Relationships between Pressure and Flow in the Umbilical and Uterine Circulations of the Sheep

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SUMMARY We studied the relationship of fetal and maternal vascular pressures to umbilical and uterine blood flow in the unanesthetized ewe and in the sheep fetus in utero by placing electromagnetic flow transducers around both the common umbilical and uterine arteries. Reductions in umbilical arterial pressure or elevations in umbilical venous pressure decreased umbilical blood flow without affecting either the uterine arterial blood flow or other maternal cardiovascular variables which were studied. Elevations in uterine venous pressure or reductions in uterine arterial pressure decreased uterine arterial flow but these interventions had no effect on umbilical blood flow until fetal hypoxemia and bradycardia occurred. When the bradycardia of the fetal hypoxic response was inhibited by atropine, alterations in maternal vascular pressure had no effect on umbilical arterial flow. These data do not support the presence of a "sluice" or "waterfall" effect in the umbilical-placental circulation of the sheep fetus in utero.

THE Poiseuille-Hagen law, which describes the relationship of flow, resistance, and perfusion pressure in rigid tubes, conventionally is used to analyze organ blood flow. 1 Recently both theoretical 2-3 and other experimental 4-5 analyses have defined another hemodynamic system variously termed the waterfall, 6 capilleron, 6 or sluice 7 model. This model states that blood flow (Q') through a system of collapsible channels which are surrounded by a pressure (Pc) exceeding venous outflow pressure decreases umbilical blood flow inversely proportional to the resistance of the rigid vascular elements (R), but is unaffected by flow pressure (Pc) as long as Pc is greater than Pc, Q' = (Pc - Pc)/R, when Pc ≥ Pc.

Power and Longo 8 and Motoyama et al. 9 proposed that the uterine vascular system that surrounds the umbilical circulation of the sheep fetus generates a placental tissue pressure; this exceeds umbilical venous pressure and thereby regulates umbilical blood flow by this sluice mechanism. Their conclusions are based on experimental data obtained from acute studies, most of which involved perfusion of isolated placenomes.

To test the validity of the waterfall theory in vivo and study the relationship of fetal and maternal vascular pressures to umbilical and uterine blood flow in the sheep, we developed a preparation for the study of variables affecting placental flows in the standing, unanesthetized ewe and the fetal lamb in utero.

Methods

Operations were performed on 18 pregnant Western ewes with time-dated gestations of 100-140 days. They were fasted 24-48 hours, given epidural anesthesia with 2 ml of 1% tetracaine HCl (20 mg), and placed supine on the operating table. Polyvinyl catheters (inner diameter, 0.132 cm; outer diameter, 0.229 cm) were inserted through the maternal femoral artery and vein and advanced into the descending aorta and inferior vena cava. The ewes were given an intravenous infusion of 1000 ml of 10% dextrose in 0.9% saline during the operative procedure. Sodium pentobarbital (60-300 mg) was administered intravenously for sedation as required. A midline abdominal incision was made and the pregnant uterine horn exposed. A small hysterotomy was made to expose the fetus. Catheters were inserted into the fetal hindlimb artery and vein and advanced into the descending aorta and inferior vena cava, respectively. Catheters also were placed in the common umbilical vein, the amniotic cavity, and a large branch of the uterine vein draining the pregnant horn.

In each of the preparations a specially constructed electromagnetic flow transducer (Clark) was placed around the common umbilical artery of the fetus, as previously described. 10 In six of these preparations we monitored trends in uterine blood flow by placing an electromagnetic flow transducer around the middle sacral artery of the ewe, distal to the origin of the iliac arteries; this artery branches to form the right and left uterine arteries.

Balloon catheters were inserted to modify umbilical and uterine vascular pressures and were positioned so that pressure was measured on the placental side of the balloon. We used a No. 6 Swan-Ganz catheter, passed through a hindlimb artery, in the descending aorta of the ewe; a No. 4 Fogarty embolectomy catheter in the fetal descending aorta; and a balloon catheter, 1.4 cm in diameter, constructed from a polyvinyl tube (o.d., 0.254 cm) in the inferior vena cava of the ewe proximal to the entry of the uterine veins. The end hole of a No. 4F Swan-Ganz catheter was plugged with epoxy resin and a side hole was cut proximal to the balloon; the tip of this catheter was advanced 3 cm into the common umbilical vein. Positions of all catheters were verified by postmortem examination.

