Stress Hormone Responses During 24-Hour Hypoxemia in Preterm Goat Fetus

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Fetal endocrinological responses to chronic hypoxemia are useful in elucidating the process of growth restriction at earlier stages of fetal development. The purpose of this study was to observe endocrinological responses to prolonged (24-h) non-acidemic hypoxemia in preterm goat fetuses. Fetal hormonal changes were examined in chronically instrumented goat fetuses at gestational day 96-102 (0.7 gestation) during continuous nitrogen infusion into the maternal trachea to create prolonged fetal hypoxemia. Plasma levels of arginine vasopressin (AVP), epinephrine, norepinephrine, adrenocorticotropic hormone (ACTH) and cortisol were measured, along with fetal heart rate (FHR) and fetal blood pressure (FBP). Fetal arterial pO₂ declined significantly from 25.0 ± 1.0 mmHg at baseline to 15.3 ± 1.0 mmHg after 2 h of hypoxemia, then remained at this level. FHR increased significantly throughout the experiment, but FBP remained unchanged. AVP and ACTH levels rose significantly after 2 h of hypoxemia, and declined to the control values after 12 h. There was no significant increase in the epinephrine level during 24-hr hypoxemia. In contrast, norepinephrine significantly increased after 2 h of hypoxemia and remained at the elevated levels throughout the remainder of the experiment. Thus, preterm fetuses could respond to acute hypoxic stress by increasing the plasma levels of AVP, norepinephrine and ACTH. However, despite the rapid increase in ACTH, the level of cortisol in the fetal plasma was significantly elevated only after 18 h of hypoxemia. The chemoreceptors of preterm fetuses, which regulate the release of cortisol or epinephrine, may be less sensitive to hypoxic insults.

Intrauterine growth restriction occurs as a clinical expression of fetal exposure to a sustained hostile environment. Growth-restricted fetuses that have been subjected to chronic hypoxemia are widely held to be able to redistribute cardiac output to vital organs such as the brain, heart, and adrenal glands. These redistribution effects are caused by arginine vasopressin (AVP) (Iwamoto et al. 1979) and norepinephrine (Reuss et al. 1982) in fetal lambs. We have reported that levels of AVP, epinephrine, norepinephrine, cortisol and ACTH, as stress hormones, initially rose with hypoxic stress in goat fetuses at gestational day 123-131 (Fujimori et al. 1994). Thereafter, AVP, epinephrine and ACTH gradually declined and normalized, whereas epinephrine and cortisol
remained significantly elevated during prolonged (24-h) non-acidemic hypoxemia (Fujimori et al. 1994).

The current status of perinatal medicine technology affords increasing opportunities to care for ever more immature or severely growth-restricted fetuses. We believe that observation of endocrinological responses to chronic hypoxemia is helpful in elucidating the processes of redistribution at an earlier stage of development. We have expanded our previous study (Fujimori et al. 1994) to less mature goat fetuses at gestational day 96-102. At this stage of development, the fetal hypothalamic-pituitary-adrenal (HPA) axis (Wintour 1984; Norman et al. 1985) is still immature. The present study described the responses of stress hormones during prolonged (24-h) non-acidemic hypoxemia in goat fetuses at gestational day 96-102 and compared our findings to responses in near-term fetuses.

**Materials and Methods**

**Animal preparations**

Studies were performed at Fukushima Medical University, Fukushima, Japan, using 12 pregnant Nippon Sanen-Goats of known gestational age. Goats were maintained in an air-conditioned room and given free access to food and water prior to and during the experiments, in accordance with the guidelines for the use and care of animals approved by the Animal Research Committee at Fukushima Medical University.

Surgery was performed at gestational day 92-98 (full term, 145 days) after a 24-h maternal fast. Anesthesia was induced using intramuscular administration of atropine sulfate (1 mg/body) and xylazine (0.2 mg/kg), and was maintained with intravenous ketamine (3 mg/kg) at 30-min intervals. A midline skin incision was made using aseptic technique. The fetal head was delivered through a hysterotomy incision and covered with a surgical glove filled with warm saline. Catheters (vinyl tubing, size V3; Biolab Products, Lake Havasu City, AZ, USA) were inserted into the fetal carotid artery and jugular vein unilaterally. Catheters (Imamura Co., Tokyo; outer diameter [OD], 1.7 mm; inner diameter [ID], 0.9 mm) were also inserted into the amniotic cavity and maternal femoral vein. Electrodes attached to polyvinyl-coated stainless steel wires (Cooner, Chatsworth, CA, USA) were placed on the fetal trunk to record fetal electrocardiograms. Fetal catheters, electrodes and maternal catheters were exposed through an incision in the left flank of the maternal goat. A polyvinyl catheter (OD, 4.7 mm; ID, 3.5 mm) for nitrogen infusion was introduced into the maternal trachea by way of an aseptic midline ventral neck incision.

