Liver and Ductus Venosus Blood Flows in Fetal Lambs in Utero

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SUMMARY We evaluated the circulation of the liver and ductus venosus, using the radionuclide-labeled microsphere technique, in 24 chronically prepared fetal lambs. We placed catheters in fetal descending aorta and inferior vena cava, and in a carotid artery and an umbilical vein; in 11 fetuses, we also inserted a catheter in a mesenteric vein that drained into the portal vein. After allowing 2–4 days for recovery from the stresses of anesthesia and operation, we measured blood flow to the fetal liver and its various lobes and through the ductus venosus. Total blood flow to the liver was 435 ± 122 ml/min per 100 g liver (mean ± SD), of which hepatic arterial flow represented 9%, portal venous flow 18%, and umbilical venous flow 73%. Hepatic arterial and umbilical venous flows were approximately equally divided between left and right lobes, although portal blood flow was directed almost exclusively to the right lobe. The right lobe received 40% more total blood flow than the left, even though the left lobe weighed more than the right. Approximately 53% of umbilical venous blood flow but less than 9% of portal venous blood flow entered the ductus venosus; umbilical venous flow therefore accounted for more than 98% of ductus venosus blood flow. Ductus venosus flow showed a strong linear correlation with umbilical blood flow. However, there was no relationship between ductus venosus flow and gestational age. The results suggest that the liver receives a large blood flow primarily because of a large umbilical venous contribution. It is not clear whether the fetal liver requires this large flow and peculiar lobar distribution for normal function and growth. It is unlikely, however, that the ductus venosus functions actively to maintain a stable blood flow to the fetal liver.

THE LIVER of the fetus receives its blood supply from the hepatic artery, portal vein, and umbilical vein. Total blood flow to the fetal liver must be high, because a large umbilical venous blood flow passes through the liver. Nevertheless, the actual flow that reaches the liver from all three vascular sources has not been measured previously. The relative contributions of hepatic arterial and portal and umbilical venous blood flows to the various lobes of the liver also have not been studied quantitatively.

Anatomically, the left lobe of the liver is supplied by branches of the umbilical vein, while the right lobe is supplied by portal venous branches (Fig. 1). Except for occasional small branches, no umbilical blood vessels extend into the right lobe, and no portal blood vessels reach the left lobe. Branches of the hepatic artery supply both lobes, but arterial flow to the whole liver is small. This would imply that the left lobe is supplied by the most highly oxygenated blood that the fetus receives, while the right lobe receives primarily blood that is low in oxygen. These anatomical data have been used to explain the observation that degenerative changes in the liver associated with fetal asphyxia are more pronounced in the right than in the left lobe.

A variable portion of umbilical venous and portal venous blood flow can bypass the fetal liver and enter the ductus venosus, which provides a direct communica-
artery and vein. These catheters were advanced to descending aorta and inferior vena cava, respectively. We placed a catheter in a cotyledonary branch of the umbilical vein in the horn of the uterus and advanced the catheter 10-12 cm so that the tip was in a main umbilical vein. In 14 of the 24 fetuses, we inserted a catheter in a carotid artery. In 11 of the 24 fetuses, we also placed a catheter in a small mesenteric vein in the following manner. We made a 3-cm incision in the left lower quadrant of the fetal abdomen and fixed the cut skin edges to the uterine muscle and amniotic membrane to prevent loss of amniotic fluid. After entering the peritoneal cavity and withdrawing several loops of small bowel, we located a vein within the vascular arcade that supplies the gut. We inserted a polyvinyl catheter (0.015-inch i.d., 0.035-inch o.d.) and advanced it approximately 5 cm so that the catheter tip was directed toward the portal vein. After closing the fetal abdomen, we placed a catheter in the amniotic sac, closed the uterine incision, and brought the catheters out subcutaneously to the ewe’s flank. Postoperatively, each ewe received penicillin and kanamycin intravenously and intraamniotically for 2 days. Vascular catheters were flushed with heparin daily to ensure catheter patency. Two to four days after surgery, we studied the fetuses of the unanesthetized ewes. We studied only fetuses with normal descending aortic blood gases (pH ≥ 7.35, Po₂ ≥ 20 torr, Pco₂ ≤ 45 torr). We measured blood flows with 15-µm diameter radionuclide-labeled microspheres and arterial blood references samples.

