Effects of Hyperbaric Oxygen on Uteroplacental and Fetal Circulation

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ABSTRACT
The effects of hyperbaric oxygen (at 3 atmospheres absolute) on uteroplacental and fetal circulations were studied in pregnant ewes near term. The ewe was given spinal anesthesia, the fetus was marsupialized to the abdominal walls to protect the umbilical circulation, and the fetal head was covered with a saline-filled glove to prevent breathing. During hyperbaric oxygenation, maternal arterial blood $P_{O_2}$ rose to 1,300 mm Hg while umbilical vein blood $P_{O_2}$ rose to 300 mm Hg; umbilical arterial $P_{O_2}$ rose to only 50 mm Hg. Maternal and fetal arterial pressures did not change significantly, but uteroplacental and umbilical flows decreased slightly. Ductus arteriosus blood flows decreased strikingly when the oxygen tension of the pulmonary blood rose; net pulmonary blood flow increased markedly because of a decrease in pulmonary vascular resistance produced by oxygen. Ascending aortic flow increased, but effective fetal cardiac output (aortic plus ductus arteriosus flows) decreased. These studies indicate that the fetal pulmonary vascular bed is sensitive to oxygen in that it undergoes vasodilatation when the oxygen tension of the blood passing through it rises; the ductus arteriosus responds to the same stimulus by constricting. Hyperbaric oxygenation seems to establish a circulatory pattern in the fetus similar to that of the early neonatal period.

ADDITIONAL KEY WORDS
fetal pulmonary blood flow
cardiac output vascular resistances

We, as well as others (1-4), have shown that elevating maternal blood $P_{O_2}$ to about 500 mm Hg through lung ventilation with 100% oxygen at 1 atm increases fetal blood $P_{O_2}$ by an average of only 10 to 15 mm Hg. We have further shown that, during such a relative maternal hyperoxia, uteroplacental and umbilical blood flows and their respective vascular resistances do not change significantly (1).
In the present study, the effects of hyperbaric oxygen on uteroplacental and fetal hemodynamics were investigated. Specifically, we attempted to answer the following questions:
(1) Is it possible through hyperbaric oxygenation of the pregnant ewe to increase fetal blood $P_{O_2}$ above levels reached with 100% oxygen at 1 atm? If so, what would be the effects on uteroplacental and fetal circulations?
(2) Since it has been shown by many investigators that elevation of blood $P_{O_2}$ is the main stimulus for ductus arteriosus closure after birth, what would be the consequences to the fetus if its blood $P_{O_2}$ could be increased sufficiently to close this vessel prior to lung expansion and establishment of neonatal circulation? This question is pertinent because ductus flow constitutes about 50% of effective fetal cardiac output (5, 6).

Material and Method
Experiments were carried out on 28 crossbred
pregnant ewes each weighing between 65 and 80 kg. Three experiments (13, 23, and 24) were discontinued because of either surgical complications (ductus avulsion) or electronic difficulties. Although the animals were thought to be near term, according to fetal weight four of the lambs were premature. Each ewe was starved for 18 to 24 hours prior to the experiment. The surgical procedure was carried out inside a hyperbaric chamber which has a total capacity of 2,300 cubic feet and was sufficient to accommodate the animal, surgical and laboratory equipment and several members of the research team. Spinal anesthesia, using 8 mg of tetracaine hydrochloride, was induced in the ewe; supplemental doses of anesthetic were administered when needed through an indwelling spinal catheter. One maternal carotid artery was cannulated under local anesthesia for the recording of arterial pressure and for collecting arterial blood samples anaerobically. An endotracheal tube was inserted through a tracheostomy to assist maternal respiration 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 and was marsupialized to the uterine wall to protect the umbilical circulation. The fetal head was covered with a saline-filled glove to prevent breathing. A catheter was inserted into a major umbilical vein through one of its intercotyledonary branches, and another into the fetal descending aorta via the femoral artery. These were used for anaerobic sampling of umbilical venous and aortic blood and for recording fetal arterial pressure. These technical steps were carried out on all of the animals. Depending on the aim of the experiment, one of the following two surgical procedures was performed.