After surgery and before initiating the experiments, 1 g of cefitoxime sodium was administered to maternal goats through the femoral vein catheter every 12 h. All studies were carried out after at least the fourth postoperative day on the 12 fetuses at gestational day 96-102.

**Experiment protocol**

All study protocols were approved by the Animal Research Committee at Fukushima Medical University. To avoid the influence of diurnal variation on fetal behavioral states and fetal endocrinological responses, all experiments were started at approximately the same time: between 15:00 and 16:00. Fetal blood pressure (FBP) and intra-amniotic pressure were measured using a pressure transducer (Disposable Transducer Kit, Model DT-NN; Spectramed Medical Products, Singapore, Singapore) and fetal heart rate (FHR) was measured using an Atom Instrument cardiotachometer (Atom, Tokyo). These data were recorded continuously on a chart recorder (Polygraph 360 system and Omnicorder 8M14; Nippon Denki Sanei, Tokyo). Mean FBP, corrected for intra-amniotic pressure, and FHR were analyzed every 10 min over a 30-min period prior to blood sampling.

Fetal hypoxemia was induced by nitrogen infusion at 2-4 l/min into the maternal trachea catheter, which lowered the maternal inspired oxygen fraction (FiO₂) (Gleed et al. 1986). Nitrogen flow was regulated to maintain fetal arterial pO₂ at approximately 15 mmHg. Fetal endocrinological and biophysical responses under hypoxemic conditions were measured at each sampling point (baseline-control period, 2 h, 6 h, 12 h, 18 h, 24 h, and recovery [2 h after conclusion of nitrogen administration]). At these sampling points, 0.4 ml of fetal arterial blood was anaerobically drawn from the carotid artery; pH, pO₂, and pCO₂ were measured using a blood gas analyzer (Corning 170 blood gas analyzer; Corning Medical Instruments, Medfield, MA, USA) with the temperature corrected to 38°C. An additional 4.0 ml of arterial blood was drawn into a syringe treated with ethylene-diaminetetraacetic acid sodium for hormonal analysis. The specimen was immediately centrifuged at 3,000 revolutions/ min for 15 min at 4°C. The plasma was separated and
stored at -80°C until analysis. The remaining blood cells were suspended in sterile saline solution to obtain the original blood volume and were infused into the fetuses. Control (normoxemic) experiments were conducted at the same sampling points using the same protocol without nitrogen infusion into the maternal trachea.

Immunoreactive AVP, ACTH, and cortisol concentrations in fetal plasma were subsequently measured using an AVP-RIA Kit (Mitsubishi Petrochemical, Tokyo) (Yoshida et al. 1987), Areugo ACTH Kit (Nichols Institute, San Juan Capistrano, CA, USA) (Zahradnik et al. 1989), and Gamma Coat Cortisol Kit (Clinical Assay, Cambridge, MA, USA) (Nishikawa et al. 1980), respectively. Concentrations of catecholamines, epinephrine and norepinephrine in fetal plasma were measured after extraction with high performance liquid chromatography by electrochemical detection (Maruta et al. 1984).

**Statistical analysis**

All data are presented as a mean plus or minus one standard error of the mean (S.E.M.). Statistical analysis was performed by means of two-way analysis of variance (ANOVA) with repeated measurements to compare controls to experimental subjects. When a significant F value was obtained, Dunnett’s pairwise multiple comparison t-test was used to compare mean values with baseline control values. Statistical tests were performed using SPSS software (version 12.0; SPSS, Tokyo). Values of p < 0.05 were considered statistically significant.

**RESULTS**

Mean gestational age was 99.7 ± 0.5 days (n = 6) for the control (normoxemic) period and 98.8 ± 0.8 days (n = 6) for the experimental (hypoxemia) period.