Blood Flow to Liver and Through Ductus Venosus

In the 11 fetuses with portal vein catheters, we determined blood flow and its distribution to the fetal liver, as well as portal and umbilical venous blood flow through the ductus venosus. We measured blood pressure in descending aorta, inferior vena cava, portal vein, and umbilical vein, amniotic fluid pressure, and fetal heart rate for at least 30 minutes. When these were stable, 1 ml of blood was withdrawn from each vascular catheter to measure blood gases. A complete set of measurements of blood gases was obtained in only seven instances. We injected 15-µm microspheres, labeled with different radionuclides, simultaneously into the inferior vena cava, portal, and umbilical venous catheters, while obtaining a descending aortic blood reference sample (and carotid arterial sample in those fetuses with a carotid arterial catheter).

Serial Studies of Ductus Venosus Blood Flow

It was apparent after a few studies that portal blood flow through the ductus venosus was small and that umbilical venous blood contributed almost all of the flow through the ductus venosus. Since we also wanted to evaluate ductus venosus flow serially through gestation, we determined only the umbilical venous contribution to blood flow through the ductus venosus in an additional 11 fetuses. In four of these, we injected microspheres, labeled with different radionuclides, into the umbilical venous catheter 2-4 times during a single day to assess diurnal variation. In three fetuses, microspheres were injected into the umbilical vein daily for 2-3 days to determine any daily variations in ductus venosus flow. In the remaining four fetuses, we injected microspheres into the umbilical vein at 3- to 6-day intervals beginning at 118-128 days gestation and progressing toward term (147 days) to evaluate ductus venosus flow during the last 3 weeks of gestation. To calculate blood flow per kilogram of fetal body weight in these latter four growing fetuses, we estimated fetal weight from gestational age, using the data of Barcroft. Prior to each microsphere injection, we measured descending aortic, inferior vena cava, and umbilical venous blood pressures, amniotic fluid pressure, and fetal heart rate for at least 30 minutes. When these were stable, 1 ml of blood was obtained from each vascular catheter for evaluation of blood gases. During microsphere injections, descending aortic (and carotid arterial, where available) blood reference samples were withdrawn to calculate actual blood flows. The volume of blood removed was replaced with maternal arterial blood.

Measurements of Pressures, Heart Rate, and Blood Gases

We measured all pressures with Statham P23Db pressure transducers and heart rate with a cardiotachometer triggered by the fetal arterial pressure pulse, and recorded these on a Beckman direct-writing recorder. Mean blood pressures were obtained electronically. Blood gases (pH, Po₂, and Pco₂) were measured with standard electrodes and a blood gas meter (Radiometer).

Preparation of Tissues

Upon completion of each study, ewes were killed with sodium pentobarbital and potassium chloride, and the entire uterus and its contents were removed. Each fetus was dissected in a uniform manner and all animal tissues were analyzed. We divided the fetal liver into left, right, and caudate lobes. The line of demarcation between left and right lobes extends between the fossae of the inferior vena cava and the gall bladder. The line is just to the right of the ductus venosus. A small portion of
the caudate lobe lies to the left of this line; since it was difficult to determine how much of this tissue was caudate lobe, we included this part with the left lobe. The remainder of the caudate lobe was dissected and evaluated separately.

The fetal organs, carcass, and placenta were processed as previously described. The amounts of each nuclide in each tissue sample were measured with a well-type gamma scintillation counter and a 512-channel pulse-height analyzer (Searle Analytical Co.).