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This part of the study was carried out on 9 animals. The uterine artery supplying the horn containing the marsupialized fetus was exposed through an inguinal incision. To prevent local spasm during placement of the flow transducer, the adventitia of a small segment of the artery was infiltrated with a solution containing 1.6 mg/ml of phenoxybenzamine and 25 mg/ml of hexylcaine. This local infiltration probably had no effect on the total innervation of the whole uterus and its circulation since the segment of the uterine artery adjacent to the infiltrated area would still go into spasm upon manipulation. The infiltrated segment of the uterine artery was then fitted with an electromagnetic flow transducer. The common umbilical vein was isolated inside the fetal peritoneal cavity through a supr-um-
the vessel walls and the flow transducer often
became poor or was totally lost because of ductus
erteriosus constriction (see results). Whenever
this was observed, either visually or through poor
tuning or both, the flow transducer used to mea-
sure ductus flow was replaced by one with a
smaller diameter; this usually restored the tun-
ing and the flow signal to the pattern seen before
contact was lost.

In the experiments on fetal pulmonary hemo-
dynamics, a Rochester-type catheter was placed
into the main pulmonary artery and was secured
in situ with a purse-string suture; this catheter
served for anaerobic sampling of pulmonary ar-
tery blood, and for recording pulmonary artery
pressure. In some cases, another Rochester cathe-
ter was inserted into the left atrium to allow pres-
sure recording. Technical details on all of these
procedures have been previously reported (5-9).

The experimental protocol consisted of three
consecutive periods as follows:

1. A control period with the ewe breathing
ambient air spontaneously or with her respiration
supported by compressed air with a Bird respira-
tor. The latter was used only when a greater than
usual degree of atelectasis was suspected as evi-
denced by a control blood PO2 lower than 70 mm
Hg. We have used this negative-positive type
respirator for several years and have observed
that it does not significantly affect the maternal
or fetal circulation. The average duration of the
control period was 60 minutes (range 35 to 102
minutes).

2. A hyperbaric oxygenation period with the
ewe breathing 100% oxygen administered with the
Bird respirator. Chamber pressure was increased
to 3 atmospheres absolute (ATA) (in two experi-
ments, the pressure was raised to 4 atm). The
time lapse to reach the desired pressure was 10 to
15 minutes, and the average time during which
the chamber was maintained at the elevated pres-
sure was 50 minutes (range 28 to 91 minutes).

3. A recovery period during which either the
ewe breathed ambient air or her respiration was
supported with compressed air. Chamber pres-
sure was reduced back to 1 ATA in accordance
with a modified U. S. Navy decompression table.
The period of time after return to 1 ATA averaged
50 minutes, and ranged from 14 to 130 minutes.

Throughout all of these periods, samples of
maternal and fetal bloods were collected simul-
taneously at frequent intervals in syringes in
which the dead space was filled with heparin.
The blood withdrawn from the fetus was re-
placed by equal amounts of maternal blood. All
blood samples were analysed within one minute
of being withdrawn.

Blood PO2 was measured using the polaro-
graphic electrode and amplifier (Instrumentation
Laboratory model 125-A). Blood pH and Pco2
were measured using the electrode (Instrumenta-
tion Laboratory model 123) and amplifier. Temperature was maintained at 37.5 ±
.05°C by a constant temperature water bath
(Instrumentation Laboratory model 127). During
compression and decompression, air temperature
deviated from control values for 7 to 10 minutes,
and water jacket temperature was sometimes al-
tered for 1 to 2 minutes. No gas tension measure-
ments were made until temperature stability had
been regained. Oxygen and CO2 electrodes were
standardized against assayed gases (approximate-
ly 5% CO2, 95% O2 and 10% CO2, 90% N2) inside
the chamber. Gas phase standardization was car-
ried out with each change in chamber pressure.

Pressure stability within the chamber was main-
tained at ±0.1 lb/in² during the hyperbaric
phase. Multiple pressure gauges were used, all
agreeing within ±0.1 lb/in² of each other. Stan-
dardization of these gauges against a mercury
column yielded agreement within less than ±
0.125 lb/in² over the range of operating pressure.

Pulsatile and mean (electronic integrator)
blood pressures and flows from mother and fetus
were recorded at five minute intervals throughout
all the periods of study. The cables connecting
the strain gauges and the flow transducers inside
the chamber to the flowmeters and the Offner
recorder outside the chamber were passed through
a seal. Technical details of blood analyses and of
pressure and flow recordings were previously re-
ported (1, 5-9).

