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Effect of Halothane on Regional Cerebral Blood Flow and Cerebral Metabolic Oxygen Consumption in the Fetal Lamb In Utero

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The effects of halothane on maternal and fetal hemodynamics, distribution of fetal cardiac output, regional cerebral blood flow, and fetal cerebral oxygen consumption were studied in the ewe (N = 9) using radionuclide-labeled microspheres. An adjustable uterine artery occluder was used to produce a controlled state of fetal asphyxia. Measurements were taken during three periods of study: 1) control, 2) asphyxia, and 3) asphyxia plus 15 min of 1% maternal halothane. The fetal cardiovascular response to asphyxia was acidosis, hypoxia, hypertension, bradycardia, and preservation of vital organ blood flows. There was a significant drop in maternal blood pressure when halothane was administered but uterine blood flow was maintained, 308 $ml \cdot min^{-1}$ during asphyxia *versus* 275 $ml \cdot min^{-1}$ with halothane. Fetal blood pressure during asphyxia plus halothane (54 mmHg) was significantly lower than that during asphyxia alone (59 mmHg), while heart rate was significantly higher: 172 beats per minute (bpm) *versus* 125 bpm ($P < 0.05$). Despite these changes, the administration of halothane during asphyxia did not produce a reduction in vital organ flows. Cerebral blood flow was maintained: 357 ± 37 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ during asphyxia alone and 344 ± 26 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ after halothane administration (P = NS, mean ± SEM). Cerebral oxygen delivery also was maintained: 8.3 ± 0.8 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ during asphyxia alone *versus* 9.7 ± 1.5 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ after halothane, compared with 11.2 ± 1.1 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ during the control period. Cerebral oxidative metabolism ($CMRO_2$) decreased significantly from 4.1 ± 0.6 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ during control to 2.8 ± 0.4 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ during asphyxia alone, but no further significant change occured after halothane (2.0 ± 0.3 $ml \cdot 100\ g^{-1} \cdot min^{-1}$). Fetal myocardial blood flow was maintained: 625 ± 93 $ml \cdot 100\ g^{-1} \cdot ml^{-1}$ during asphyxia alone *versus* 529 ± 79 $ml \cdot 100\ g^{-1} \cdot min^{-1}$ after halothane administration. The authors conclude that the addition of 1% maternal halothane in the briefly asphyxiated fetal lamb does not abolish the protective reflexes of increased coronary and cerebral blood flow and decreased $CMRO_2$. **Key words: Anesthesia: obstetric. Anesthetics, volatile: halothane. Brain: blood flow; metabolic rate of oxygen. Complications: fetal asphyxia. Hemodynamics, fetal: cardiovascular; cerebral blood flow; organ blood flow. Hemodynamics, maternal: heart rate; MABP; uterine blood flow.)**

PERINATAL ASPHYXIA exposes the fetal brain to the risk of permanent brain damage. General anesthesia in modern obstetrics is often reserved for emergency situations in which the fetus is at the greatest risk for asphyxia, such as umbilical cord prolapse, maternal hemorrhage, breech extraction, and fetal distress. Unfortunately, we do not yet know which anesthetic agents best optimize the fetal milieu during such emergencies. Recent studies have examined the response of the asphyxiated fetal lamb to halothane using an umbilical cord occlusion model,[1,2] which mimics umbilical cord compression. We used a recently developed technique of uterine artery occlusion,[3] which mimics any situation in which uterine blood flow is reduced. As a first step in evaluating various anesthetic agents during reduced uterine blood flow, we studied the effect of halothane on maternal and fetal cardiovascular hemodynamics, fetal regional blood flow, and cerebral metabolic oxygen consumption.

Materials and Methods

These studies were approved by the Committee on Animal Research at the University of California, San Francisco.

