Pediat Res. 16: 504–507 (1982)

# MECHANISM OF ARGININE VASOPRESSIN RELEASE IN THE SHEEP FETUS

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This work was supported in part by research grants AM01237, HD08783, and HD11149 and by postdoctoral training grant HD07190 from the National Institutes of Health, Bethesda, MD. Dr. DeVane's current address is the Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, FL.

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## SUMMARY

Maternal and fetal plasma concentrations of arginine vasopressin (AVP) during asphyxial and hypoxemic episodes were ascertained between 130 and 140 days of gestation in chronically catheterized sheep. During an acute asphyxial stress, i.e., decreased $PaO_2$ and pHa and increased $PaCO_2$, maternal AVP in plasma was unaltered, whereas fetal arterial plasma concentrations rose from 1.6-2.2 μU/ml to 34-385 μU/ml and were associated with massive expulsion of meconium into the amniotic fluid. Mild hypoxemia, induced while the mother breathed a gas mixture consisting of 85% nitrogen and 15% oxygen, did not affect either maternal or fetal plasma AVP concentrations. The use of 10% inspired oxygen resulted in 60% and 50% reductions in maternal and fetal $PaO_2$, respectively ($P < 0.05$). In this instance, the maternal plasma AVP levels were unchanged, whereas the fetal plasma AVP concentration rose from a mean of 2.61 ± 0.14 (SE) to 10.2 ± 2.59 μU/ml ($P < 0.025$) within 30 min. Expulsion of meconium into the amniotic fluid did not occur. No evidence of either fetal-maternal placental transfer or fetal-placental clearance of plasma AVP was obtained. Although hypoxemic stress resulted in an elevation of fetal plasma AVP concentration, it does not appear to be the sole factor responsible for AVP release during intrauterine stress. It is suggested that substantial elevations in fetal plasma AVP concentrations may play an integral role in the fetal expulsion of meconium into the amniotic fluid.

## SPECULATION

Elevations in fetal plasma concentrations of arginine vasopressin are reflective of intrauterine stress and may be representative of an adaptive mechanism whereby the fetus responds to hypoxemia and asphyxia. Measurement of fetal plasma arginine vasopressin, i.e., cord plasma levels, may serve as an indicator of the degree or severity of intrauterine stress. Moreover, increases in arginine vasopressin during fetal asphyxia could be important in the fetal expulsion of meconium into the amniotic sac, thereby establishing the situation necessary for meconium aspiration.

## INTRODUCTION

Several investigators have shown that during human and ovine parturition there is release of arginine vasopressin (AVP) by the fetus (1, 4,7,13,14,21,28). Others have observed elevated plasma concentrations of AVP in the fetal lamb after maternal hypoxemia (2,24), fetal hypovolemia (3,11,31), occlusion of the umbilical cord (9), and infusion of hypertonic saline to the fetus (5,30).

We recently observed a higher concentration of AVP in arterial as well as venous cord plasma from human infants who were subjected to various types of intrauterine stress during pregnancy, labor, and/or delivery than in arterial or venous cord plasma from infants who were not stressed (10). This relationship was observed in infants delivered prior to the onset of labor as well as after the onset of labor. In an effort to identify the specific mechanisms involved in this apparent stress-induced release of AVP in the human infant, we have conducted studies in the chronically instrumented pregnant ewe and fetus. We sought to ascertain whether asphyxia, i.e., the presence of hypoxemia with acidosis and/or hypercapnea, was associated with AVP release in the sheep fetus and, having established this, to study one component of asphyxia, viz., hypoxemia, to determine whether hypoxemia was responsible for the AVP release seen in association with asphyxial stress.