Results

1. EFFECTS OF THE PROCEDURE
ON THE EWE AND FETUS

The effects of the surgical procedure, in-
cluding anesthesia, on the ewe and her fetus
were no different from those previously re-
ported (1, 5-9). Control maternal PO2, Pco2,
pH and arterial pressure were within the
ranges of values observed by us and by others.
The maternal arterial PO2 was low in exper-
iment 2, but blood pressure was within
the normal range. No obvious deleterious effects
on the persons who remained with the animal
inside the hyperbaric chamber were observed.

2. EFFECTS OF HYPERBARIC OXYGENATION
ON MATERNAL AND FETAL BLOOD GAS TENSIONS

The data on maternal artery and umbilical
vein blood gas tensions and pH during the
three periods of study are presented in Table
1. Figure 1 depicts the relationship between
maternal arterial and umbilical vein blood
PO2, and Figure 2 presents the relationship

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### Table 1

**Effects of Hyperbaric Oxygen on Ewe and Her Fetus**

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*One uterine artery blood flow (ml/kg of fetus/min). The values given in this and subsequent tables represent the average of several readings. C = control period; H = hyperbaric period when Po2 of the blood from the ewe and umbilical vein had reached the peak; R = recovery period after decompression.*
between umbilical artery and umbilical vein bloods in simultaneously collected samples.

Maternal arterial blood $\text{Po}_2$ rose from a control average of 73 mm Hg to an average of 1,160 mm Hg during the hyperbaric period with a wide individual variation; arterial $\text{Po}_2$ returned to control values after decompression. Maternal arterial blood $\text{Pco}_2$ increased...
and pH decreased significantly ($P < .001$) during hyperbaric oxygenation; both parameters returned to control values after decompression (Table 1).

Umbilical vein $P_{O_2}$ rose during the hyperbaric period from an average of 26 mm Hg to 319 mm Hg with a large individual variation (Table 1, Fig. 1); it returned to control values during the recovery period. Despite this marked increase in umbilical vein $P_{O_2}$, pulmonary artery blood $P_{O_2}$ (Table 3) and umbilical artery blood $P_{O_2}$ increased about two-to-three-fold with a wide scatter (Table 1, Fig. 2). Other fetal blood gases changed in a similar manner to those of the mother; blood $P_{CO_2}$ increased and pH decreased significantly during hyperbaric oxygenation ($P < .001$). These changes were evident in the umbilical vein, aortic and pulmonary artery blood. Blood $P_{CO_2}$ and pH returned to near control values after decompression (Tables 1 and 3).

**3. EFFECTS OF HYPERBARIC OXYGENATION ON MATERNAL AND FETAL CIRCULATIONS**

**Uteroplacental Hemodynamics**

Maternal arterial pressure did not change significantly throughout the three periods of study (Table 1). Uteroplacental blood flow (measured in only one uterine artery), however, decreased from an average of 216 to 179 ml/kg/min ($P > .05$). During the recovery period, uteroplacental blood flow returned to an average of 205 ml/kg/min but only a few measurements were made (Table 1). The significance of the changes in uteroplacental blood flow is, however, questionable ($P > .05$).

**Fetal Circulation**

**Umbilical Hemodynamics.**—Fetal arterial pressure was not affected appreciably by hyperbaric oxygenation. Total umbilical blood flow, however, decreased by about 15% (Table 1). Although the magnitude of this decrease falls within the error of the electromagnetic

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**FIGURE 3**

Segments of a record illustrating the pattern of changes in phasic and integrated maternal and fetal arterial pressures, and fetal ascending aortic and ductus arteriosus flows. The polarity of the flowmeter was adjusted so that ductus arteriosus flow above zero indicates right-to-left shunt. Note the progressive increase in aortic flow during hyperbaric oxygenation. Note also the marked decrease in ductus arteriosus flow and the development of a negative component which required changing the zero base line; net ductus arteriosus flow became left to right (mean below zero base line) after 20 minutes at 3 atm. Ductus arteriosus flow resumed control pattern during recovery.
### Effects of Hyperbaric Oxygen on Fetal Systemic Circulation

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<th>Flow, ductus arteriosus (ml/kg/min)</th>
<th>Effective card. output (ml/kg/min)</th>
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<td>248 ± 16</td>
<td>41 ± 3</td>
<td>31 ± 3</td>
<td>7.36 ± .02</td>
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*Flows measured in main pulmonary artery, ascending aorta and ductus arteriosus. C, H, and R as in Table 1.
method of measuring venous flow (± 15%), it might be meaningful since the changes in the hyperbaric period consistently followed the same direction, namely, a decrease \((P < .05)\). After decompression, fetal arterial pressure decreased slightly and umbilical vein blood flow remained low. The significance of the changes observed in the recovery period is, however, questionable considering the small number of determinations and also the length of the experiment and the possible onset of deterioration of the experimental preparation.