Calculation of blood flow to fetal organs (excluding liver), carcass, and placenta (umbilical blood flow) were performed by computer (IBM 360). Our methods for calculating blood flow to the liver and through the ductus venosus are given in the Appendix. We calculated cardiac output, using descending aortic and carotid arterial blood reference samples. When only descending aortic blood reference samples were available, cardiac output was approximated by methods described previously. We used the paired t-test and linear regression analyses to analyze our data statistically.

Results

Quantification of Arteriovenous and Veno-Venous Shunts in the Liver

We selected microspheres 15 μm in diameter, since larger ones obstruct a greater proportion of the microcirculation. However, several anatomical studies in fetal lambs have shown that liver sinusoids are approximately 12-15 μm in diameter. These studies have also described hepatic artery-hepatic vein anastomoses (10-20 μm in diameter) and umbilical or portal vein-hepatic vein anastomoses (approximately 30 μm in diameter), but they have not noted hepatic artery-portal vein connections. Therefore, to determine (1) whether the sinusoids of the fetal liver trap 15-μm microspheres and (2) how much, if any arteriovenous or veno-venous shunting exists, we simultaneously injected 50- and 15-μm microspheres with different radionuclide labels into the umbilical vein and into the inferior vena cava of the two remaining fetuses. There were no significant differences between distribution of 50-and 15-μm microspheres to the whole liver or to the left, right, or caudate lobes. This demonstrated that (1) microspheres of 15-μm diameter are trapped by the sinusoids of the fetal liver and (2) there is little arteriovenous or veno-venous shunting in blood vessels of less than 50-μm diameter in the fetal liver.

Blood Respiratory Gases and Vascular Pressures

Table 1 shows blood respiratory gases and mean arterial and venous blood pressures. We found no significant differences between inferior vena caval and portal venous blood gases. We also found no consistent differences between portal and umbilical venous mean blood pressures; inferior vena caval pressure was always less than either portal (t = 4.37, P < 0.005) or umbilical venous (t = 4.17, P < 0.005) pressures.

Liver Blood Flow

Table 2 shows the weights of the liver and its various lobes in the 11 fetuses with portal venous catheters. The liver constituted approximately 3.3% of fetal body weight. Of special note is that the left lobe weighed more than the right lobe (t = 5.68, P < 0.001). Table 3 presents the results of our studies on normal blood flow to the fetal liver. Total blood flow to the liver was 315 ± 92 ml/min (mean ± SD), of which hepatic arterial flow contributed 9%, portal venous flow 18%, and umbilical venous flow 73%. Almost all portal blood flow to the liver was directed to the right and caudate lobes, although hepatic arterial and umbilical venous flows to the liver were approximately equally divided between the left and right portions of the liver. Approximately 40% of total flow supplied the left lobe, 51% the right, and 9% the caudate lobe. Total liver blood flow was directly related to liver weight (r = 0.61, P < 0.05), fetal weight (r = 0.76, P < 0.005), and gestational age (r = 0.86, P < 0.001).

Flow per unit of liver weight was large (435 ± 122 ml/min per 100 g). The right lobe of the liver received approximately 40% more blood flow per 100 g of tissue than the left lobe, even though the left lobe weighed more than the right. Blood supply to the caudate lobe was essentially the same as that of the right lobe.

Figure 2 shows the relative proportions of hepatic arterial, portal venous, and umbilical venous blood flow to each portion of the liver. Since anatomically the caudate is primarily a part of the right lobe, we have combined right and caudate lobe blood flows in Figure 2 for comparison. Within the right portion of the liver (right plus caudate lobes), the hepatic artery contributed 10%, the portal vein 30%, and the umbilical vein 60% of the
TABLE 3  **Blood Flow to the Liver, Supplied by the Hepatic Artery, Portal Vein, and Umbilical Vein, in Normal Fetal Lambs in Utero**