SURGICAL PREPARATION

Nine lambs were studies *in utero* at 120–127 days gestation (term = 145 days). Dorset ewes were surgically prepared as follows. Anesthesia was achieved with tetracaine administered into the lumbar subarachnoid space and iv infusion of ketamine while the ewe breathed oxygen by mask. An incision was made in the groin through which polyvinyl catheters (PVCs) were inserted into maternal femoral artery and vein. The uterus was exposed through a midline abdominal incision and a wire occlusion loop was secured to the com-

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mon uterine artery. A Doppler flow probe (Gould Statham, Oxford, CA) was placed distal to the occluder on the artery supplying the gravid horn and after proper adjustment used as a direct measurement of uterine blood flow. The fetus was then exposed through a hysterotomy incision, and PVCs were placed in the common brachiocephalic trunk *via* axillary artery, inferior vena cava *via* hindlimb vein (for microsphere injection), femoral artery and the sagittal sinus anterior to the cranial lambdoidal suture. Finally, all incisions were closed and the catheters tunnelled subcutaneously to the maternal flank. Each animal was allowed to recover for 40–96 h prior to study.

PROTOCOL AND MEASUREMENTS

Maternal and fetal blood pressure, uterine artery blood flow, intra-amniotic pressure, fetal heart rate, and electrocardiogram were measured continuously throughout the study on a Grass® Model 8 (Quincy, MA) or Beckmann® R411 Dynograph Recorder (Schiller Park, IL) multichannel recorder. Maternal femoral arterial blood gases and fetal axillary artery, femoral artery, and sagittal sinus blood gases were measured at the beginning of the control period and 5 min before and after each of three microsphere injections to ensure stability of the fetal lamb. A Corning® 158 *p*H/Blood Gas Analyzer (Medfield, MA) and OSM2 Hemoximeter Radiometer (Copenhagen, Denmark) saturation analyzer were used. No studies were performed unless fetal axillary arterial *p*H was greater than 7.35 and fetal P_{O_2} was greater than 15 mmHg at the beginning of the control period.

During the control period, ewes were placed in the left lateral decubitis position to breathe room air for 30 min while blindfolded to help induce calm. At the end of the control period, the first injection of radionuclide-labeled microspheres was made into the fetal inferior vena cava over a period of 15 s. Withdrawal of blood from the fetal femoral and axillary arteries began 20 s before injection of microspheres, and continued for a total of 90 s (Harvard® Infusion Pump, Millis, MA). These samples were subsequently used to calculate blood flow to organs above and below the ductus arteriosus using the method of Rudolph and Heymann.[4] The fetus was transfused with maternal blood after this and subsequent microsphere injections, and after blood withdrawal to prevent hypovolemia.

After the control period, fetal asphyxia was produced by gradually tightening the uterine artery occluder until a transient fetal bradycardia occurred or uterine artery blood flow was reduced to 50% of control. Blood gases were taken and analyzed every 10–15 min, and the occluder adjusted to achieve a stable acidosis, *i.e.*, *p*H range, 7.10–7.20 with a change of less than ± 0.03 over 15 min. The uterine artery remained partially occluded throughout the experiment.

When a stable fetal asphyxia was achieved, a second microsphere injection was made. Halothane (5%/O_2) was administered by face mask to induce anesthesia, and succinylcholine (1 mg/kg iv) was given to facilitate intubation of the trachea. The induction-to-intubation time was noted. After tracheal intubation, additional halothane (1% inspired) was administered for 15 min by mechanically controlled ventilation through a circle system. Maternal end-tidal halothane gas samples were analyzed with a Beckman LB-2 Infrared-Medical Gas Analyzer (Fullerton, CA) at 5, 10, and 15 min. At 15 min, a third microsphere injection was made into the fetal circulation.

