THE RELATIONSHIP BETWEEN ARTERIAL AND TISSUE PO_2 IN THE FETAL LAMB[1]

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The relationship between arterial and tissue PO_2 is not well understood in the adult, let alone in the fetus. Figure 1 shows the pathway for oxygen through the maternal lungs and pulmonary circulation to the systemic circulation. For the fetus, there is an additional step of transfer across the placenta to fetal blood, and thence via the fetal heart to systemic circulation and fetal tissues. It should also be noted that well oxygenated blood from the placenta is mixed with deoxygenated blood in the fetal circulation before it is distributed to fetal tissues thus further reducing the concentration of oxygen in fetal blood circulating to tissues. It can be assumed that both in mother and fetus there will be a marked drop in PO_2 between arterial blood and tissues as oxygen diffuses to the oxygen consuming sites in the mitochondria. This cascade of oxygen is illustrated diagramatically in the lower part of Figure 1. The major difference which emerges between mother and fetus is the low PO_2 of fetal blood compared with maternal blood. This is likely to impose an even lower tissue PO_2 on the fetus than that found in the adult and values reported for fetal tissues have ranged from 1 to 20 mmHg (1-6).

Our studies have been carried out in fetal sheep and we have been measuring both blood and tissue PO_2. The questions that we have posed are as follows:

1. What are the absolute values for tissue PO_2 in the fetal lamb?
2. What is the correlation between blood and tissue PO_2?
3. What factors can affect this correlation such as increasing gestational age and duration of implantation of electrodes, and how does hypoxemia and asphyxia affect tissue PO_2?
4. What are the absolute values for PO_2 in the newborn lamb?

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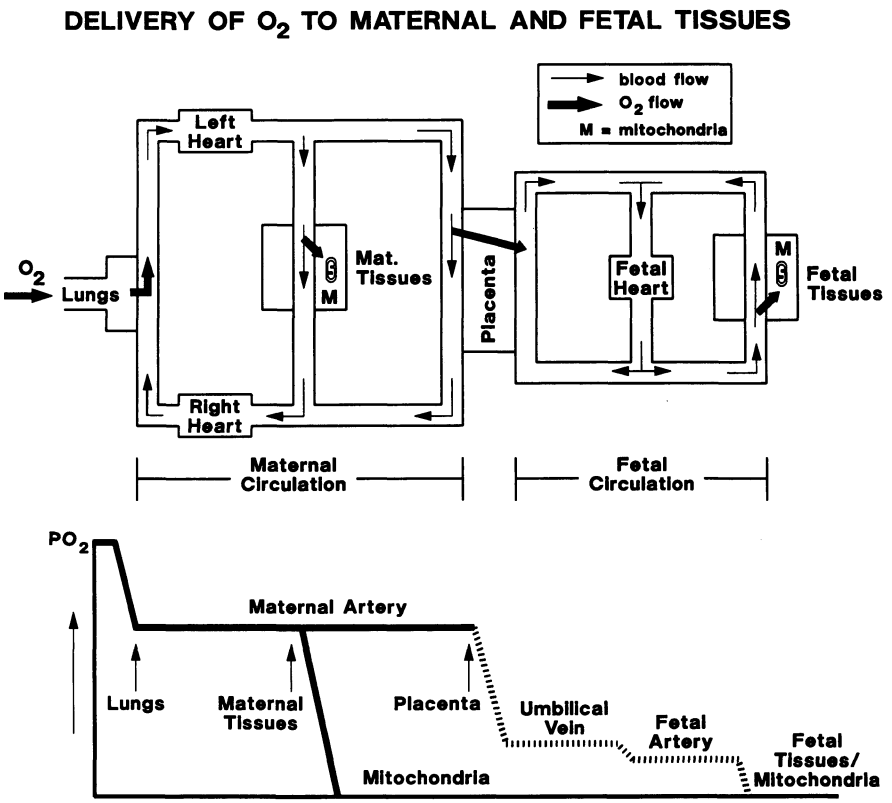

Figure 1

Upper: The pathway for oxygen can be traced via maternal lungs, left heart and systemic circulation to maternal tissues. For the fetus, there is an additional step of transfer across the placenta and thence via fetal heart to systemic circulation and fetal tissues.

Lower: Illustrates the cascade of oxygen from air via maternal lungs to maternal arterial blood and tissues. Note the sharp drop in $P0_2$ as oxygen diffuses from blood to maternal tissues and mitochondria. There is also a sharp drop in $P0_2$ across the placenta and a further drop takes place as oxygen diffuses from fetal blood to fetal tissues and mitochondria.