<table>
<thead>
<tr>
<th></th>
<th>Left lobe</th>
<th>Right lobe</th>
<th>Caudate lobe</th>
<th>Whole liver</th>
<th>Percent of combined ventricular output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic artery (ml·min⁻¹)</td>
<td>9 ± 15</td>
<td>18 ± 26</td>
<td>1 ± 1</td>
<td>28 ± 40</td>
<td>2.2</td>
</tr>
<tr>
<td>(ml·min⁻¹·100 g⁻¹)</td>
<td>23 ± 34</td>
<td>54 ± 68</td>
<td>18 ± 12</td>
<td>36 ± 45</td>
<td></td>
</tr>
<tr>
<td>Portal vein (ml·min⁻¹)</td>
<td>1 ± 2</td>
<td>43 ± 20</td>
<td>13 ± 9</td>
<td>57 ± 21</td>
<td>4.5</td>
</tr>
<tr>
<td>(ml·min⁻¹·100 g⁻¹)</td>
<td>4 ± 6</td>
<td>138 ± 50</td>
<td>256 ± 163</td>
<td>80 ± 25</td>
<td></td>
</tr>
<tr>
<td>Umbilical vein (ml·min⁻¹)</td>
<td>116 ± 33</td>
<td>100 ± 64</td>
<td>14 ± 9</td>
<td>230 ± 71</td>
<td>18.0</td>
</tr>
<tr>
<td>(ml·min⁻¹·100 g⁻¹)</td>
<td>329 ± 124</td>
<td>306 ± 140</td>
<td>290 ± 169</td>
<td>319 ± 95</td>
<td></td>
</tr>
<tr>
<td>Total (ml·min⁻¹)</td>
<td>126 ± 46</td>
<td>161 ± 78</td>
<td>28 ± 12</td>
<td>315 ± 92</td>
<td>24.7</td>
</tr>
<tr>
<td>(ml·min⁻¹·100 g⁻¹)</td>
<td>356 ± 129</td>
<td>498 ± 150</td>
<td>564 ± 175</td>
<td>435 ± 122</td>
<td></td>
</tr>
</tbody>
</table>

n = 11; values are mean ± sd.

Total flow per 100 g. The hepatic artery contributed 6% and the portal vein 1% of the flow per 100 g to the left lobe, while the umbilical vein supplied almost all of the flow (93%).

**Ductus Venosus Blood Flow**

Figure 3 shows the amounts of umbilical and portal venous blood flow that entered the ductus venosus in the 11 fetuses with portal vein catheters. We found that 53% (mean ± 9% sd, range 36-64%) of umbilical venous return bypassed the liver to enter the ductus venosus. Only 9% (mean ± 13% sd, range 0-43%) of portal venous blood flow passed through the ductus venosus. Since portal flow per kilogram of fetal body weight is low relative to umbilical venous flow, this contribution to ductus venosus flow is small; umbilical venous return to the fetus, therefore, accounts for more than 98% of ductus venosus flow.

Ductus venosus blood flow showed no consistent trend in the four fetuses in which we measured it 2-4 times in a single day. When we evaluated ductus venosus flow (per kilogram of fetal weight) as a function of gestational age, we could find no correlation in either the series of 15 fetuses in which we measured flow on a single day only (11 fetuses with portal venous catheters, and in the first study in four fetuses in which flow was determined 2-4 times in a single day) or in the series of seven fetuses in which we determined ductus flow either at daily intervals (three fetuses) or at 3- to 6-day intervals (four fetuses). Ductus venosus blood flow per unit weight, however, correlated closely with umbilical blood flow per unit weight (Fig., 4A and B) even though the proportion of umbilical venous return to the fetus that entered the ductus venosus showed no relationship to umbilical blood flow.
caudate lobes is surprising, since umbilical venous blood has been reported previously in acute studies on fetal lambs. Portal venous blood supplies the right and caudate lobes almost exclusively; this is consistent both with the anatomical arrangement of the portal venous circulations within the portal sinus. The function of the ductus venosus remains unclear at present. In some species (horse, pig), the ductus is obliterated very early in fetal development, yet in most species it is patent until after delivery. It may function to ensure an adequate venous return to the fetal heart when umbilical venous return fluctuates. Chacko and Reynolds and Dickson have suggested that the ductus venosus modulates umbilical and portal venous blood pressures to maintain an equilibrium between them for proper flow relationships in the liver and ductus venosus. Ductus venosus blood flow would therefore be related to pressures in the umbilical and portal circulations. Although we noted that umbilical and portal venous blood pressures were approximately equal, which would support this con-