At the end of the experiment, the ewe was killed with Euthanol® and succinylcholine. The fetus was autopsied and the fetal organs were removed, carbonized, ground, and then placed in counting vials. The organ samples were counted for radioactivity and the resulting counts used with fetal samples to calculate organ blood flow. If microspheres are homogenously distributed in the arterial supply of an organ and are completely removed with one passage through the organ, organ blood flow can be calculated by the equation:[5]

$$F = Fa \times (i \text{ organ}/i \text{ arterial}),$$

where F = organ flow ($ml \cdot 100\ g^{-1} \cdot min^{-1}$); Fa = withdrawal rate of the reference arterial blood sample ($ml \cdot min^{-1}$); *i* organ = microsphere content of the organ tissue ($cpm \cdot 100\ g^{-1}$); and *i* arterial = microsphere content of the total reference arterial blood sample (cpm). The total of all organ blood flows was considered the cardiac output of the fetus. However, true biventricular output was probably higher by approximately 10%, because we took no reference sample from the lung and, therefore, could not calculate lung blood flow into total organ flow.

The fetal brain was fixed in formalin, then dissected into parts and processed as the other organs. The position of the sagittal sinus catheter was confirmed at autopsy. The O_2 content of arterial and venous blood was calculated according to the formula: O_2 content = Hb ($g \cdot 100\ ml^{-1}$) × 1.34 × % saturation + (.003 × P_{O_2} [mmHg]). Cerebral O_2 delivery was calculated as the product of hemispheric cerebral blood flow ($ml \cdot 100\ g^{-1} \cdot min^{-1}$) × (Ca O_2 $ml \cdot 100\ ml^{-1}$) × 0.01, where CaO_2 = axillary arterial O_2 content. Cerebral O_2 consumption ($CMRO_2$) was calculated from hemispheric cerebral blood flow using a modification of the Fick equation (CBF $ml \cdot 100\ g^{-1} \cdot min^{-1}$) × $C(a\text{-}v)O_2$ ($ml \cdot 100\ ml^{-1}$) × 0.01, where $C(a\text{-}v)O_2$ = axillary artery minus sagittal sinus O_2 content.

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TABLE 1. Maternal and Fetal MABP and Heart Rate During Control Period Production of Fetal Asphyxia, and Administration of Maternal Halothane*

	Control	Asphyxia	Halothane & Asphyxia
Maternal			
MABP N = 8	90 ± 6	96 ± 6	79 ± 7†‡
Uterine Blood Flow N = 6	631 ± 105	308 ± 44†	275 ± 51†
Heart rate N = 8	104 ± 9	99 ± 9	110 ± 5
Fetal			
MABP N = 9	51 ± 4	59 ± 4†	54 ± 4‡
Heart rate N = 9	174 ± 7	125 ± 7†	172 ± 16‡

* Mean ± SE pressures in mmHg, rate in beats per minute, blood flow in ml · min^{-1}.
† $P < 0.05$ = significantly different from control.
‡ $P < 0.05$ = significantly different from asphyxia.

TABLE 2. Maternal and Fetal Blood Gases and Acid-base Data During Control Period, Production of Fetal Asphyxia, and Administration of Maternal Halothane*

	Control	Asphyxia	Halothane & Asphyxia
Maternal			
*p*H	7.52 ± 0.01	7.53 ± 0.01	7.46 ± 0.03†‡
BE	5.3 ± 1	7.0 ± 0.9	3.9 ± 1.7†‡
[H^+]	19.8 ± 0.5	29.2 ± 0.6	35.4 ± 2.1†‡
P_{O_2} mmHg	79 ± 3	93 ± 10	394 ± 42†‡
P_{CO_2} mmHg	33 ± 2	34 ± 2	40 ± 2†‡
Hemoglobin	8.8 ± 0.3	9.2 ± 0.2	8.6 ± 0.4
Fetal (axillary art)			
*p*H	7.38 ± 0.01	7.14 ± 0.02†	7.02 ± 0.03†‡
BE	3.3 ± 1.2	−8.8 ± 1.0†	−13.8 ± 0.8†‡
[H^+] nmole/L	41.8 ± 1.4	72.9 ± 3.1†	97.7 ± 5.8†‡
P_{O_2} mmHg	19 ± 1	17 ± 2	23 ± 3
P_{CO_2} mmHg	50 ± 3	62 ± 6†	68 ± 5†
SA_{O_2} %	45 ± 5	20 ± 2†	25 ± 3†
Content O_2 ml · 100 ml	6.0 ± 0.5	2.8 ± 0.2†	3.4 ± 0.4†
Hemoglobin (N = 9)	9.9 ± 0.3	10.5 ± 0.3	10.1 ± 0.20

* N = 8 Maternal, N = 9 Fetal, Mean ± SE.
† $P < 0.05$ = significantly different from control.
‡ $P < 0.05$ = significantly different from asphyxia.