## MATERIALS AND METHODS

### Animals

Seven ewes of mixed breed were used in this investigation. The studies were performed between the 130th and 140th days of gestation (term 145-150 days) of ewes bearing singleton fetuses. The surgical procedures performed on the ewe and fetus for the conduct of these studies have been described in detail by Rosenfeld et al. (17,18). Briefly, after induction of spinal anesthesia, the uterus was exposed through a midline abdominal incision, and one hind leg of the fetus was delivered through a small uterine incision. Polyvinyl catheters (0.9 mm id x 1.4 mm od) were inserted (a) 6.5 cm into the femoral artery, the tip lying in the lower aorta, (b) 12.0 cm into the femoral vein, the tip lying in the vena cava, and (c) 2.0 cm into one umbilical vein near the insertion of the umbilicus into the abdominal wall of the fetus, the tip lying within the common umbilical vein. The umbilical vein, in contrast to the femoral artery and femoral vein, was not ligated in order to avoid obstruction of fetal placental venous return in the catheterized vein. Another catheter was placed in the amniotic sac, and ampicillin (250 mg) was instilled in the amniotic cavity. The leg of the lamb was replaced in the amniotic sac, and the uterus was then closed and returned to the abdominal cavity of the ewe.

Electromagnetic flow probes (Micron Instruments, Inc., Los Angeles, CA) were implanted around both main uterine arteries (17), and a polyvinyl catheter was inserted into the main uterine vein of the pregnant horn via a peripheral tributary vein. All catheters and flow probe leads were exteriorized through a stab wound in the abdominal fascia of the ewe and her abdomen closed. Through separate incisions in the groins, catheters were inserted 15 cm into both maternal femoral arteries so that the open ends lay just distal to the aortic trifurcation, and 30 cm into both maternal femoral veins so that the tips lay just below the diaphragm in the inferior vena cava. The flow probe leads and all catheters were brought out to the flank through a subcutaneous tunnel and placed in a canvas pouch attached to the skin with steel pins. The catheters were flushed daily with 0.15 M NaCl containing heparin (250 U/ml) and sealed with sterile metal pins. The ewes were given penicillin G (500,000 U) and streptomycin (0.5 gm) on the day of surgery and on each of the next 2 days. The fetus was given ampicillin (50 mg, iv) every other day.

After the operation, each ewe was maintained in a stall in the laboratory and given feed and water ad lib. Throughout the study, her body weight remained constant or increased. The animals were studied only after they were considered to have recovered from the trauma of surgery and anesthesia, as judged by a normal response of uterine blood flow to 17β-estradiol (1 μg/kg, iv) (19). No animal was studied before the 6th day after surgery and until 24-48 hr after estrogen treatment.

### Asphyxia experiments

In 4 sheep (Group I), fetal asphyxia was induced by the iv administration of sodium pentobarbital to the ewe. After a control period of 20 min, pentobarbital (900 mg) was injected as a bolus into the ewe via a femoral vein catheter, causing rapid unconsciousness and a precipitous fall in blood pressure and uterine blood flow. Nine minutes later, a second bolus of pentobarbital (900 mg) was injected, shortly after which the ewe was killed with a lethal dose of pentobarbital.

Mean arterial pressure (MAP) in the lower abdominal aorta of the ewe and fetus was monitored continuously through interpolated pressure transducers (type 4-327-0109, Bell and Howell, Pasadena, CA), and the signals were recorded on a two-channel pen-recorder (Brush, model 220, Gould, Inc., Cleveland, OH). Heart rates were obtained at intervals from a direct recording of the phasic signal from these transducers. Uterine blood flow was monitored with square-wave electromagnetic flowmeters (model 1000, Micron Instruments, Inc., Los Angeles, CA) and recorded on a second two-channel recorder electronically integrated with the measurements of MAP and heart rate. Heparinized blood samples for AVP and blood gas analysis were collected from the arterial catheters of the ewe and the fetus during the control period and at 1, 3, 6, 11, and 14 min after the initial administration of pentobarbital. In some animals, samples of blood also were collected from the uterine and umbilical vein catheters for AVP determination.

### Hypoxemia experiments

In 3 animals (Group II), several episodes of controlled maternal hypoxemia were induced by delivering pre-mixed gas containing either 15% or 10% oxygen in nitrogen into a large transparent polyethylene bag fitted over the ewe's head. The gas mixture was delivered at a brisk flow rate to prevent carbon dioxide accumulation in the bag. Three experiments were performed on each animal, using 15% oxygen in one experiment and 10% oxygen in two experiments. A recovery period of 24 hr was allowed after exposure to 15% oxygen and 48 hr after exposure to 10% oxygen. At no time did the ewes become excited while the air bag was in position.