Discussion
Liver Blood Flow
We have determined the blood flow to the fetal liver and through the ductus venosus of fetal lambs in utero. Blood flow to the whole liver is quite high, principally because of a large umbilical venous flow contribution. The circulations of the right and caudate lobes are similar to each other, a finding that supports the concept that the caudate is functionally, as well as anatomically, a part of the right lobe of the liver.

Hepatic arterial flow contributes approximately 2% of combined ventricular output to total liver blood flow, as has been reported previously in acute studies on fetal lambs. Portal venous blood supplies the right and caudate lobes almost exclusively; this is consistent both with the anatomical arrangement of the portal venous vascular system and with cineangiographic studies. The large umbilical venous contribution to the right and caudate lobes is surprising, since umbilical venous blood vessels do not extend to the right side of the liver. This large blood flow must cross the portal sinus to be distributed by portal blood vessels to the right side of the liver (Fig. 1). Because umbilical venous flow across the portal sinus (left to right) is high, this may explain why little portal blood reaches the left lobe or the ductus venosus via the portal sinus. The small amount that does reach the left lobe and ductus venosus may do so because the portal sinus in fetal lambs is wide (0.5–0.9 cm in diameter) and allows portal venous and umbilical venous blood to stream in opposite directions within it. In addition, during atrial systole, increased right atrial pressure is distributed retrograde through the thoracic inferior vena cava and ductus venosus to the umbilical recess. This intermittent change in venous pressure might also influence the hemodynamic relationship between the umbilical and portal venous circulations within the portal sinus.

Our finding that almost half of the umbilical venous blood flow to the fetal liver supplies the right side disagrees with cineangiographic observations on anesthetized fetal lambs that umbilical venous blood crosses the portal sinus but does not enter the parenchyma of the right lobe. The use of anesthetic agents may have influenced those cineangiographic results. The demonstration of a large umbilical flow to the right lobe makes it difficult to understand why fetal asphyxia affects the right lobe more than the left lobe. It is possible that the right and left lobes react differently to asphyxic stress.

There are some quantitative similarities between the circulation of the liver of fetal and adult sheep. In adult ewes, hepatic arterial flow to the whole liver is extremely small, approximately 2 ml/min per 100 g liver. Total portal blood flow is approximately 100–150 ml/min per 100 g liver. Therefore, total flow to the liver of adult sheep is similar to the total of hepatic arterial and portal venous flows that we have obtained in fetal lambs (116 ml/min per 100 g liver). The fact that portal blood flow accounts for over 95% of total liver flow in adult sheep is very different from studies in adult dogs or humans where portal blood flow contributes only about 60–75% of the total. The reason for this difference may be related to the peculiarities of the sheep's four-chambered digestive system. The major difference in the magnitude of liver blood flow between adult and fetal sheep is the umbilical venous supply to the fetal liver.

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

**Figure 4.** Ductus venosus blood flow (ml·min$^{-1}$·kg$^{-1}$ fetus) compared with umbilical blood flow (ml·min$^{-1}$·kg$^{-1}$ fetus). A: 15 fetuses with blood flow measured on a single day; B: 7 fetuses with blood flow determined either daily or at 3 to 6-day intervals.

There was no relationship between flow through the ductus venosus (total flow, flow per kg body weight, or flow as a percentage of umbilical venous blood flow) and mean blood pressure in the portal or umbilical vein. In those fetuses in which we measured ductus venosus flow more than once, changes in portal or umbilical blood pressure were not associated with consistent changes in flow. In addition, ductus venosus flow showed no obvious relationship to total liver blood flow; liver flow was not maintained by variations in blood flow through the ductus venosus.