DATA ANALYSIS

The following data were compared: control values *versus* values obtained during asphyxia alone, control *versus* asphyxia plus halothane, and asphyxia alone *versus* asphyxia plus halothane. Using a repeated measures analysis of variance, if the overall F test was significant, individual comparisons between individual periods were made using the Newman-Keuls' test.[6] Where sample sizes were smaller, appropriate F and q values were used. Differences were considered statistically significant when $P < 0.05$.

Results

Tables 1–3 summarize the maternal and fetal cardiovascular and arterial blood gas measurements and fetal organ blood flows. Maternal heart rate did not change significantly during the three periods of the study (table 1). During asphyxia plus halothane, maternal Pa_{O_2} increased significantly, while *p*H decreased significantly (table 2). There was no significant difference in uterine blood flow between asphyxia alone and asphyxia plus halothane, despite a significant decrease in maternal blood pressure during asphyxia plus halothane.

Partial uterine artery occlusion produced a stable acidosis in 36 ± 7 min (mean ± SE). At that time, fetal mean arterial blood pressure (MABP) increased significantly from a control value of 51 ± 4 mmHg to 59 ± 4 mmHg ($P < 0.05$), and fetal heart rate decreased significantly from 174 ± 7 to 125 ± 8 bpm (table 1). Fetal *p*H decreased from a control value of 7.38 ± .01 to 7.14 ± .02, and fetal P_{CO_2} rose from 50 ± 3 to 62 ± 6 mmHg ($P < 0.05$). Fetal P_{O_2} did not change significantly during either period of asphyxia (table 2).

Total brain blood flow increased significantly from 214 ± 19 ml · 100 g^{-1} · min^{-1} during control to 357 ± 37 ml · 100 g^{-1} · min^{-1} during axphyxia alone, indicating a significant fall in cerebral vascular resistance (table 4). Regional brain blood flow during both periods of asphyxia increased from control in subcortical areas, especially in the brainstem, by a much greater percentage (102%) than flow to the hemispheres (61%) (fig. 1).

TABLE 3. Fetal Regional Blood Flows and Calculated Fetal Cardiac Output at Control During Production of Fetal Asphyxia and Administration of Maternal Halothane*

Organ System ml · 100 g^{-1} · min^{-1}	Control	Asphyxia	Halothane and Asphyxia
Heart	286 ± 24	625 ± 93†	529 ± 79†
Brain	214 ± 19	357 ± 37†	344 ± 26†
Thymus	85 ± 11	41 ± 6†	52 ± 12†
Adrenal	306 ± 50	852 ± 199†	686 ± 143†
Gut‡	83 ± 7	44 ± 7†	58 ± 11†
Spleen	429 ± 101	162 ± 70†	158 ± 64†
Kidney	213 ± 22	102 ± 19†	103 ± 16†
Placenta	197 ± 33	232 ± 57	183 ± 47
Carcass§	27 ± 3	11 ± 2†	10 ± 2†
Calculated fetal cardiac output ml · min^{-}	919 ± 109	711 ± 83†	708 ± 91†

* Mean ± SE, N = 9.
† $P < 0.05$ = significantly different from control.
‡ Includes stomach, small and large bowel.
§ Includes musculo-skeletal system and skin.

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TABLE 4. Regional Brain Blood Flow*

Brain Region ml·100 g^{-1}·min^{-1}	Control	Asphyxia	Halothane and Asphyxia
Cerebral hemisphere	193 ± 22	304 ± 33†	285 ± 23†
Cerebellum	246 ± 20	441 ± 45†	426 ± 31†
Brainstem‡	344 ± 26	682 ± 76†	675 ± 45†
Total brain	214 ± 19	357 ± 37†	344 ± 26†

* Mean ± SE, n = 9.
† $P < 0.05$ = significantly different from control.
‡ Includes only medulla.