Prior to exposure of the ewe to the experimental gas mixture, there was a 30-min control period during which the ewe breathed room air or compressed air delivered to the head bag (control period), after which the ewe was exposed to the experimental gas mixture for 30 min (experimental period). At the end of this period, the ewe again was allowed to breathe room air (recovery period). Fetal and maternal MAP and heart rate and maternal uterine blood flow were monitored continuously as described above. Heparinized arterial blood samples for AVP and blood gas analysis were collected from the ewe and fetus at 30 and 15 min before, at 5, 10, 15, and 30 min during, and at 5, 15, 30, and 60 min after the period of breathing the experimental gas mixture. In these experiments, the packed red cells, obtained after centrifugation of the blood samples, were reconstituted to the original volume with sterile isotonic saline and infused into the fetus and ewe before the next sample was taken (18). This prevented significant changes in circulating blood volume during these experiments, particularly in the fetus.

### Assays

Blood samples (3.0 ml) were collected in heparinized plastic syringes and immediately transferred to sterile plastic centrifuge tubes (1.9 ml). After centrifugation at 10,000 x g for 60 sec in a Beckman microfuge, the plasma was removed, and a 1-ml aliquot was mixed with 2 ml of cold acetone. The plasma-acetone mixture, in which we have found AVP to be stable for at least 4 wk, was centrifuged at 3,000 x g for 20 min to precipitate the denatured proteins. The supernatant fluid was removed and extracted with diethyl ether using a modification of the procedure of Robertson et al. (22). The aqueous phase was evaporated to dryness under a stream of nitrogen. The residue was dissolved in 400 μl of 0.15 M phosphate buffer, pH 7.2, and 100 μl or less of the solution was assayed for AVP. The mean recovery of AVP from sheep plasma was 70% during all phases of these experiments. The recovery was taken into consideration in the calculation of the results.

AVP in plasma extracts was measured using a radioimmunoassay procedure described by Skowsky et al. (26) as modified by Weitzman et al. (29). Antiserum to AVP, R-71 (a gift from Dr. Richard E. Weitzman, Harbor General Hospital, Torrance, CA), was used at a final dilution of 1:150,000. A radiolabelled tracer, $^{125}$I-AVP, was prepared from synthetic AVP (Bachem Inc., Torrance, CA) and purified by ion-exchange chromatography as described by Weitzman et al. (29). Bovine posterior pituitary extract (supplied by Dr. Aubrey S. Autschorn, United States Pharmacopia, Rockville, MD) was used as the reference preparation. The lower limit of sensitivity of the assay was 0.2 μU of AVP, and 1.5 μU of AVP caused a 50% displacement of radiolabelled ligand. The coefficient of variation of the interassay variability was 7.9%. The coefficient of variation of the intra-assay variability was 8.9%.

Serial amniotic fluid samples (3 ml) were withdrawn from the catheter in the amniotic sac in 7 of the 9 hypoxic studies. These samples were examined macroscopically for meconium.

Arterial blood samples (0.5 ml) for blood gas and acid-base determinations were obtained in heparinized glass syringes and kept on ice until analyzed using a blood gas analyzer (model 113, Instrumentation Laboratory, Wilmington, MA). The hematocrit was measured on these samples by the method of Wintrobe.

### Data analysis

The paired Student's t test and analysis of variance with repeated measures (ANOVA) followed by Duncan's Multiple Range test were used in the

statistical analysis of the data. Data are presented as the mean ± one standard error of the mean (SE).