Electrodes Used to Measure Oxygen Tension

The electrodes we have used have been both intravascular and chronically implanted tissue PO_2 electrodes. The intravascular PO_2 sensor is a commercially available polarographic electrode mounted in the tip of a double-lumen catheter (Venus Oxygen Probe - Orange

Medical Instruments Ltd., High Wycombe, England). It is a Clark-type electrode and is difficult to maintain for long periods of time in chronic fetal sheep preparations because heparinization of fetal blood has to be continuously maintained.

The tissue PO_2 sensor is a custom-made galvanic electrode made available to us through the courtesy of Professor S. P. Bessman, University of Southern California at Los Angeles. This is a fairly large electrode measuring 3 mm which is housed in an acrylic disc of 1 cm diameter (Figure 2). Unlike the Clark electrode, the galvanic electrode does not require a polarization current placed across the anode-cathode pair, i.e., it is a self-generating $P0_2$ electrode from which current or voltage can be measured directly (7). The electrode is placed within tissue layers, e.g. subcutaneous tissue, or on the surface of muscle or dura mater overlying cerebral cortex, and we believe that it measures tissue fluid $P0_2$. This method represents a different approach to the measurement of tissue P02 and cannot be compared with measurements by needle electrodes introduced in a blind fashion into different locations within the tissue, both intracellular and extracellular. It is comparable with the Clark type heated transcutaneous electrode (8) with respect to its size and the area of tissue to which it is applied. However, the galvanic electrode is not heated and measurements represent actual readings obtained at the temperature of the tissue, i.e. about 39-40°C in the fetal lamb.

After removal of the electrode from subcutaneous tissues, one can see a smooth pocket of tissue which surrounds the electrode and is separated from it by a thin layer of tissue fluid. Figure 2 shows the appearance of the dura overlying cerebral cortex in a newborn lamb after reflecting the galvanic O_2 electrode which had been applied before birth.

Results

Typical recordings from a fetal lamb in which a dural PO_2 electrode had been implanted are shown in Figure 3. Note that tissue PO_2 is extremely low, with a baseline around 4 mmHg. Note also the repetitive dips in PO_2 which are characteristic of a normally functioning electrode and a fetal lamb in good condition. The dips in tissue PO_2 appear to be associated with bursts of uterine electromyographic activity which represent uterine contractions. Episodes of mild tachycardia are also associated with the dips in PO_2, as we have previously reported (9).

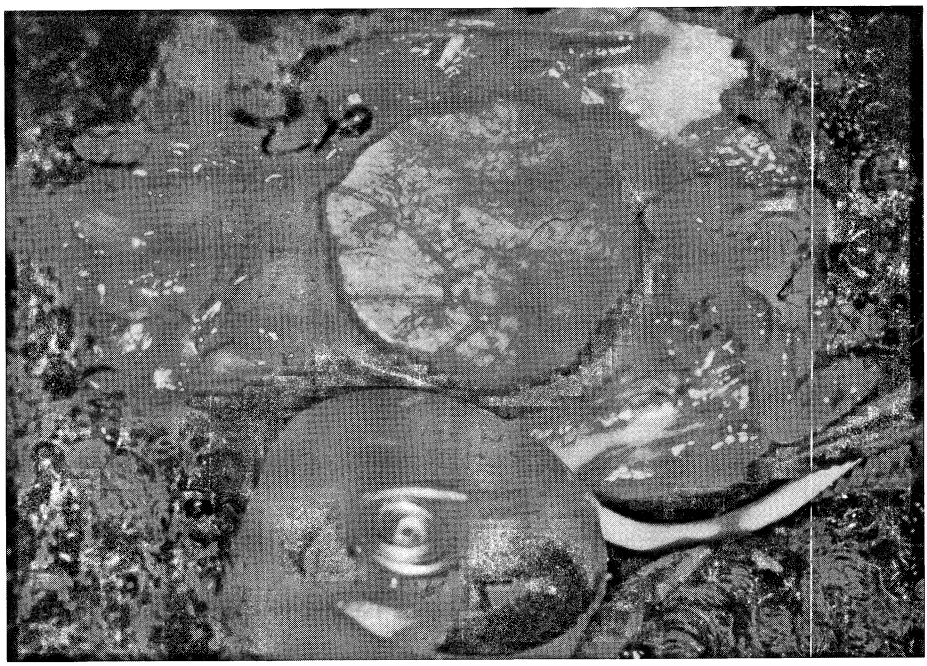

Figure 2

Galvanic $P0_2$ electrode reflected from its site of implantation on the dura overlying cerebral cortex in a newborn lamb aged 5 days. The electrode had been implanted 9 days before birth. Diameter of burr hole in skull and acrylic disc housing $P0_2$ electrode is 1 cm.