Myocardial and adrenal organ blood flows during both periods of asphyxia also were significantly higher than flows during control (table 3). Blood flows to the immediately nonvital organs, such as kidneys, gut, spleen, thymus, and carcass (musculoskeletal system and skin), declined significantly from control. Calculated fetal cardiac output decreased from 919 ± 109 ml·min^{-1} during control to 711 ± 83 ml·min^{-1} during asphyxia alone, and 708 ± 91 ml·min^{-1} during asphyxia plus halothane.

Cerebral O_2 consumption (hemispheres), which was 4.1 ± 0.6 ml·100 g^{-1}·min^{-1} during control, decreased during asphyxia alone to 2.8 ± 0.4 ml·100 g^{-1}·min^{-1} (table 5). Fetal axillary arterial O_2 content also decreased significantly from 6.0 ± 0.5 ml·100 ml^{-1} during control to 2.8 ± 0.2 ml·100 ml^{-1} during asphyxia (table 2). Despite the drop in arterial O_2 content, cerebral O_2 delivery did not change significantly from control: 11.2 ± 1.1 ml·100 g^{-1}·min^{-1} *versus* 8.3 ± 0.8 ml·100 g^{-1}·min^{-1} during asphyxia ($P > 0.05$ but < 0.1) (table 5).

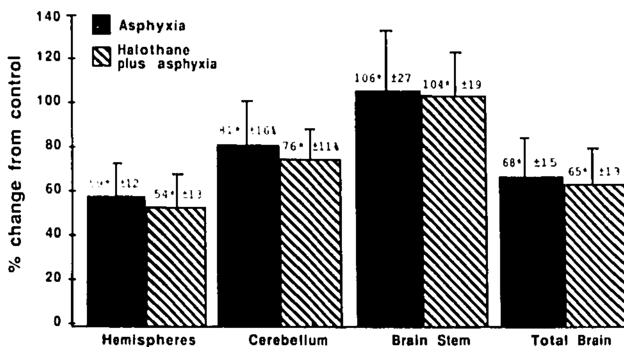

FIG. 1. Changes from control regional cerebral blood flow following asphyxia and asphyxia plus halothane. Blood flow to all areas of the brain increased when asphyxia was induced, but remained unchanged with the induction of anesthesia with halothane. The brainstem received the greatest increase in blood flow.

TABLE 5. Cerebral Metabolic Measurements*

	Control	Asphyxia	Halothane & Asphyxia
Arterial O_2, ml/100 ml	6.0 ± 0.5	2.8 ± 0.2‡	3.4 ± 0.4‡
Cerebral A-V O_2 difference, ml/100 ml	2.2 ± 0.2	1 ± 0.2‡	0.8 ± 0.2‡
Cerebral blood flow† ml·100 g^{-1}·min^{-1}	193 ± 22	304 ± 33‡	285 ± 23‡
Cerebral O_2 delivery† ml·100 g^{-1}·min^{-1}	11.2 ± 1.1	8.3 ± 0.8	9.7 ± 1.5
Cerebral O_2 consumption§ ml·100 g^{-1}·min^{-1}	4.1 ± 0.6	2.8 ± 0.4‡	2.0 ± 0.3‡

* Mean ± SE (N = 9, except † where N = 7).
‡ $P < 0.05$ = significantly different from control.
§ Hemisphere.

Maternal induction-to-tracheal intubation time with 5% halothane/O_2 was 4.3 ± 0.3 min. End-tidal halothane levels after administration of 1% halothane/O_2 were 0.62 ± .01, 0.67 ± .01, and 0.68 ± .01 vol% at 5, 10, and 15 min, respectively (N = 5). The addition of halothane produced the following changes: fetal MABP decreased significantly from asphyxial levels toward control, while heart rate increased to control levels (table 1); fetal *p*H dropped significantly to 7.14 ± .02 during asphyxia alone, and 7.02 ± .03 during asphyxia plus halothane (table 2); fetal P_{O_2} remained unchanged (table 2); fetal P_{CO_2} and arterial O_2 content increased significantly from control, but were similar to values obtained during asphyxia alone (table 2).