## RESULTS

Effect of acute asphyxial stress on AVP release

In each of the 4 animals studied in Group I, the iv administration into the ewe of a large dose of sodium pentobarbital resulted in immediate unconsciousness and marked hypoventilation. Within 1 min after the injection of sodium pentobarbital, maternal MAP and uterine blood flow were less than 50% of the preinjection values. The fetus at this time exhibited mild-to-moderate bradycardia and hypertension. A further decrease in MAP and uterine blood flow followed the second dose of pentobarbital with only minimal additional cardiovascular changes in the fetus. The arterial oxygen tension in the ewe fell progressively until the experiment was terminated at 10 min with the last dose of pentobarbital. In contrast, the maternal arterial $PCO_2$ was unchanged, 36 ± 6 mm Hg initially and 34 ± 1 mm Hg just prior to death. The acute placental hypoperfusion and maternal arterial hypoxemia were associated with a more gradual, yet progressive fall in both fetal arterial $PO_2$ and pH (Figure 1), and a rise in arterial $PCO_2$ from 42 ± 3.7 mm Hg to 84 ± 7.7 mm Hg. In all cases, a massive expulsion of meconium was observed before fetal demise.

Prior to the maternal administration of sodium pentobarbital, the arterial plasma concentrations of AVP in the 4 ewes and their fetuses ranged from 1.4-2.0 and 1.6-2.2 μU/ml, respectively. After the administration of pentobarbital, there was little change in the maternal arterial plasma concentration of AVP, ranging from 1.7-4.0 μU/ml. However, there was a marked increase in the fetal arterial plasma concentration of AVP, ranging from 34-385 μU/ml. The relative time course of the typical changes in the arterial plasma concentration of AVP in the fetus and its mother is illustrated in Figure 1.

Effects of acute hypoxemia on AVP release

To study one component of asphyxial stress in the release of AVP in the fetus, experimental hypoxemia was induced by having the ewe breathe a mixture of oxygen and nitrogen of known composition (Group II). In Figure 2, we have illustrated the sequential changes observed in maternal and fetal $PaO_2$, arterial plasma concentration of AVP, arterial blood pH, heart rate, and mean arterial blood pressure in relation to the period when the ewe breathed a gas mixture consisting of 15% oxygen and 85% nitrogen for 30 min. Three such experiments were performed. During the experimental period, maternal $PaO_2$ rapidly fell over 5 min from 94.8 ± 5.84 to 55.2 ± 2.62 mm Hg (ANOVA, $P < 0.05$) and was unchanged at 30 min (52.5 ± 2.08 mm Hg). The reduction in fetal $PaO_2$ was nearly proportional to that in maternal blood, a decrease from 19.9 ± 1.40 to 13.8 ± 1.36 mm Hg at 30 min (ANOVA, $P < 0.05$). During the recovery period, the maternal and fetal $PaO_2$ quickly returned to values seen during the control period. The control levels of arterial plasma AVP for the fetus and ewe were similar, 2.9 ± 0.42 μU/ml and 2.8 ± 0.32 μU/ml, respectively. There was no change in the plasma concentration of AVP associated with the changes in either the maternal or fetal blood $PaO_2$ values. Moreover, no appreciable change was seen in arterial pH and $PCO_2$ (Table I), hematocrit, MAP, or heart rate in either the ewes or fetuses, and there was no change in uterine blood flow.

These same animals (Group II) were studied again using the experimental protocol outlined above, but with a gas mixture consisting of 10% oxygen and 90% nitrogen (N = 6). The results of these studies are illustrated in Figure 3. A more marked fall in both maternal and fetal $PaO_2$ was observed at 5 min, decreases from 92.6 ± 2.6 and 20.5 ± 0.57 mm Hg to 42.5 ± 1.6 and 12.9 ± 0.96 mm Hg, respectively (ANOVA, $P < 0.001$). As in the previous experiments, the values remained relatively stable thereafter, and at 30 min were 35.9 ± 1.74 and 10.2 ± 0.75 mm Hg, respectively. During the episode of hypoxemia, the mean fetal plasma AVP concentration gradually rose from 2.6 ± 0.14 to 10.2 ± 2.59 μU/ml (ANOVA, P = 0.025) within 30 min after the induction of hypoxemia. There was no significant change in the maternal plasma AVP concentration. Associated with the rapid fall in fetal $PaO_2$ was a simultaneous increase in fetal MAP from 46.8 ± 1.78 to 53.2 ± 4.02 mm Hg (ANOVA, P = 0.001) and a fall in fetal heart rate from 166 ± 4.4 to 144 ± 12 beats per min (ANOVA, $P < 0.025$). There were no significant changes in either fetal arterial pH or $PCO_2$ (Table I) or hematocrit, and there was no evidence of meconium release by the fetus into the amniotic fluid either during or after the hypoxemic episodes. Maternal MAP and uterine blood flow were unaltered, whereas heart rate rose significantly at 5 min (ANOVA, $P < 0.005$) and remained elevated throughout the experimental period. During the recovery period, all variables returned to values similar to those seen in the control period.