**Systemic Hemodynamics**—Table 2 lists data on the effects of hyperbaric oxygenation on blood respiratory gases, fetal arterial pressure, ductus arteriosus and ascending aortic flows, and the algebraic sum of the two which we have termed “effective cardiac output.” Figure 3 illustrates the pattern of changes in phasic flow including ductus blood flow direction during the three periods of study. Figure 4 presents integrated values in a representative experiment for fetal "effective cardiac output" and its respective components.

In these studies, the changes in umbilical vein blood \(P_{O_2}, P_{CO_2}, \text{pH}\) and in fetal arterial pressure during the hyperbaric and recovery periods were similar to those observed in the previous series of experiments (Table 2). In the control period, ductus arteriosus flow was always from right to left and its magnitude averaged 126 ml/kg/min. During hyperbaric oxygenation and concomitant with the rise in fetal blood \(P_{O_2}\), ductus flow decreased markedly reaching an average of 41 ml/kg/min \((P < .001)\). The decrease was related to ductus constriction which required changing the flow transducer to one with a smaller diameter. The phasic flow became irregular in that positive flow pulses alternated with negative ones (Fig. 5). This alternating flow pattern is similar to that seen in previous studies during fetal lung inflation (5-7). It is related to the complex dynamics of ductus blood flow in the

![Figure 4](http://circres.ahajournals.org/)

*Figure 4*  
A representative experiment showing the effects of hyperbaric oxygen on fetal effective cardiac output and its two respective components. Note the marked rise in aortic flow that occurred simultaneously with the decrease in ductus arteriosus flow (values below zero indicate left-to-right flow). Effective cardiac output decreased slightly during hyperbaric oxygenation. All returned to control values during decompression.
### Table 3: Effects of Hyperbaric Oxygen on Fetal Pulmonary Hemodynamics

| Patient no. | 16* | 17f | 21t | 22 | 25 | 26* | 27 | 28 | Average
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<tr>
<td>Eipt. no.</td>
<td>16*</td>
<td>17f</td>
<td>21t</td>
<td>22</td>
<td>25</td>
<td>26*</td>
<td>27</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>
| Weight (kg) | 4.6 | 3.2 | 4.5 | 1.1 | 3.9 | 1.75 | 4.1 | 4.25 | 4.1 ± 0.3
| *Flow measured in left pulmonary artery, ascending aorta and ductus. $^+$Negative sign means flow from left to right. C, H, I, and R as in Table 1. |
presence of a narrow pressure gradient between the pulmonary artery and aorta and the presence of asynchrony between the two ventricles (8). Net ductus flow either approached zero or in certain instances became negative (left to right) (Fig. 3). Ascending aortic flow increased by about 50% ($P < .001$) during hyperbaric oxygenation and returned to control values during decompression (Table 2, Figs. 3 and 4). Because of the decrease in ductus flow and the simultaneous increase in ascending aortic flow, fetal "effective cardiac output" did not change significantly (Table 2, Fig. 4).

**Pulmonary Hemodynamics.**—Table 3 presents data on fetal pulmonary hemodynamic parameters and on fetal arterial pressure and pulmonary blood gases during the three periods of study. Figure 5 illustrates the pattern of changes in phasic pulmonary artery and ductus flows; Figure 6 presents integrated values in a representative experiment for systemic and pulmonary artery pressure, and ductus and main pulmonary artery flows.