All catheters and flow transducer cables were led to the flank of the ewe and protected by a Teflon pouch sewn to the
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skin. The uterus and abdominal wall were sutured, and the ewe was allowed to recover. Procaine penicillin G (400,000 U) and dihydrostreptomycin (0.5 g) (Distrilycin, 2 ml) were administered intramuscularly to the ewe on the day of surgery. Kanamycin (400 mg) and potassium penicillin (1 million U) were administered into both the amniotic cavity and the inferior vena cava of the ewe on each of the first five postoperative days.

Observations were made 2–7 days postoperatively while the ewe stood undisturbed in her cage; pressures were measured with Statham P23Dc transducers and flows with Statham SP2202 blood flowmeters (frequency response, flat to 100 Hz; percent error, ±5%; reproducibility, ±2%) and recorded on a Beckman type RM direct-writing recorder.

Heart rate was recorded by a Beckman type 9857B cardiometer. Fetal arterial blood pH, P02, and PCO2 were measured with a Radiometer gas analyzer and appropriate electrodes. Fetal hematocrits also were measured. Of the 18 fetuses, five which had arterial blood pH <7.3, P02 <19 mm Hg, or PCO2 >50 mm Hg were excluded. All fetal pressures were corrected to amniotic fluid pressure as zero reference. Mean fetal aortic pressure was assumed to equal mean common umbilical arterial pressure.

Uterine or umbilical venous pressure was elevated and uterine or umbilical arterial pressure was reduced by inflation of the appropriate balloons. In the 13 preparations satisfactory technical recordings, fetal arterial blood pH, P02, and PCO2, and balloon function were obtained on 23 separate study days, during each of which balloons were inflated repeatedly. Since two balloon catheters were placed in four ewes, we were able to study uterine venous pressure elevation in eight preparations, umbilical venous pressure elevation in three, umbilical arterial pressure reduction in three, and uterine arterial pressure reduction in three.

Serial measurements of fetal arterial blood gas were made during each type of pressure alteration. The magnitude and duration of balloon inflation were varied in each study.

Since, in the first three animals studied, balloon inflations produced changes in fetal heart rate and consequent changes in umbilical arterial flow, we administered 0.4 mg of atropine sulfate into the fetal inferior vena cava prior to balloon inflation in the later studies; these included all balloon inflations performed in the fetus.

The relationship between the degree and duration of uterine venous pressure elevation and umbilical blood flow was examined in a 2 x 3 chi-square table in which each entry was >5.

Linear regression curves were derived relating either elevation of uterine or umbilical venous pressure or reduction of uterine or umbilical arterial pressure to percentage change in uterine or umbilical blood flow. The confidence limits of the slope (Sx) and the points about the line were used to test whether or not the line intersected the origin of the x and y axes. The slope of the line relating uterine venous pressure to percent reduction in uterine arterial flow was determined by the x/y ratio method, since the standard deviation of the points about the line increased as the x value increased.

Results

In Table I are listed values for fetal vascular pressures, fetal heart rate, maternal vascular pressures, umbilical blood flow, fetal arterial blood gases, and hematocrits, with their appropriate statistical variables.

Umbilical blood flow prior to manipulation was 187 ml/min per kg of fetal weight, a value not significantly different from the average umbilical flow of normal fetuses whose umbilical blood flow was measured by the same technique. Vascular pressures and arterial blood gases were similar to those recorded in other chronic preparations in utero. For all fetuses pH was ≥7.30, P02 ≥19 mm Hg, and PCO2 ≤50 mm Hg.

UTERINE VENOUS PRESSURE ELEVATION

On 60 occasions, mean uterine venous pressure was elevated to levels of 17–70 mm Hg in eight preparations.

![FIGURE 1 The relationship between uterine venous pressure elevation and the percentage decrease in uterine arterial blood flow, as measured in four preparations. Each data point represents one pressure elevation. Sx = standard error of the ratio, y/x. Sy = standard error of the slope.](http://circres.ahajournals.org/doi/figure/1)
Uterine blood flow was measured in four preparations and fell by 12–82% within 1–2 seconds (Fig. 1). When uterine venous pressure was increased to levels less than 30 mm Hg, umbilical arterial blood flow was not affected even when these levels were maintained for longer than 120 seconds. However, some pressure elevations greater than 30 mm Hg produced a late fall in umbilical arterial blood flow (Fig. 2).