Employing the data obtained in the experiments described above, we have compared the fetal $PaO_2$ with the simultaneous fetal arterial plasma concentrations of AVP obtained in the control period and at 15 and 30 min in the experimental period. These data are presented in Figure 4. It is of interest that there was essentially no change in the fetal arterial concentrations of AVP of those fetuses who experienced pure hypoxemia, i.e., a low $PaO_2$ without simultaneous alterations in either pHa or $PaCO_2$, until the $PaO_2$ fell below 12 mm Hg; then, the highest observed value was 18.7 μU/ml. In contrast, those fetuses who experienced an asphyxial episode, i.e., hypoxemia associated with acidosis and/or hypercapnea, not only had elevated plasma concentrations of AVP at oxygen tensions >12 mm Hg, but also had significantly greater plasma concentrations of AVP at lower oxygen tensions (Figure 4). It also is evident from the figure that the relationship between the arterial plasma concentration of AVP and oxygen tension in the hypoxemic fetuses is nonlinear.

With the placement of catheters in the maternal and fetal compartments as described, we were able to obtain simultaneous serial blood samples representative of the umbilical artery and vein and uterine artery and vein (18), permitting us to study the fetal-placental clearance and fetal-maternal transfer of AVP. During the control period of the hypoxemia studies, the AVP concentrations in all 4 sampling sites were not statistically different (umbilical artery = 2.7 ± 0.15 μU/ml; umbilical vein = 3.6 ± 0.92 μU/ml; uterine artery = 2.8 ± 0.29 μU/ml; uterine vein = 2.8 ± 0.47 μU/ml). In 3 hypoxemia experiments performed in one fetus, we were able to analyze 30 paired serial samples representing the umbilical artery and vein. The mean fetal-placental arteriovenous difference was -0.033 ± 0.21 μU/ml ($P > 1.0$). There also was no significant maternal-placental arteriovenous concentration differences observed ($P > 1.0$) when a similar analysis of paired uterine arterial and venous samples was performed. In addition, we did not observe any evidence of fetal-maternal transfer of AVP (Figures 1 and 3).

## DISCUSSION

In the fetal lamb, the presence of AVP in the pituitary gland and in plasma from early gestation to term has been observed by Skowksy et al. (25, 27). Alexander et al. (4) found a significant elevation in the plasma concentration of bioassayable AVP in the fetal lamb prior to the initiation of parturition. However, Stark et al. (28) observed an elevated concentration of AVP in plasma of the fetal lamb only after the onset of labor; in some fetuses exposed to antepartum asphyxia, these investigators found an increase in the plasma concentration of AVP which was inversely related to the fetal arterial oxygen tension. It is noteworthy that significant elevations of AVP in umbilical cord plasma of human infants also have been demonstrated (7,13,14,21). In addition, we (10) have noted a signficantly higher concentration of AVP in cord plasma from infants who were believed to have been subjected to intrauterine stress than from those who were believed not to have been subjected to such stress.

In the present investigation, we observed that pentobarbital-induced maternal hypoventilation and uterine hypoperfusion resulted in fetal asphyxia, i.e., hypoxemia, acidosis, and hypercapnea. In this circumstance, there was a marked increase in the plasma concentration of AVP in the fetal lamb quite similar in magnitude to the concentration of AVP observed in the cord plasma of human infants subjected to intrauterine stress during pregnancy, labor, and/or delivery (10,13). Therefore, we sought to define the specific stimuli which cause this apparent asphyxia stress-induced release of AVP in the fetus.