Pulmonary artery blood $Po_2$ rose during hyperbaric oxygenation from an average of 16 to 47 mm Hg ($P < .001$); $Pco_2$ increased and pH decreased significantly (Table 3). In the control period, pulmonary artery pressure was usually higher than aortic pressure (Table 3, Figs. 5 and 6). Because of this difference, ductus arteriosus flow was always right to left (Fig. 5); its magnitude, however, was somewhat lower than in the previous series and averaged 96 ml/kg/min (Table 3). Main pulmonary artery flow averaged

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**Figure 5**

Segments of a record illustrating the changes induced by hyperbaric oxygen in phasic and integrated pressures and flows in the fetal pulmonary circulation. Note the slight decrease in pulmonary artery pressure, and the striking fall in ductus arteriosus flow which developed an irregular pattern with a large negative component during hyperbaric oxygenation. This complex pattern is very similar to that seen after lung expansion. Both pattern and magnitude of ductus flow returned to normal in the recovery period. Main pulmonary artery flow increased slightly during hyperbaric oxygen but returned to the control value during recovery.
Data on a representative experiment showing the changes in the pressure gradient across the ductus arteriosus and in ductus arteriosus and pulmonary flows during the hyperbaric and decompression periods. Note the reversal in the pressure gradient in favor of the systemic circuit together with the marked fall in ductus arteriosus flow during hyperbaric oxygenation (ductus arteriosus flow values below zero indicate left to right flow). During decompression, the pressure gradient returned to the control pattern and ductus flow increased strikingly.

Pulmonary blood flow decreased.

153 ml/kg/min; these values are within the range of data previously reported (6, 7).

During hyperbaric oxygenation, mean pulmonary arterial pressure fell by an average of 5 mm Hg (Table 3); aortic pressure, however, did not change significantly (Figs. 5 and 6, Table 3). Consequently, the pressure gradient across the ductus arteriosus either decreased considerably or reversed in favor of the systemic circulation (Figs. 5 and 6). Ductus arteriosus flow decreased strikingly as in the previous series. Here again, the phasic flow complex began to exhibit a negative component that led, in certain instances, to reversal of flow from left to right (Fig. 5). Main pulmonary artery flow showed variable changes but usually increased (Table 3). Net pulmonary blood flow, estimated from the algebraic difference of main pulmonary artery and ductus arteriosus flows, nearly tripled during hyperbaric oxygenation (Table 3). The increase was related to a marked fall in pulmonary vascular resistance. Left atrial pressure increased by about 2 mm Hg during hyperbaric oxygenation.

During the recovery period, ductus arteriosus blood flow returned to near control values in magnitude and direction (Table 3, Figs. 5 and 6). Main pulmonary artery flow decreased during this period in the three cases in which it was measured; net pulmonary blood flow decreased significantly in the cases in which it was possible to estimate it (Table 3). In the two experiments (16 and 26) during which left pulmonary artery flow was monitored, this flow promptly increased during hyperbaric oxygenation when the pulmonary blood $\text{PO}_2$ rose (Table 3, Fig. 7); it returned to control values after decompression (Table 3).

Foramen ovale flow was estimated from the difference between "effective cardiac out-
put" and main pulmonary artery flow even though these parameters were measured in different series of animals. This flow decreased by an average of 50% during hyperbaric oxygenation. Such a decrease was also observed in the two experiments in which aortic, main pulmonary artery and ductus flows were measured simultaneously. It was probably related to a partial closure of the foramen ovale subsequent to the increase in blood return to the left side of the heart.

**Discussion**

The present data obtained from ewes studied under regional anesthesia and from unanesthetized fetal lambs provide information regarding various aspects of fetal adjustment to intrauterine life and the interrelationship of blood oxygen and fetal circulatory dynamics.

**Maternal and Fetal Gradients of Respiratory Gas Tensions**

From the present data it is clear that, despite the hyperbaric oxygen environment in which the pregnant ewe was placed, her arterial blood Po\(_2\) did not rise proportionally with the increase in alveolar Po\(_2\). A similar
HYPERBARIC OXYGEN AND FETAL CIRCULATION

The difference has been observed by us and by others in animals studied under 100% oxygen at 1 atm. Although the exact mechanism of this difference is not clear, it is believed that immobilization of the ewe in the lateral position plays an important role.

In the present studies, the umbilical vein P\textsubscript{02} was increased to levels never heretofore reported. Yet, a wide maternal-fetal P\textsubscript{02} gradient still persisted. Similarly, a large blood P\textsubscript{02} difference existed between umbilical venous and the fetal aortic bloods despite the hyperbaric oxygenation. Although the various mechanisms that contribute to maintaining these gradients will be discussed in detail in a future report, they include such factors as uteroplacental and fetal oxygen consumption, the different positions on the oxyhemoglobin dissociation curve of the maternal and fetal bloods, and dilution of umbilical vein blood with less saturated blood coming from various areas of the fetal body.