In Table 2 the amount and duration of uterine venous pressure elevation are related to changes in umbilical blood flow. The relationship between the duration and magnitude of uterine venous pressure elevation and the presence or absence of an effect on umbilical blood flow is significant by the chi-square test, \( P < 0.05 \). The delayed reduction in umbilical arterial blood flow was always associated with fetal arterial hypoxemia (Po2, 10–16 mm Hg) and bradycardia (Fig. 2). When atropine was given to the fetus prior to uterine venous pressure elevation, the fetal bradycardia associated with hypoxemia was inhibited and umbilical arterial blood flow did not fall.

Maternal arterial pressure fell by 10–65 mm Hg with uterine venous pressure elevations greater than 25 mm Hg during seven of nine inflations but did not change significantly with uterine venous pressure elevations of less than 25 mm Hg.

**UTERINE ARTERIAL PRESSURE REDUCTION**

Reductions in mean uterine arterial pressure of 15–55 mm Hg for 20–180 seconds reduced uterine arterial blood flow to 20–76% of control (Fig. 3). Umbilical blood flow changed only once when uterine arterial mean pressure was reduced by 55 mm Hg for 80 seconds. The 28% fall in umbilical blood flow which occurred 100 seconds after the initiation of uterine arterial pressure reduction was associated with a fall of fetal arterial Po2 to 14 mm Hg, hypertension, and bradycardia. Reductions in uterine arterial pressure were never associated with an increase in umbilical blood flow.

**UMBILICAL VENOUS PRESSURE ELEVATION**

Elevations in mean umbilical venous pressure of 1–35 mm Hg immediately reduced umbilical blood flow without changing uterine arterial or venous pressure, maternal heart rate, or uterine arterial blood flow (Fig. 4).

When umbilical venous pressure was raised by less than 10 mm Hg for less than 8 seconds, fetal heart rate and arterial pressure did not change. However, with more prolonged or greater elevations, fetal arterial pressure fell transiently, then rose in association with fetal bradycardia. Hypoxemia was confirmed by fetal arterial blood gas determinations at the time when bradycardia and hypertension developed. Umbilical venous Po2, however, increased by 3–7 mm Hg at the time that umbilical arterial Po2 fell.

![Figure 2](image-url)

**Figure 2** An elevation of uterine venous (UtV) pressure to 75 mm Hg for nearly 30 seconds causes fetal bradycardia and hypertension, with a secondary fall in umbilical arterial blood flow. Fetal arterial (FA) blood gases prior to and during the uterine venous pressure elevation document fetal arterial hypoxemia. MIVC = maternal inferior cava.

![Figure 3](image-url)

**Figure 3** The relationship between mean uterine arterial pressure reduction and the percentage decrease in uterine arterial blood flow. Each data point represents one pressure reduction. \( S_{y-x} \) = standard error of the points about the mean.
UMBILICAL ARTERIAL PRESSURE REDUCTION

Reductions in mean umbilical arterial pressure of 2–23 mm Hg for periods of 7–70 seconds caused an immediate fall in umbilical blood flow of 6–66%, but had no effect on uterine blood flow (Fig. 5).

When umbilical arterial pressure was reduced by less than 12 mm Hg for 10 seconds or less, fetal hypoxemia and bradycardia were not noted. However, with more prolonged or greater pressure reductions, fetal arterial hypoxemia ensued and was accompanied by fetal bradycardia and fetal arterial hypertension above baseline levels after the balloon was released. Umbilical venous PO₂ rose 3–9 mm Hg when umbilical arterial PO₂ fell. The response of umbilical blood flow to umbilical arterial pressure reduction was instantaneous, and the level of umbilical flow followed umbilical arterial pressure in a parallel, stepwise fashion.

Discussion

Power and Longo [1] proposed that the uterine circulation in sheep generates a placental tissue pressure which above a certain level exerts a critical effect on fetal umbilical-placental blood flow. They suggested that the pressure exerted by this surrounding tissue can exceed umbilical venous pressure and thereby establish a "sluice" or "waterfall" relationship between the uterine and umbilical circulations. They invoked this mechanism in the human to explain clinical obstetrical syndromes associated with alterations in uterine arterial or venous pressure, viz., the supine hypoten sive syndrome or uterine contractions. In both instances, they suggested, uterine venous pressure elevation increased surrounding tissue pressure, thus intensified a placental waterfall system and reduced umbilical blood flow or elevated umbilical arterial pressure, or both. They further proposed that changes in fetal heart rate commonly noted during uterine contractions and the supine hypertension syndrome are due to fetal baroreceptor and chemoreceptor reflexes precipitated by reduced umbilical flow, elevated fetal arterial pressure, and fetal hypoxemia.

