to the expression for $\frac{dq}{dx}$ and integrating,

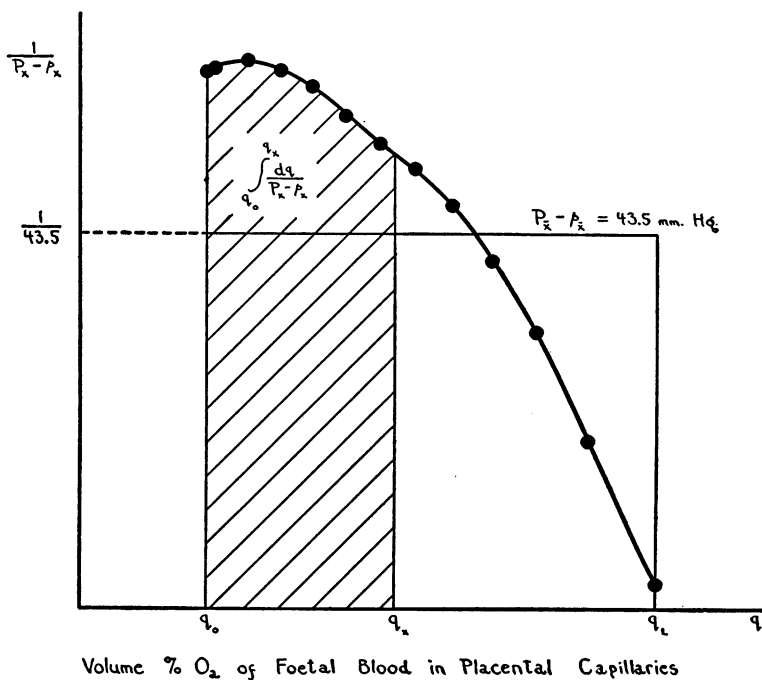
$$\frac{x}{L} = \frac{i}{100k} \int_{q_0}^{q_x} \frac{dq}{P_x - p_x}.$$

If the integral is evaluated, we can show how the oxygen tension varies in both the maternal and fetal capillaries from the arterial to the venous ends. To evaluate the integral, we need the actual maternal and fetal blood dissociation curves for oxygen, as determined in the laboratory, and the relationship between q_x and Q_x already derived. Of course, the oxygen content of arterial and venous maternal and fetal blood are also required. To illustrate the procedure, we utilize the data reported in 1952 by Barron and Alexander⁴ for sheep #5, recomputing per cent oxygen saturation values from smoothed dissociation curves.

For each arbitrary value of q_x between fetal artery and vein, we compute the corresponding values of p_x (from the fetal blood dissociation curve), Q_x (from the formula for it just derived above), P_x (from Q_x and the maternal blood dissociation curve), and so $1/(P_x - p_x)$. Since the integral to be evaluated represents the area under the curve formed from $1/(P_x - p_x)$ as a function of q_x , we measure this area for successive values of q_x in Figure 2, which shows the needed relationship for sheep #5. The data and computations derived from them are summarized in Table 1.

OXYGEN TENSION IN MATERNAL AND FETAL SHEEP CAPILLARIES

Since x/L , relative distance along the placental capillaries from the fetal arterial to venous end, is proportional to the integral which has just been evaluated from Figure 2 in Table 1, we show in Figure 3 the functional relationship between P_x and p_x , the oxygen tension in maternal and fetal blood, and our measure of capillary distance (x/L), the integral. Here we see how rapidly oxygen pressure falls in maternal capillaries as the



Maternal Venous	$Q_0 = 9.00$	volume % O_2
" Arterial	$Q_L = 19.12$	" " "
Foetal Arterial	$q_0 = 1.84$	" " "
" Venous	$q_L = 8.45$	" " "
$P_{\bar{x}} - p_{\bar{x}} = 43.5$ mm. Hg O_2 pressure		

FIG. 2. The area under the curve expressing the relationship of $1/(P_x - p_x)$ to q_x gives the value of the required integral, which is proportional to distance along fetal capillaries. The value of $1/(P_x - p_x)$ which gives a rectangle based on q_0 to q_L having the same area as that under the curve on the same base is shown. It gives the integrated mean O_2 diffusion pressure for the placenta of the sheep under consideration as 43.5 mm. Hg.

blood first enters from maternal arteries to meet the emerging fetal blood. Later, we shall determine quantitatively the advantage of having maternal and fetal blood flow in opposite rather than the same direction through their contiguous vessels.