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cept, we were unable to correlate ductus venosus blood flow with umbilical or portal venous pressure or umbilical-portal venous pressure differences. In addition, there was no obvious relationship of ductus venosus flow to total or lobar liver flows. Thus it is unlikely that the ductus changes its caliber and therefore its resistance to maintain a stable blood flow to the liver.

In our studies, the proportion of umbilical venous blood flow that passed through the ductus venosus varied within a more narrow range (36-64%) than has been reported previously in acute experiments on fetal sheep (34-91%). Human fetuses (8-92%), and fetal rhesus monkeys (30-71%). This large variability could be because those studies were performed on fetuses that were subjected to the acute influences of anesthetic and operative stresses. In sheep and human fetuses, larger umbilical venous blood flows were associated with a higher proportion of umbilical venous flow through the ductus venosus. Studies on fetal rhesus monkeys showed the opposite result; i.e., larger umbilical venous flows were associated with a smaller proportion of umbilical flow through the ductus. We were unable to show a relationship between that portion of umbilical venous return to the fetus that passes through the ductus and umbilical venous blood flow. Nor could we demonstrate an association between ductus venosus blood flow, corrected for fetal body weight, and gestational age. Nevertheless, the linear relationship between ductus venosus blood flow (per unit fetal weight) and umbilical blood flow (per unit fetal weight) suggests that, at least within the normal range for umbilical flow, the ductus venosus acts passively.

Our observation on undisturbed fetal lambs in utero that less than 10% of portal venous blood flow reaches the ductus venosus supports Amoroso et al. who analyzed the oxygen content of blood samples from portal vein, umbilical vein, and ductus venosus of anesthetized fetal lambs. They concluded that little, if any, portal blood enters the ductus. This also is consistent with our finding that more than 98% of ductus venosus blood is derived from umbilical venous blood.

It would be of additional interest to study the normal circulatory patterns of the newborn liver to determine when its circulation assumes that of the adult liver. Since the umbilical circulation ceases after birth, the major blood supply of the liver, and of the left lobe in particular, must come from the portal vein. Emery has shown that, in the presence of asphyxia in human newborns, the left lobe of the liver is particularly sensitive to degenerative changes, a finding that he relates to the sudden cessation of highly oxygenated umbilical venous blood and its replacement with poorly oxygenated portal venous blood.

In conclusion, we have determined the normal blood flow and its distribution to the fetal liver and ductus venosus in unanesthetized fetal lambs in utero. Blood flow to the liver is high, primarily because of a large umbilical venous blood flow. The question then arises, is this extremely large blood flow (and oxygen delivery) necessary for normal liver function and growth? In adult sheep, dog, and man, oxygen consumption by the liver is high (2-7 ml O₂/min per 100 g liver). It is not known what comparable values in the fetus are, but it is possible that specialized functions of the fetal liver, e.g., hematopoiesis, iron storage, steroid synthesis and metabolism, require a large blood flow and oxygen delivery. It also is not known whether or not each lobe of the liver receives its particular flow pattern because of certain unique functions that each lobe performs. If so, this could explain why the right lobe, which is smaller than the left one in fetal life, receives a much larger flow than the left lobe. This same phenomenon has been observed in adult sheep as well.

It would be important to determine what effect asphyxia, with its resultant fetal hypoxemia and decreased umbilical blood flow, has on blood flow to the fetal liver and ductus venosus. We have preliminary studies that show that marked decreases in umbilical blood flow produce decreases in total flow to the liver with a more striking reduction of flow in the right than in the left lobe. These studies suggest that perfusion of the left lobe by umbilical venous blood may be maintained at the expense of the right lobe. Furthermore, ductus venosus blood flow decreases linearly with reductions in umbilical blood flow. These findings could have important consequences in instances where umbilical flow decreases in response to fetal stress.