It is generally believed that fetal hypoxia causes the release of AVP. Indeed, Rurak (24) and others (2,28) have demonstrated a relationship between fetal plasma AVP concentration and the arterial oxygen tension. However, in these studies it appears that the hypoxemia-induced release of AVP in the fetus was confounded by the presence of other factors such as acidosis or hypercapnea. In fact, Rurak (24) clearly showed that the rise in fetal AVP was best related to the changes in both arterial pH and $PO_2$. The hypoxemic paradigm in our investigation produced neither acidosis nor hypercapnea, and only the most severe pure hypoxemic stress provoked significant elevation of plasma AVP concentrations in the fetus. However, the rise in plasma AVP concentration in this instance was markedly less than that seen in association with a similar degree of hyoxemia in the context of asphyxia (Figure 4). These findings are supportive of the thesis that hypoxemia is not the sole factor responsible for the release of AVP in the fetus during intrauterine stress. In fact, while the exact set of circumstances which results in the exaggerated release of plasma AVP by the fetus remains obscure, it most probably involves a condition that would include not only hypoxemia but also acidosis, hypercapnea, or even hypotension. From these observations, it would appear that extremely high fetal plasma levels of AVP at birth are indicative of significant degrees of fetal distress. Moreover, it is likely that in the majority of instances these episodes are so brief or transient that the Apgar score or even scalp vein pH values do not correlate well with AVP concentrations, a fact noted by Polin and co-workers (21). We would suggest that the cord AVP concentration may be a better reflection of the degree of fetal stress experienced in utero than the Apgar score.

It is noteworthy that, in the human adult, hypoxemia caused either no change or a reduction in plasma AVP concentration (8,12). On the other hand, in acutely studied adult dogs under phenobarbital anesthesia, moderate hypoxia resulted in only slight increases in plasma AVP concentrations (6). During the present experiments, neither the asphyxial nor hypoxic stress resulted in a rise in maternal AVP. In the case of the former, the absence of an elevation in plasma AVP is best explained by the rapidity of the experimental protocol and its termination.

In our earlier studies of the human newborn (10), meconium-stained amniotic fluid usually was associated with the greatest elevations in cord plasma AVP concentrations. In the studies reported here, meconium passage into the amniotic sac was observed during asphyxial stress and in association with the greatest increases in fetal plasma AVP, but not during or after pure hypoxemic stress. Pharmacologic doses of vasopressin, when administered to humans, often cause stimulation of gastrointestinal smooth muscle with the expulsion of gut contents. Furthermore, infusions of vasopressin into the fetal lamb have been shown to affect gastrointestinal perfusion (15). We speculate that intra-amniotic passage of meconium in both the sheep and human fetus may be mediated by an increase in AVP concentration stimulated by intrauterine asphxial stress. In this context, Molteni et al. (20) noted that acute metabolic acidosis produced prolonged gasping respirations by the sheep fetus for 24-36 hr after recovery. Thus, we postulate that asphyxial stress may be a sufficient stimulus to cause AVP release by a compromised fetus with resultant passage of meconium into the amniotic cavity followed by gasping respirations. This cascade of events might then result in a situation conducive to the intrauterine aspiration of meconium, a situation that appears to occur in our institution 3 or 4 times each year.

In the human, there is a significant fetal-placental arteriovenous concentration difference in the plasma concentration of AVP, umbilical arterial concentration greater than umbilical venous (7,10,13,21). Furthermore, there is no evidence of fetal-to-maternal transplacental transfer of AVP. Thus, it would appear that in the human the placenta serves as a site of AVP metabolism and clearance. Although we found no evidence in the sheep of transplacental transfer of AVP from the fetal to the maternal compartment, confirming previous reports (4,5,24,28), we did not find a significant concentration gradient across the fetal placenta. This is in contrast to the report of Jones and Rurak (16), who, in studies of 3 exteriorized, acutely studied lamb fetuses, reported that the plasma concentration of AVP in the umbilical vein was consistently lower than that in the umbilical artery. However, it should be noted that the mean concentration gradient found by these investigators was 0.83 ± 0.26 mU/ml, and this was determined using a bioassay for the measurement of AVP, a method less sensitive and less accurate than the radioimmunoassay employed in our studies. Since both our data and those of Jones and Rurak (16) were obtained from stressed animals, in contrast to the data obtained from the metabolic studies of others (5,23) which are suggestive of a role for the placental clearance of AVP, the question of ovine placental clearance of AVP in the fetus remains unanswered at this time.