TABLE 1. DATA AND CALCULATIONS ON BLOOD SHEEP #5, FETUS
120 DAYS OF BARRON AND ALEXANDER²

$\frac{x}{L}$ Relative distance along capillaries from fetal arterial end in % of total capillary length	q_x Fetal O ₂ content vols. %	Actual, opposite direction of flow		Hypothetical, same direction of flow	
		p_x Fetal O ₂ tension mm. Hg	P_x Maternal O ₂ tension mm. Hg	p_x Fetal O ₂ tension mm. Hg	P_x Maternal O ₂ tension mm. Hg
0.0	1.84	8.0	44.0	8.0	100.0
2.6	1.98	8.8	44.7		
11.2	2.44	11.0	46.6	11.0	87.0
20.2	2.92	12.6	48.6		
28.8	3.39	14.0	50.6	14.0	72.5
37.6	3.88	15.0	52.8		
46.3	4.38	16.0	55.0	16.0	63.2
55.2	4.90	17.0	57.2		
64.1	5.45	18.0	60.0	18.0	57.0
73.2	6.03	19.0	64.1		
82.4	6.68	20.0	69.8	20.0	51.6
91.8	7.44	20.9	80.0		
100.0	8.45	22.0	100.0	22.0	44.0

DIFFUSION CONSTANT OF THE PLACENTA OF THE SHEEP

If we solve our previous equation for k, the diffusion constant in cc. O₂ diffusing across the placenta per minute per mm. Hg O₂ pressure difference, letting x = L, we have :

$$k = \frac{i}{100} \int_{q_0}^{q_L} \frac{dq}{P_x - p_x} .$$

To evaluate this expression, one can substitute the area for the integral when q_x is q_L in Table 1, taking care to use correct rather than arbitrary units.

For i we have, by the Fick principle :

$$i = \frac{100m}{q_L - q_0} .$$

Since there is interest in determining that particular point along the placental circulation at which the O_2 diffusion pressure gradient, if constant throughout, would permit the same rate of oxygen transport as actually occurs, we shall determine k by finding this particular value of x , \bar{x} . The corresponding value of the diffusion pressure $(P_{\bar{x}} - p_{\bar{x}})$ is called the integrated mean diffusion pressure gradient.

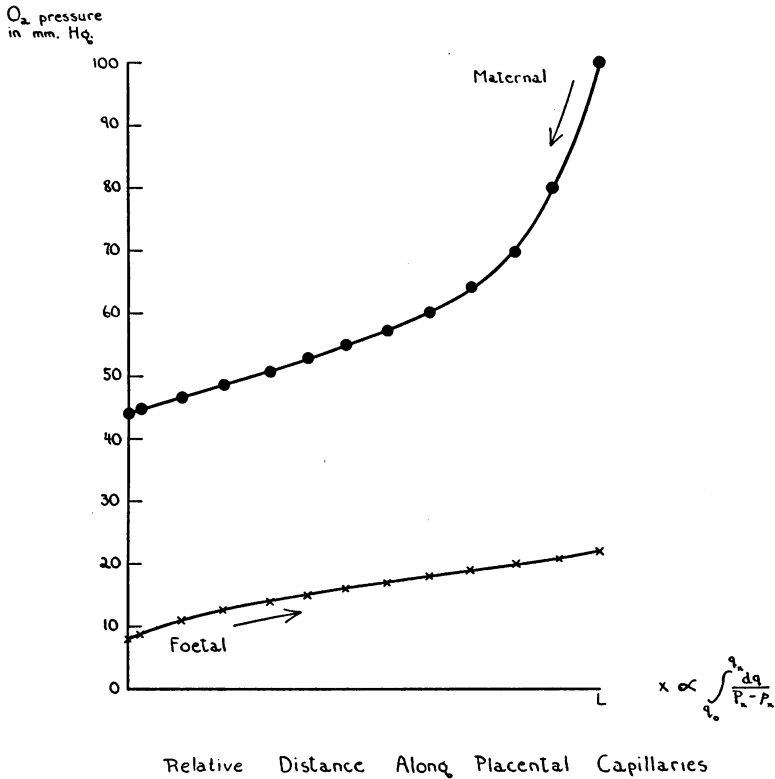


FIG. 3. The changes in O_2 tension in maternal and fetal blood in the sheep's placenta as a function of relative distance along the fetal capillaries are shown. Relative capillary distance is taken as proportional to the area under the curve shown in Figure 2, while the corresponding values of O_2 tension (both P_x and p_x) from which this curve was drawn are shown as ordinates.

In Figure 2, we find that single value of $1/(P_x - p_x)$ which will give a rectangle based on q_0 to q_L having the same area as that under the curve for the same base. \bar{x} is found to be $0.67L$. This is to say that two-thirds of the way towards the oxygenated end of the fetal stream the diffusion gradi-

ent equals the integrated mean value. At this point, the fetal blood has acquired about 60% of the oxygen it will finally receive in its passage through the placenta. The value of $P_x - p_x$, the integrated mean diffusion gradient, is 43.5 mm. Hg O_2 pressure difference. It is used to determine k :

$$k = \frac{m}{43.5}$$

Using Barcroft's figures, as quoted by Barron and Alexander³ for the oxygen consumption of a sheep fetus at 110 days, or 4.2 cc. O_2 per min. per kilo,* and allowing for a fetal weight of 1300 grams, we estimate m at 5.5 cc. O_2 /min.