Appendix

Abbreviations

- \( Q_{H_L} \) = hepatic arterial blood flow to the liver
- \( Q_{PV} \) = portal venous blood flow (total)
- \( Q_{PVV} \) = portal blood flow to the liver
- \( Q_{PVV_DV} \) = portal blood flow through the ductus venosus
- \( Q_U \) = umbilical venous blood flow (total)
- \( Q_{UV} \) = umbilical blood flow to the liver
- \( Q_{UV_DV} \) = umbilical blood flow through the ductus venosus
- \( Q_{ref} \) = blood flow in descending aortic blood reference sample
- \( Q_{ov} \) = blood flow through the ductus venosus (total)

Other subscripts (in parentheses)

- (IVC) = derived from microspheres injected in inferior vena cava
- (PV) = derived from microspheres injected in portal vein
- (UV) = derived from microspheres injected in umbilical vein

\( CPM \) = radioactivity, counts per minute, in an organ or reference (ref) sample

Liver Blood Flow Calculations

1. Hepatic arterial blood flow to the liver: \( Q_{H_L} \) is calculated from (a) injection of microspheres in inferior vena cava (IVC), and (b) descending aortic blood reference sample.

\[
Q_{H_L} = \left( \frac{Q_{ref} \times CPM_{Liver \ (IVC)}}{CPM_{ref \ (IVC)}} \right)
\]
2. Portal venous blood flow to the liver: \( Q_{PV} \) is calculated from (a) injection of microspheres in inferior vena cava (IVC), (b) injection of microspheres in portal vein (PV), and (c) descending aortic blood reference sample.

\[
Q_{PV_L} = Q_{PV} - Q_{PVUV}
\]

\[
Q_{PV} = Q_{UV} + Q_{plc} + Q_{dV} + Q_{mes}
\]

(terminated from IVC injection)

and

\[
Q_{PV_L} = Q_{PV} \left( \frac{CPM_{liver (PV)}}{CPM_{fetus + placenta (UV)}} \right)
\]

A small error is introduced in these calculations by not including the recirculation of microspheres injected into the portal vein that enter the ductus venosus rather than the liver, are returned to the heart, and reach the liver subsequently via the hepatic artery. This error is quite small (less than 0.2%), since \( Q_{PVUV} \) is usually less than 10% of \( Q_{PV} \), and \( Q_{PV} \) is rarely larger than 60 ml/min, and the fraction, \( CPM_{liver (IVC)} / CPM_{fetus + placenta (IVC)} \), is generally less than 2%.

A second small error is present in calculation of total portal venous drainage. \( Q_{UV} \) actually includes some rectal blood flow that drains into hemorrhoidal veins rather than mesenteric veins.

3. Umbilical blood flow to the liver: \( Q_{UV} \) is calculated from (a) injection of microspheres in inferior vena cava (IVC), (b) injection of microspheres in umbilical vein (UV), and (c) descending aortic blood reference sample.

\[
Q_{UV} = Q_{U} - Q_{UV}
\]

\[
Q_{U} = \left( \frac{CPM_{placenta (IVC)}}{CPM_{fetus (IVC)}} \right)
\]

\[
Q_{UL} = Q_{U} \left( \frac{CPM_{liver (UV)}}{CPM_{fetus + placenta (UV)}} \right)
\]

but \( CPM_{liver (UV)} \) is not directly available. Total \( CPM_{liver (UV)} \) (sum of \( CPM_{UV} \) of microspheres that are trapped by liver on first circulation plus proportion of \( CPM_{UV} \) of microspheres that bypass the liver through the ductus venosus) is actually measured. \( CPM_{liver (UV)} \) represents microspheres that are trapped on the first circulation only and is calculated as follows:

\[
CPM_{liver (UV)} = \frac{CPM_{liver (UV)}}{CPM_{fetus + placenta (UV)}} (CPM_{liver (IVC)})
\]

solving for \( CPM_{liver (IVC)} \):

\[
CPM_{liver (IVC)} = \left[ \frac{CPM_{liver (UV)}}{1 + \left( \frac{CPM_{liver (UV)}}{CPM_{fetus + placenta (IVC)}} \right)} \right]
\]

and

\[
Q_{UL} = Q_{U} \left[ \frac{CPM_{liver (UV)}}{1 + \left( \frac{CPM_{liver (UV)}}{CPM_{fetus + placenta (IVC)}} \right)} \right]
\]

For blood flow to a particular lobe of the liver, \( CPM \) for that lobe is substituted for \( CPM_{liver} \), for both (UV) and (IVC).