The rise in maternal blood P\textsubscript{co2} and the fall in blood pH observed in our experiments were of the same magnitude and trend as those noted by Meijne and Straub (11) in adult dogs subjected to nearly the same degree of compression. Although the exact mechanisms of these changes are obscure, they have been attributed to a decreased ventilatory rate induced by high oxygenation. This hypothesis is supported by data which show that, when the animals are hyperventilated during hyperbaric oxygenation, blood P\textsubscript{co2} decreases instead of increases (12). Whatever the cause of the changes in maternal blood P\textsubscript{co2} and pH, the fetal alterations in these parameters are most likely secondary to those occurring on the maternal side of the placenta.

HEMODYNAMIC EFFECTS OF HYPERBARIC OXYGEN

The reports on the circulatory effects of hyperbaric oxygen in adult animals are somewhat confusing. Tindall and co-workers (12) observed a decrease in internal carotid blood flow during hyperbaric oxygenation. In these studies, however, the P\textsubscript{co2} of the blood fell and it is difficult to assess the relative contributions of the fall in P\textsubscript{co2} and the rise in P\textsubscript{o2}. Renal blood flow and cardiac output are thought to decrease during hyperbaric oxygenation but the data on these changes are inconclusive (13, 14).

In the present studies, hyperbaric oxygen did not significantly alter the circulation of the pregnant ewe. The slight decrease in uteroplacental blood flow despite unchanged arterial pressure might be due to vasoconstriction produced by oxygen. But, since the changes were not statistically significant, this hypothesis requires further confirmation.

In contrast to the negligible effects in the ewe, hyperbaric oxygen produced dramatic hemodynamic alterations in the fetus. Elevation of the fetal oxygen tension promptly established a pattern of fetal circulation which closely resembled that of early neonatal life. The striking decrease in ductus arteriosus blood flow with sometimes a reversal in its direction, and the increase in ascending aortic flow were similar in many respects to the changes in systemic hemodynamics seen after lung expansion (6, 7). The fact that, in the present studies, ductus arteriosus blood flow decreased only after the P\textsubscript{o2} of the blood passing through it had increased confirms previous in vivo and in vitro observations regarding the importance of oxygen for ductus closure (5). It also suggests that other factors, mechanical or otherwise, are probably not important in contributing to closure of the ductus arteriosus after birth.

We had postulated that, if the pulmonary arterial blood P\textsubscript{o2} in the fetus could be raised sufficiently to cause ductus constriction, fetal life would be seriously compromised since ductus flow constitutes over 50% of the fetal "effective cardiac output." This was certainly not confirmed in the present studies. Although oxygen has been suggested as one of the stimuli causing pulmonary vasodilatation in the neonatal period (15, 16), its action on the intact unexpanded fetal lungs has never been clearly demonstrated. The striking increase in net pulmonary blood flow observed in the present experiment was strictly related to the rise in the P\textsubscript{o2} of the blood passing through
the lungs causing a decrease in pulmonary vascular resistance.

Quantitative comparison between the changes in fetal pulmonary circulation produced by lung expansion and those produced by oxygen in the unexpanded lungs is difficult for various reasons. Among these are the complex hemodynamic changes that occur after initiation of breathing, the technical difficulties in measuring continuously and accurately all the parameters that take part in these changes, the variation in the degree of lung expansion, and the uncertainty about the pulmonary blood Po2 at the time of measurement. Nevertheless, a rough comparison can be made between the present data and those obtained by us from two previous series of experiments in which the same methodology was employed to monitor changes in pulmonary hemodynamics after lung expansion (6, 7). In those two series, pulmonary arterial pressure decreased by about 50% after lung ventilation and net pulmonary blood flow increased by over 200%; pulmonary vascular resistance decreased 100 to 300%. During hyperbaric oxygenation, pulmonary artery pressure did not decrease by more than 5% although net pulmonary blood flow nearly doubled. The decrease in pulmonary vascular resistance must have been far below that observed after lung expansion. Even when the fetal lungs were expanded with nitrogen (5), the fall in pulmonary artery pressure and the increase in net pulmonary blood flow were initially greater than those produced by hyperbaric oxygenation. All this serves to emphasize that, while oxygen unquestionably plays an important role in the changes in pulmonary vascular tone that occur after birth, the mechanical effects of expanding the alveoli still play a major role. Just how oxygen acts on the pulmonary vessels is not clear. Preliminary experiments performed by us on the effects of hyperbaric oxygen on fetal lambs subjected to ganglionic blockade with mecamylamine suggest that the autonomic vasomotor tone may not be essential since these animals exhibited the same degree of fall in pulmonary vascular resistance as those observed in the present series.