In this way, we obtain for the diffusion constant of sheep #5:

$$k = 0.126 \text{ cc./min./mm.Hg } O_2 \text{ pressure difference.}$$

This is essentially the same as the value reported by Barron and Alexander.³

**DIFFUSION COEFFICIENT REQUIRED TO TRANSPORT OXYGEN IN SHEEP IF
MATERNAL AND FETAL BLOOD FLOWED IN SAME
INSTEAD OF OPPOSITE DIRECTION**

Here we assume the same concentrations of oxygen in artery and vein of fetal and maternal supply, only considering the effect of a reversal of flow direction of maternal blood so that in both sets of vessels blood flows in the same direction. The expression for $\frac{dq}{dx}$ is unchanged, but now the sign changes for $\frac{dQ}{dx}$:

$$\frac{dQ}{dx} = - \frac{100k}{iL} (P_x - p_x).$$

The result is:

$$Q_x = Q_0 - (q_x - q_0)i/L.$$

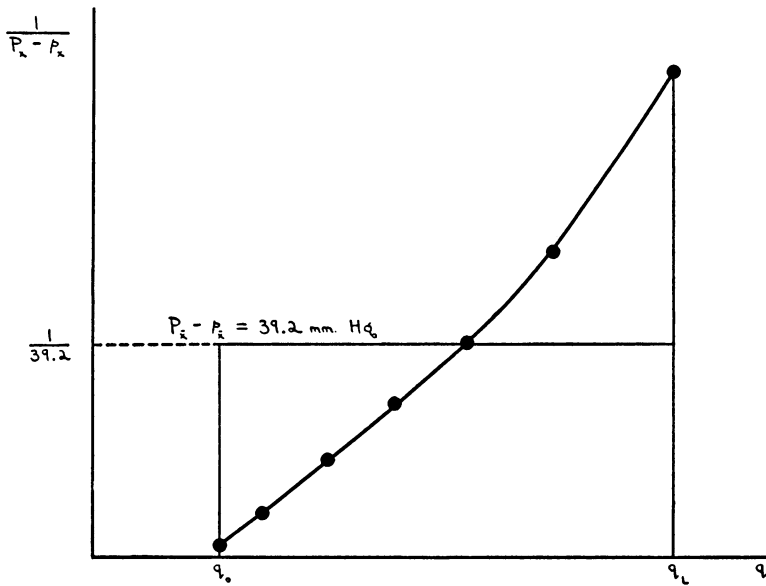
Our evaluation of $\frac{x}{L}$ remains:

$$\frac{x}{L} = \frac{i}{100k} \int_{q_0}^{q_x} \frac{dq}{P_x - p_x} \cdot$$

But the evaluation of the integral is changed by the new expression for Q_x . Otherwise the procedure is the same. Table 1 gives the pertinent data

* Sheep #5 is 120 days old, but at 136 days the fetal consumption is 4.3 cc., so that the 4.2 cc. figure still applies here.

and Figure 4 shows the graph of $1/(P_x - p_x)$ against q_x to evaluate the integral. The result is that $P_{\bar{x}} - p_{\bar{x}}$, the integrated mean diffusion gradient, becomes 39.2 mm. Hg, the steady pressure available (other conditions unchanged except diffusion constant and flow direction) to move the required oxygen supply. Such a gradient, to be effective, requires a diffusion constant of 0.139, 11% higher than the one actually prevailing with opposing direction of flow. Clearly the opposing direction of flow of maternal and fetal blood is the more efficient possibility.



Volume % O₂ of Foetal Blood in Placental Capillaries
 is Foetal and Maternal Blood Flowed in Same
 Direction in Adjacent Capillaries

K required is 0.139 cc./min./mm Hg O₂ difference
 This is 11% more than 0.125 actually found

FIG. 4. This curve is derived exactly like that of Figure 2, except that the assumption is made that the maternal blood flow direction is reversed, so that both fetal and maternal blood flow in contiguous vessels in the same direction. The initial and final values for oxygen tension in maternal and fetal blood are assumed not to have changed. The result is that the integrated mean oxygen diffusion pressure available for transport of oxygen to the fetus falls to 39.2 mm. Hg; a diffusion constant 11% higher than the actual one would be needed if the two circulations flowed in the same direction.

It is interesting that blood and water also flow in opposite directions in the gills of fish. Hazelhoff and Evenhuis⁴ found that oxygen utilization dropped from 51% to 9% when the water flow direction was experimentally shifted to the same direction as blood flow.

SUMMARY

Oxygen diffusion in the placenta of sheep has been analyzed, with a numerical example from data in the literature. The change in oxygen content of fetal and maternal blood in their course through the placenta has been described in tabular and graphic form and the method for finding the diffusion constant of the placenta illustrated.

If maternal and fetal blood flowed in the same direction rather than counter-current in contiguous vessels, it has been shown that the diffusion constant in the example chosen would have had to be 11% higher. The actual opposed flow direction is therefore more efficient than the other possibility.

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