Ductus Venosus Blood Flow Calculations

1. Actual ductus venosus blood flow is calculated from the sum of the components:

\[
Q_{DV} = Q_{UV} + Q_{PV}
\]

where

\[
Q_{UV} = Q_{U} - Q_{ul}
\]

and

\[
Q_{PV} = Q_{PV} - Q_{PV_L}
\]

2. When both portal venous (PV) and inferior vena cava (IVC) injections of microspheres are not available:

\[
Q_{UV} = Q_{U} \left[ 1 - \left( \frac{CPM_{liver (UV)}}{CPM_{fetus + placenta (UV)}} \right) \right]
\]

This introduces a maximum potential error of 6%. This error is only this large when 60% of the umbilical vein injection of microspheres enters the ductus venosus (rather than the liver), and 10% of this returns to the liver via the hepatic artery (which was present in only 1 of 11 fetuses).

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References

The Pericardium Substantially Affects the Left Ventricular Diastolic Pressure-Volume Relationship in the Dog

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SUMMARY We instrumented six dog hearts in vivo to study the relationship between left and right ventricular diastolic pressures with the pericardium closed and open. We measured left ventricular septum-to-free wall and anterior-posterior and right ventricular septum-to-free wall dimensions with implanted ultrasonic crystals, together with simultaneous high fidelity pressures. We varied diastolic pressure by infusing or withdrawing blood or by increasing right ventricular afterload with transient pulmonary artery constriction. Although left and right ventricular diastolic pressures always correlated, this correlation was significantly higher with the pericardium closed than open. We fit left ventricular diastolic pressure to an equation which included first order right ventricular pressure and fourth order left ventricular dimension terms. With the pericardium closed, the right ventricular pressure term dominated; with the pericardium open, left ventricular dimension terms dominated. Therefore, with the pericardium closed, right ventricular pressure was a more powerful predictor of left ventricular pressure than were left ventricular dimensions. In addition, the left ventricle appears much more compliant with the pericardium open. These results led us to modify the traditional view of the diastolic left ventricle as an unconstrained elastic shell of myocardium and replace it with a concept of the diastolic heart as a composite shell of stiff pericardium and compliant muscle, divided into subcompartments (ventricles) by the relatively compliant septum. The influence of the pericardium on the diastolic pressure-volume-relationship should be considered in experiments on animals and patient management when the pericardium is open or closed.

BERGLUND ET AL. suggested that the pericardium plays an important role in determining systolic function through its effects on the diastolic pressure-volume relationship. Spottntz and Kaiser demonstrated that the pericardium influences left ventricular filling pressure even at small volumes. Even so, virtually all contemporary studies of the heart's diastolic properties tacitly or explicitly treat the pericardium as a flaccid sac which encloses the heart and exerts important effects only at very large diastolic volume. A few workers used excised or isolated beating hearts with independent right and left ventricular loading to find a direct mechanical pressure coupling between the ventricles through the interventricular septum. These investigators stated that this coupling did not depend on the pericardium, but Elzinga et al. noted that leaving the pericardium closed tightened the pressure coupling. Our study integrates these lines of research by examining continuous ventricular dimensions and pressures in the in vivo dog heart. In contrast to earlier workers, we believe that the diastolic heart should be viewed as a whole, as a composite pericardium-myocardium shell, in which the pericardium plays the dominant role in determining diastolic pressure.

Theory

The traditional concept of the left ventricle during diastole considers it an unconstrained shell whose internal pressure depends on the wall muscle elasticity and mass and the ventricle's geometry. In the normally perfused
Liver and ductus venosus blood flows in fetal lambs in utero.
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