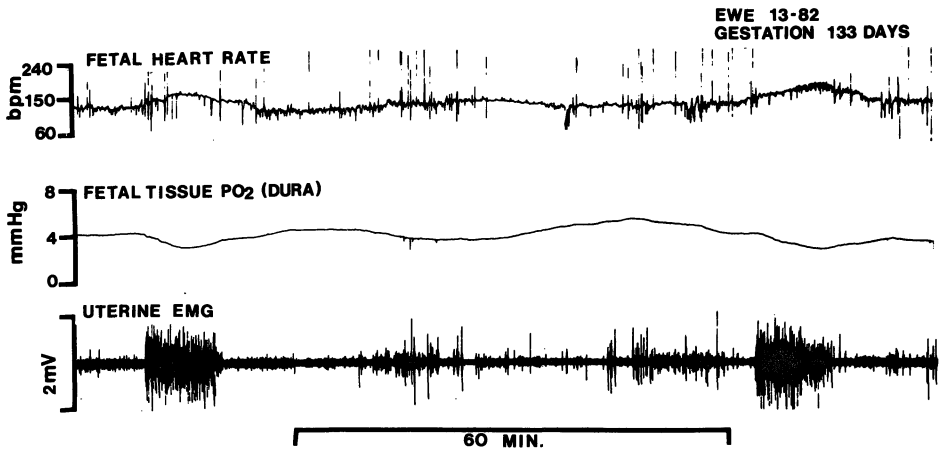

Figure 3

Simultaneous recording of tissue (dura) $P0_2$ and heart rate in a fetal lamb at 133 days gestation. Electromyographic (EMG) activity recorded from uterine wall.

Relationship between blood and tissue PO_2 under physiologic conditions

Simultaneous recordings of fetal arterial and tissue PO_2 have been examined in the fetal lamb. Figure 4 shows the computerized output from a recording of arterial blood and tissue PO_2 in a fetal lamb at 142 days gestation; the lamb was delivered in good condition 2-3 days after this recording was made. Frequent dips in PO_2 can be seen and it should be noted that tissue PO_2 faithfully reproduced the dips seen in arterial blood. Note that arterial PO_2 ranged from 17 to 22 mm Hg while tissue (subcutaneous) PO_2 ranged from 4 to 6 mmHg, i.e. a ratio of approximately 4:1.

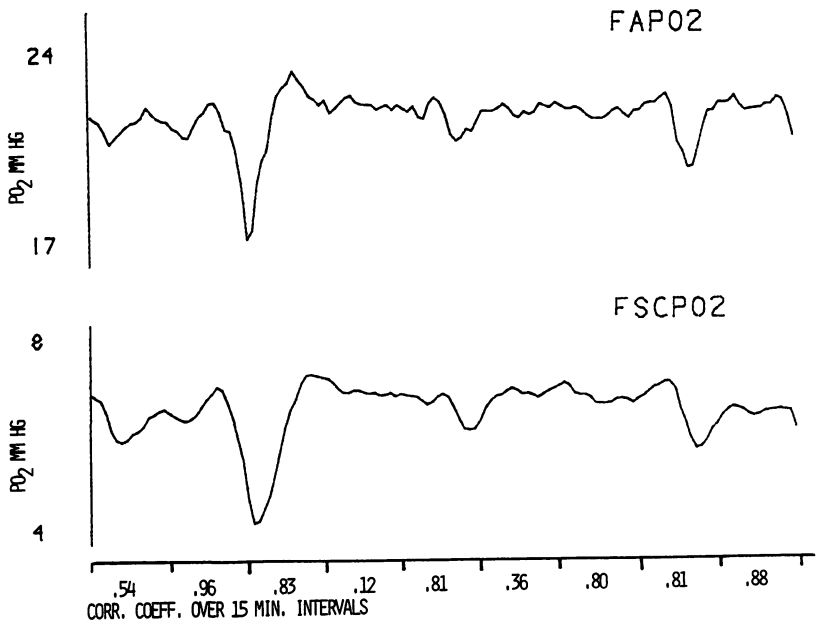

Figure 4

Computer output plot of 135 minutes recording of arterial PO_2 ($FAPO_2$) and subcutaneous tissue PO_2 ($FSCPO_2$) in a fetal lamb at 142 days gestation (term = 147 days). Data averaged over 30s intervals . Intravascular and tissue electrode implanted at 105 days gestation. Note the correlation coefficient (r) values below for arterial vs tissue PO_2 over 15 minute intervals.