A comparison of the periods of asphyxia alone and after the addition of halothane revealed that fetal organ blood flows and cardiac output were unchanged, although significantly different from control (table 3). The same pattern held for cerebral arterial blood flows (fig. 1) and fetal cerebral metabolic O_2 consumption and O_2 delivery (table 5).

Discussion

When emergency intervention for the stressed fetus requires cesarean delivery with general anesthesia, there is little information to guide the anesthesiologist in the choice of an inhalation agent. Although fetal cardiovascular and circulatory responses to asphyxial stress (maternal hypoxia or umbilical cord occlusion) have been studied,[7] the response of the stressed fetus to inhalation agents has received little attention. Data regarding fetal cerebral metabolism and cerebrovascular response to maternal anesthetics are incomplete,[1,2] al-

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though potential fetal brain damage during maternal hypoxia and anesthesia is a primary concern of any perinatologist.

In animal models, asphyxiation of the fetus has resulted in acidosis, bradycardia, hypertension, and redistribution of cardiac output to vital organs, especially the brain.[7] Studies using an umbilical cord occlusion model[1,2] to explore the effect of maternal halothane on the asphyxiated fetus have produced conflicting results. One study reports a decrease in cerebral blood flow and cerebral O_2 delivery,[1] while another reports no change in cerebral blood flow.[2] Other models of fetal asphyxia to date include fetal hypovolemic hypoxia,[5] maternal hypoxia,[8-10] and umbilical cord occlusion.[11] In the present study, we occluded the uterine artery to model any clinical situation in which uterine perfusion is impaired, *e.g.*, maternal hypotension, uterine hypertonus or tetany, and uterine artery vasoconstriction secondary to endogenous or exogenous vasoactive amines. To investigate further the condition of the fetus, we studied cerebral metabolic O_2 consumption to evaluate the effects of any possible change in cerebral blood flow or cerebral O_2 delivery with asphyxia and anesthesia.

We found that asphyxia increased fetal cerebral, myocardial, and adrenal blood flow, while shunting blood away from the kidney, gut, spleen, and carcass. The increase in H^+ ion and P_{CO_2} probably facilitated the increase in cerebral blood flow by causing cerebral vasodilatation. The fetus became hypertensive and bradycardic with the onset of asphyxia, despite a decrease in cardiac output, a finding similar to that of other investigators.[2,7,9-11]

With the addition of maternal halothane, the normal fetal bradycardia and hypertension in response to asphyxia were reversed and fetal MABP and heart rate returned toward control values. Recent evidence indicates that fetal bradycardia in response to hypoxia is mediated primarily through peripheral chemoreceptor, rather than baroreceptor stimulation.[7] Halothane appears to reverse the normal asphyxial response, either by desensitizing the peripheral neural receptors, or by inhibition of the central vasomotor response.

Unlike Palahniuk *et al.*,[1] we found that administration of halothane to the asphyxiated fetus did not significantly change cerebral blood flow (fig. 1). However, the Palahniuk study was marked by greater asphyxial depression before and after the addition of halothane: fetal MABP, *p*H, and %O_2 saturation were 58 mmHg, 7.05, and 16.5% O_2, respectively, during asphyxia alone, and 35 mmHg, 6.85, and 9.8% O_2 following halothane. The greater depression observed by these investigators may have been due to a prolonged induction time. (No time from mask induction-to-tracheal intubation was reported.) In our study, cerebral blood flow following halothane was similar to that during asphyxia, especially in the subcortical regions (table 4). The fact that cerebral blood flow remained elevated above control during halothane, despite a significant drop in blood pressure and no change in cardiac output, suggests that, in our model, the fetus retains some cerebral vasomotor capacity despite asphyxial stress. Cerebral blood flow was maintained either by autoregulation or by the vasodilating actions of halothane, H^+ ion, P_{CO_2}, lactic acid, or metabolites.[2,12,13]