ACKNOWLEDGEMENTS

The authors thank Marc Jackson, Sonnya Coultrup, Jodie Roberts, and Gaye Burnsed for technical assistance and Anita Crockett for editorial assistance. We are indebted to Dr. Richard E. Weitzman for the generous gift of the antiserum to AVP and for his advice and counsel on the establishment of the assay for AVP.

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Table I. Maternal and fetal arterial blood gas values during the control period and after 30-min exposure to the experimental gas mixture (mean ± SE)

| | $PaO_2$ | $PaCO_2$ | pHa |
|---|---|---|---|
| Maternal ($F_iO_2$ = 0.15)* | | | |
| Control | 94.8 ± 5.84 | 26.6 ± 1.59 | 7.52 ± 0.04 |
| 30 min | 52.5 ± 2.08 | 23.8 ± 1.47 | 7.52 ± 0.06 |
| Maternal ($F_iO_2$ = 0.10)+ | | | |
| Control | 92.6 ± 2.60 | 32.4 ± 0.94 | 7.51 ± 0.01 |
| 30 min | 35.9 ± 1.74 | 29.0 ± 0.55 | 7.53 ± 0.02 |
| Fetal ($F_iO_2$ = 0.15)* | | | |
| Control | 19.9 ± 1.40 | 37.2 ± 1.39 | 7.47 ± 0.03 |
| 30 min | 13.8 ± 1.36 | 35.7 ± 2.73 | 7.46 ± 0.03 |
| Fetal ($F_iO_2$ = 0.10)+ | | | |
| Control | 20.5 ± 0.57 | 41.6 ± 0.91 | 7.43 ± 0.01 |
| 30 min | 10.2 ± 0.75 | 38.2 ± 1.49 | 7.42 ± 0.04 |

*N = 3
+N = 6

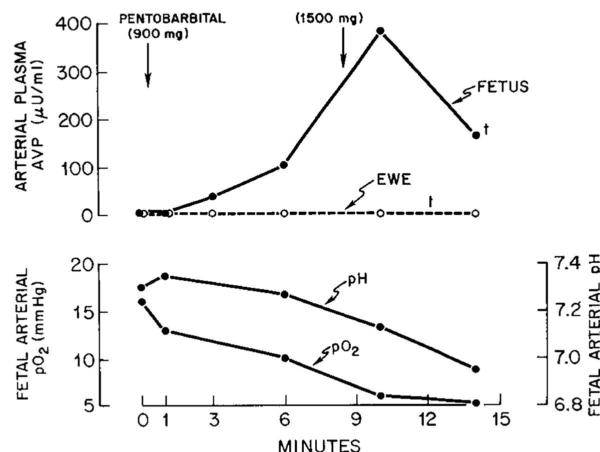


Figure 1. Typical effect of acute asphyxial stress on ovine fetal (●) and maternal (O) plasma arginine vasopressin concentrations.

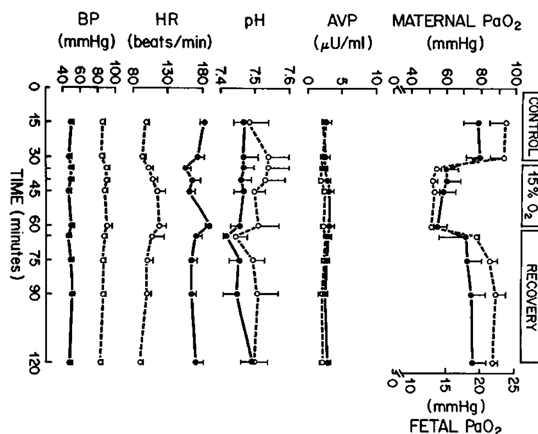


Figure 2. Effect of maternal breathing of 15% inspired oxygen on fetal (●) and maternal (O) arterial oxygen tension, plasma arginine vasopressin, and other parameters. Mean ± SE are presented (N = 3). Statistical analysis is noted in the text.