In order to document the relationship between arterial and tissue PO_2 in more detail, the correlation coefficient (r) between these two variables was examined over 15 minute intervals. The r values are shown below the recording in Figure 4. The correlation coefficient was generally high with r values greater than or equal to .80. On the other hand, correlation was

less significant when there was little deviation or no dips in PO_2. This is not unexpected since correlation requires deviation in values to show significance and the r value will be zero if two straight lines are correlated.

Mean fetal arterial PO_2 was measured over many days from the time of implantation of electrodes in five pregnant ewes up to the time of delivery. This interval ranged from 8-40 days. All lambs were born in good condition at or near term. Figure 5 shows mean values of PO_2 representing 6-30 hours of recording at various intervals from implantation of electrodes. Arterial blood PO_2 remained relatively stable up to term. Tissue PO_2, however, showed a sharp decline from the time of implantation of electrodes and did not stabilize until about 10-15 days later.

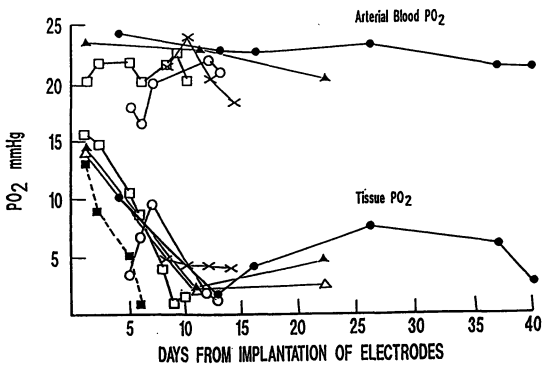

Figure 5

Mean fetal arterial and tissue PO_2 in 5 fetal lambs from the time of electrode implantation (105-129 days gestation) until delivery or electrode failure. Each point represents mean value for 6 - 30 hours of data. ×, △, ○, ■, ●, represent subcutaneous tissue PO_2 electrodes in 5 fetal lambs and ▲, □, represent dural PO_2 electrodes in 2 of the 5 fetuses.

The mean correlation coefficient (r) between arterial and tissue PO_2 plotted against elapsed time from implantation of electrodes and gestational age (days from delivery) is shown in Figure 6. Correlation improved with increasing time from implantation and with increasing gestational age. It is not clear at the present time which factors, i.e. increasing time from implantation of electrodes or increasing fetal maturity, had the most important influence on the relationship between arterial and tissue PO_2. However, it is clear that it improved with time. This may reflect the development of a good micro-circulation around the electrode.

Alternatively, increasing fetal maturity with more deviation in oxygen tension (dips in PO_2) due to increased uterine activity, may have heightened the relationship between blood and tissue PO_2.

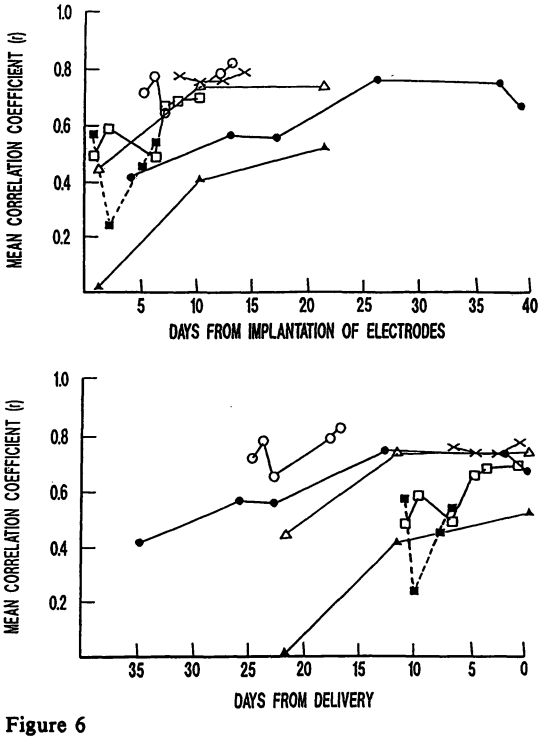

Figure 6

Effect of elapsed time from implantation of electrodes (above) and increasing fetal maturity (below) on mean correlation coefficient (r) between arterial blood and tissue PO_2 in 5 fetal lambs. Each point represents mean r values for 8 - 60 periods of 30 minutes each. Note the trend towards higher r values with increasing time from implantation of electrodes. ×, △, ○, ■, ●, represent subcutaneous tissue PO_2 electrodes and ▲, □, represent dural PO_2 electrodes in 2 of the 5 fetuses.