We developed a model to study the relationship of maternal and fetal vascular pressures to both uterine and umbilical blood flows in standing, unanesthetized ewes and their fetuses in utero. The accuracy, methodology, and advantages of monitoring instantaneous changes in umbilical blood flow in the fetal lamb in utero by placing an electromagnetic flow transducer around the common umbilical artery have been described previously. [10] We have established that an electromagnetic flow transducer placed around the middle sacral artery of the ewe reflects trends in uterine arterial flow. Although the measured flow values are 80–85% of those derived from simultaneous radionuclide microsphere injections, the continuous recording of uterine arterial blood flow which the flow transducer provides allowed us to study instantaneous changes in the trend of uterine blood flow.

Our studies show that uterine, but not umbilical, blood flow is decreased instantaneously by elevation of uterine venous pressure or reduction of uterine arterial pressure. A variable and delayed fall in umbilical blood flow consequent to fetal hypoxemia can result from the reduced uterine arterial flow. The bradycardia of fetal hypoxemia [12] may be responsible for the late fall in umbilical flow, because its prevention by atropine abolishes the decrease in umbilical blood flow associated with the hypoxic response.

The maternal hypotension which is consequent to elevation of uterine venous pressure by inflation of the inferior vena cava balloon in the ewe is probably related to decreased systemic venous return. The contribution made by reduced systemic venous return to the reduction of cardiac output and systemic arterial pressure was not systematically analyzed in this study.

Umbilical blood flow is directly, reproducibly, and instantaneously decreased by elevation of umbilical venous pressure or reduction of umbilical arterial pressure. Fetal pressure alterations had no measurable effect on uterine blood flow or the other maternal cardiovascular variables monitored. Even though umbilical arterial and venous pressure alterations could result in fetal hypoxemia and bradycardia, the fall in umbilical flow was not a consequence of the bradycardia, because atropine, which prevented the bradycardia, did not abolish the fall in umbilical flow caused by fetal pressure manipulations.

Moreover, since the fall in umbilical blood flow was immediate, it could not have been related to alterations in flow patterns or a fall in venous return or cardiac output.
The late occurrence of fetal systemic hypotension which occurred only after prolonged balloon inflations also suggests this.

It is noteworthy that fetal arterial hypoxemia resulting from umbilical venous or arterial pressure changes was accompanied by an elevation of umbilical venous PO2. Both umbilical venous pressure elevation and umbilical arterial pressure reduction slow the circulation of blood through the fetal placental vascular bed. The elevations in umbilical venous oxygen tension noted during those periods of reduced flow velocity support the presence of a time-dependent diffusion limitation to transplacental oxygen transfer. When umbilical flow is slowed, the time for equilibration between fetal and maternal oxygen tension increases and umbilical venous PO2 rises.

The umbilical-placental circulation in the fetal lamb does not act as a collapsible circuit in which surrounding tissue pressure is determined by the uterine circulation. These findings differ from those of Power and Longo, who perfused isolated placemomes with hypoxic maternal blood (PO2, 15 mm Hg), using low, constant, nonpulsatile flows (0.31–2 ml/min). They were dealing with an already hypoxic umbilical-placental circulation prior to any pressure manipulations. Also, the pressure changes they noted were small and not subjected to statistical analysis.

The pressure-flow relationships we describe for sheep offer an alternative to the “sluice” theory to explain several clinical obstetrical syndromes. Uterine blood flow may be reduced during uterine contractions by maternal hypotension, or in the supine hypotensive syndrome when uterine venous pressure is elevated while systemic arterial pressure falls. Low uterine arterial flow from whatever cause can lead to fetal hypoxemia, bradycardia, and a secondary fall in umbilical blood flow. Umbilical cord compression, on the other hand, may reduce umbilical flow directly, both by increasing umbilical venous pressure and decreasing distal umbilical arterial pressure. Changes in fetal heart rate might then result from fetal hypoxemia secondary to decreased umbilical flow, arterial hypertension, or a reduction in umbilical venous return and, therefore, in fetal arterial pressure if the cord compression preferentially obstructs the umbilical vein.

The uterine and umbilical circulations react independently to changes in their inflow and outflow pressures. Changes in fetal vascular pressures and umbilical blood flow do not alter uterine arterial or venous pressure and do not affect uterine blood flow. Uterine flow reductions, however, can indirectly decrease umbilical blood flow when fetal hypoxemia occurs. Our data indicate that fetal cardiovascular dynamics and baroreceptor- and chemoreceptor-mediated reflexes, rather than uterine vascular pressures, are the critical determinants of umbilical blood flow in the fetal lamb.

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