The significant drop observed in fetal blood pressure during asphyxia plus halothane was accompanied by continued deterioration in fetal acid-base status (table 2). These findings are comparable to those of Palahniuk *et al.*,[1] whose method of induction was similar to ours (4% halothane/O_2 by mask *vs.* 5% halothane/O_2 by mask). However, our results differ from those obtained by Yarnell *et al.*,[2] who performed a tracheostomy and induced anesthesia with only 1% halothane for 15 min. The size of the induction bolus and the added time to intubation might account for the difference between the Yarnell findings and our own. Our time from induction-to-tracheal intubation was 4.3 ± 0.3 min, after which we reduced administration of halothane from 5% to 1% for 15 min.

Another reason for the difference in findings may be that our acidotic preparation was not stable, and might have indicated a further increase in acidosis with additional asphyxial time. There were no matched controls in our experiment. However, subsequent to this study, using the same preparation, we continued the "stable" asphyxial time to 30 min, and observed no marked deterioration in *p*H. A more likely explanation for the observed drop in *p*H and increase in H^+ ion is that halothane decreased vascular resistance, flushing metabolites from the peripheral to the central circulation. That halothane decreased systemic vascular resistance was evidenced by the decline in fetal MABP with no change in cardiac output.

We did not administer supplemental O_2 to the animals until the induction of anesthesia, in order to mimic the clinical situation (emergency cesarean section) in which 100% O_2 may not be given until just before induction. Fetal P_{O_2} was not significantly different in any study period. However, hemoglobin saturation decreased significantly during asphyxia, and did not improve significantly with the addition of maternal halothane/O_2 (table 2). These findings agree with those of other investigators who have found that O_2 content decreased during fetal acidosis.[11] Acidosis shifts the oxygen saturation curve to the right; thus, even if P_{O_2} is maintained or increased, adequate oxygen supply to all tissues is not guaranteed. However, the fetus has a protective mechanism for maintaining vital organ integrity in the face of decreased oxygen content; that is, blood flow increases to the brain, heart, and adrenals, thereby

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increasing O_2 supply, while O_2 use decreases, as seen in a reduced cerebral metabolic consumption of oxygen.

Our data demonstrate that the addition of 1% maternal halothane over 15 min does not produce a significant change in $CMRO_2$ during asphyxia. Values obtained during asphyxia alone were 2.8 ± 0.4 ml · 100 $g^{-1} \cdot min^{-1}$ *versus* 2.0 ± 0.3 ml · 100 $g^{-1} \cdot min^{-1}$ after halothane ($P > 0.05$ but < 0.08). The tendency toward a reduction in $CMRO_2$ with the addition of halothane might be due to the nonlinear response of $CMRO_2$ to anesthetic induction.[12,14] Changes may have become significant if additional time had elapsed. Any decline in $CMRO_2$ might be viewed as protective if anaerobic pathways are not being used. Michenfelder *et al.*, using much higher concentrations and a different species (5–9% inspired halothane in dogs), demonstrated a decrease in $CMRO_2$ due to an alteration in oxidative phosphorylation and increases in cerebral lactate levels thought to be detrimental.[13] This finding has not been verified in fetal or neonatal models. We did not measure cerebral lactate levels, cerebral glucose consumption, or cerebral concentrations of adenosine triphosphate, nor monitor cerebral electroencephalogram; therefore, we cannot determine whether the tendency toward decreased $CMRO_2$ is beneficial or detrimental to cerebral cellular integrity. Further study is necessary in this area.

We conclude that maternal halothane administered to the pregnant ewe in low concentrations does not abolish normal fetal responses to asphyxia and maintains regional cerebral blood flow, cerebral oxygen supply, and lower cerebral metabolic oxygen consumption when the duration of anesthesia is less than 15–20 min. Maternal halothane can therefore be used with greater confidence for cesarean delivery after a relatively short term of fetal asphyxia induced by reduced uterine artery blood flow.

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