Relationship between blood and tissue PO_2 under pathological conditions

Maternal hypoxemia was studied by administering 10% O_2 to the pregnant ewe. Figure 7 shows a recording of maternal tissue PO_2 from the surface of the uterus and fetal tissue PO_2 from subcutaneous tissue and the surface of fetal muscle. It can be seen that maternal tissue

PO_2 returned quite rapidly towards baseline values, whereas fetal tissue PO_2 returned slowly following the period of hypoxemia. The delay in reoxygenation of fetal tissues may be due in part to the extra step in oxygen transfer across the placenta and in part to the admixture of well oxygenated umbilical venous blood with deoxygenated blood before distribution to fetal tissues.

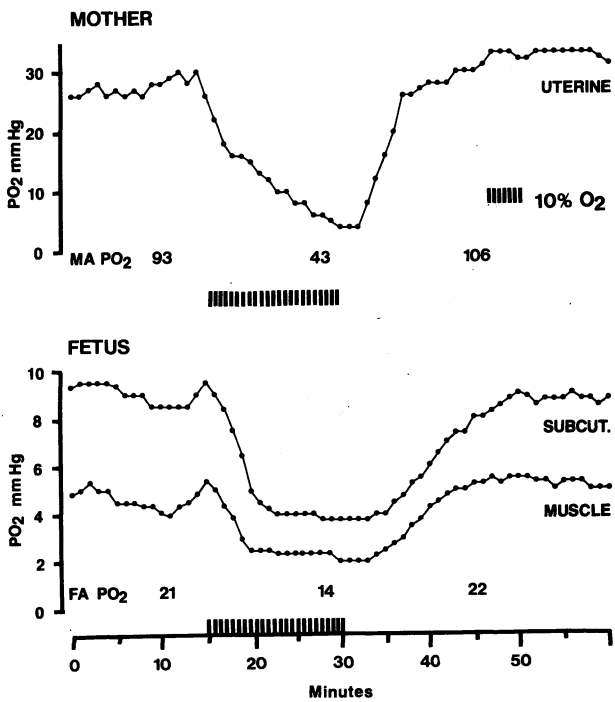

Figure 7

Effect of administration of 10% 0_2 to a pregnant ewe, on maternal tissue $P0_2$ (uterine wall) and fetal tissue $P0_2$ (subcutaneous and muscle). Note the slow return to baseline tissue $P0_2$ values in the fetus compared with the mother. Intermittent blood samples obtained from maternal carotid artery ($MAP0_2$) and fetal carotid artery ($FAP0_2$).

We have also used the model of umbilical cord compression as a means of studying fetal hypoxia. Figure 8 shows the results of an experiment in which fetal arterial blood PO_2 and tissue PO_2 were examined simultaneously during a moderate degree of umbilical cord

compression for 30 minutes; arterial pH fell from 7.36 to 7.27 during this period. Note that fetal arterial PO_2 initially fell rapidly but began to increase again during compression although pH continued to fall. The increase in blood PO_2 can probably be attributed in part to a shift to the right in the fetal oxygen dissociation curve due to the development of acidosis.