Whatever the mechanism, the pulmonary vasodilatation that occurred during hyperbaric oxygenation was responsible for absorbing that fraction of blood flow which was diverted from the ductus arteriosus when the latter constricted. Obviously, the increase in net pulmonary blood flow led to an increase in blood returning to the left side of the heart and, hence, to an increase in aortic flow.

As stated before, the slight decrease in umbilical blood flow observed during hyperbaric oxygenation falls within the error of the method used to measure venous flow. Assuming, however, that it is real, it could be due to a multiplicity of factors such as changes in the fetal cardiac output, constriction in the umbilical vein and its tributaries or ductus venosus, or spontaneous alterations in the umbilical circulation related to the condition of the experimental preparation. Because the umbilical circulation accepts about 65% of the fetal cardiac output and practically determines the fetal systemic resistance (6, 17), a significant constriction in the umbilical arteries and its tributaries should have increased the fetal arterial pressure. The fact that the latter practically remained unchanged during hyperbaric oxygenation speaks against a major direct effect of oxygen on the umbilical circulation.

Certain authors (16) have postulated that blood PCO2 plays a role in controlling pulmonary vascular resistance before and after birth. It is unlikely that the rise in fetal blood PCO2 observed in these experiments contributed much to the pulmonary vasodilatation that occurred during hyperbaric oxygenation. The reasons are, first, an increase in PCO2 should have caused vasoconstriction and not vasodilatation; and second, in many instances, pulmonary vasodilatation occurred before any significant change in blood PCO2.

The present observations provide ground for a great deal of speculation about the meaning of, and the reasons for, certain anatomical and physiological peculiarities of fetal life in utero. The first aspect to be considered,
which has puzzled investigators for the last fifty years, is the meaning of the low oxygen tension of fetal blood. It appears now that such a low tension has a dual purpose. It contributes toward maintaining a high fetal pulmonary vascular resistance which diverts the greatest portion of the right ventricular output away from the lungs and it serves to maintain a widely dilated ductus arteriosus which channels the diverted blood toward the systemic circulation. Just how oxygen exerts such a diametrically opposing action on two contiguous vascular structures is not known.

The second is the purpose of the ductus arteriosus and the foramen ovale. The present observations show that the fetal circulation can be transformed into the so-called "transitional circulation" of early neonatal life without jeopardizing fetal life. Of course, the present experiments were acute in nature and the decrease in ductus arteriosus flow was temporary. Whether the fetus would have become compromised if the ductus arteriosus were constricted chronically cannot be stated. At any rate, we are inclined to believe that the purpose of the ductus arteriosus is not only to divert blood from the lungs, but also to provide the fetus with the relatively high cardiac output necessary to meet its overall metabolic demands.

It is generally believed that the foramen ovale shunts highly oxygenated blood toward the left side of the heart and from there to the brain. However, over the years we have not been impressed by the very slight difference between carotid and descending aortic Po2 which in our view would not justify the existence of the foramen ovale. Furthermore, we have recently shown (18) that the relatively high PCO2 and low Po2 of fetal blood are the main factors responsible for maintaining a high cephalic blood flow in the fetus. In fact, a rise in blood Po2 such as occurs after birth promptly constricts cephalic circulation and decreases its blood flow. For these reasons, we are inclined to believe that the main purpose of the foramen ovale may not only be to provide oxygenated blood to the brain but also it probably serves to divert blood from the right to the left side of the heart. This blood is required to provide the volume and pressure necessary for development of the left ventricle and for maintaining the fetal systemic pressure at a level adequate to perfuse the various fetal parts including the placenta. For, if the foramen ovale were not present, the volume of blood returning to the left heart through the fetal pulmonary veins might not be sufficient to prepare the left ventricle for its dominant role after birth.

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References


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