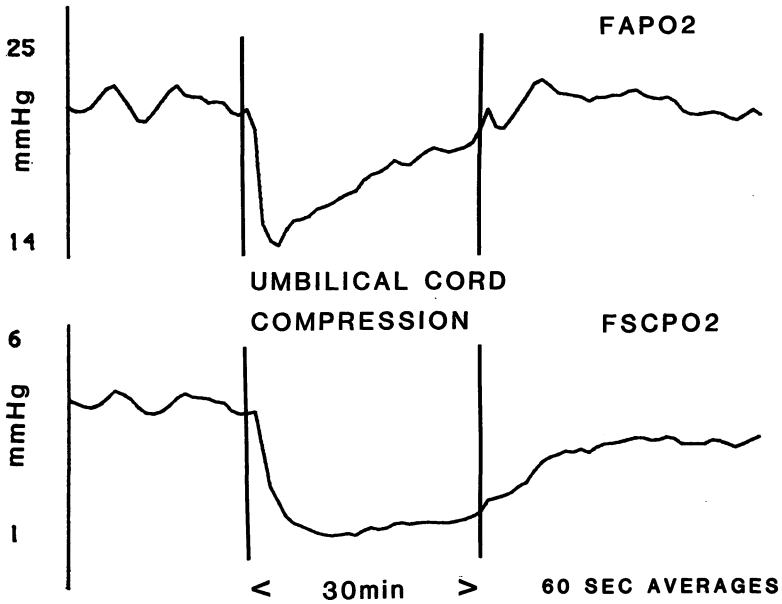

Figure 8

Computer outplot of fetal arterial PO_2 ($FAP0_2$) during a typical experiment in which the umbilical cord was partially compressed for 30 minutes. The correlation coefficient (r) for the control (pre-compression) period was 0.77 and for each successive 30 minute period was -.15, .39 and .90. Thus correlation between blood and tissue $P0_2$ was poor during compression and the initial 30 minutes of the recovery period.

Despite the rise in blood PO_2, subcutaneous tissue PO_2 remained depressed throughout the period of cord compression. When the cord was released, tissue PO_2 increased slowly in comparison with arterial PO_2, which was rapidly restored to pre-compression values. Although the explanation for this phenomenon is not yet clear, it can be postulated that the failure of tissue PO_2 to reflect blood PO_2 may depend on factors which alter blood flow to the tissue, e.g. peripheral vasoconstriction due to catecholamine release.

Tissue PO_2 in the newborn lamb

We have also had an opportunity to measure newborn tissue PO_2 following delivery of fetal lambs with implanted PO_2 electrodes. Figure 9 shows the record from a newborn lamb in which PO_2 electrodes were implanted approximately 10 days before delivery. Note that at one day of age, muscle and subcutaneous tissue PO_2 had risen to values 3-5 times those found in the fetus, i.e. to 15-35 mm Hg compared with from levels of < 5 mm Hg before birth.

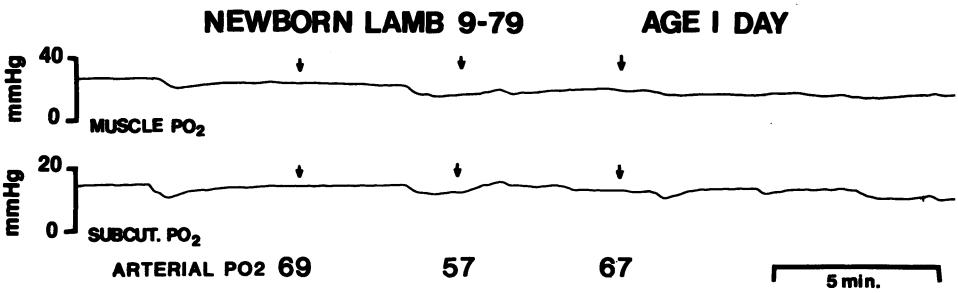

Figure 9

Muscle and subcutaneous tissue PO_2 recorded in a newborn lamb aged 1 day. Galvanic tissue electrodes implanted in the fetus before birth. Carotid arterial blood samples obtained at points indicated by arrows for measurement of PO_2 in vitro.

Intermittent dips of tissue PO_2 were again seen, as in fetal PO_2 recordings, and these appeared to correlate with arterial PO_2 levels measured in vitro. The nature and cause of these dips is not clear at the present time.

Conclusions

1. Absolute values of tissue PO_2 in the fetal lamb are generally <10 mm Hg and frequently <5 mm Hg.
2. Tissue PO_2 increases in the newborn lamb, as anticipated, after birth.
3. There is a high degree of correlation (0.75 or better) between fetal arterial and tissue PO_2 under the following conditions: (i) normal physiologic; (ii) tissue electrodes implanted for at least 7-14 days; (iii) increasing fetal maturity.

4. Correlation between fetal arterial blood and tissue PO_2 is heightened during PO_2 dips, which occur under normal physiologic conditions in the fetal lamb, and with increasing frequency as term is approached.
5. Fetal tissue PO_2 remains depressed after maternal hypoxemia and after fetal asphyxia induced by umbilical cord compression. Recovery to baseline is slow in fetal tissue compared with fetal arterial blood. Thus it is possible that tissue PO_2 may provide us with a better indication of fetal status than blood PO_2 under conditions of hypoxemia or asphyxia.

Acknowledgements

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