**Maternal blood gases and pH**

Maternal arterial pO₂ was significantly reduced from 93.4 ± 5.2 mmHg to 45.3 ± 4.7 mmHg after 2 h of hypoxemia and remained at that level throughout the experiment (p < 0.001) (Table 1). Maternal arterial pCO₂ exhibited a significant decrease during the experiments except at 18 h (Table 1). Maternal arterial pH initially showed a tendency to increase, but this was not statistically significant. Maternal blood gases and pH returned to or approached baseline-control values during the 2 h after nitrogen was discontinued (recovery period) (Table 1). In normoxemic controls, no parameters were significantly altered during the entire 24 h and recovery (Table 1).

**Fetal blood gases and pH**

Fetal arterial pO₂ was significantly reduced from 25.0 ± 1.0 mmHg to 15.3 ± 1.0 mmHg after 2 h of hypoxemia and remained at that level throughout the experiment (p < 0.001) (Table 2). Fetal arterial pCO₂ exhibited a slight and non-significant decrease during the experiment (Table 2). Fetal arterial pH initially showed a tendency to increase except at 6 h, at which time the difference was statistically significant (p < 0.05) (Table 2). Fetal blood gases and pH returned to or

### Table 1. Maternal arterial blood gases and pH values during control or experiments.

<table>
<thead>
<tr>
<th></th>
<th>Baseline-control</th>
<th>2-h</th>
<th>6-h</th>
<th>12-h</th>
<th>18-h</th>
<th>24-h</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>Control (normoxemia)</td>
<td>7.51 ± 0.02</td>
<td>7.50 ± 0.01</td>
<td>7.50 ± 0.02</td>
<td>7.48 ± 0.02</td>
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<tr>
<td></td>
<td>Hypoxemia</td>
<td>7.48 ± 0.01</td>
<td>7.52 ± 0.01</td>
<td>7.52 ± 0.01</td>
<td>7.52 ± 0.01</td>
<td>7.50 ± 0.03</td>
<td>7.42 ± 0.03</td>
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<td>pO₂ (mmHg)</td>
<td>Control (normoxemia)</td>
<td>92.1 ± 3.4</td>
<td>88.7 ± 2.9</td>
<td>85.0 ± 2.4</td>
<td>85.6 ± 8.7</td>
<td>88.1 ± 5.9</td>
<td>90.7 ± 3.3</td>
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<td></td>
<td>Hypoxemia</td>
<td>93.4 ± 5.2</td>
<td>45.3 ± 4.7***</td>
<td>45.6 ± 3.5***</td>
<td>46.6 ± 5.4***</td>
<td>39.5 ± 2.4***</td>
<td>58.2 ± 4.4***</td>
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<tr>
<td>pCO₂ (mmHg)</td>
<td>Control (normoxemia)</td>
<td>26.3 ± 5.3</td>
<td>31.5 ± 3.2</td>
<td>31.8 ± 3.7</td>
<td>29.1 ± 3.4</td>
<td>31.6 ± 5.1</td>
<td>25.1 ± 4.7</td>
</tr>
<tr>
<td></td>
<td>Hypoxemia</td>
<td>29.7 ± 2.0</td>
<td>19.6 ± 3.0**</td>
<td>19.9 ± 3.5**</td>
<td>23.7 ± 1.3*</td>
<td>29.3 ± 1.8</td>
<td>22.6 ± 3.5*</td>
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</table>

Data is presented as a mean ± standard error.

*p < 0.05 vs Baseline-control by Dunnett’s test, **p < 0.01 vs Baseline-control by Dunnett’s test, ***p < 0.001 vs Baseline-control by Dunnett’s test.
approached baseline-control values during the 2 h after nitrogen was discontinued (recovery period). In normoxemic controls, no parameters were significantly altered during the entire 24 h and recovery (Table 2).

**Table 2. Fetal arterial blood gases and pH values, fetal heart rate (FHR), mean fetal blood pressure (m-FBP) during control or experiments.**

<table>
<thead>
<tr>
<th></th>
<th>Baseline-control</th>
<th>2-h</th>
<th>6-h</th>
<th>12-h</th>
<th>18-h</th>
<th>24-h</th>
<th>Recovery</th>
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</thead>
<tbody>
<tr>
<td>pH</td>
<td>Control (normoxemia)</td>
<td>7.37 ± 0.02</td>
<td>7.36 ± 0.03</td>
<td>7.37 ± 0.01</td>
<td>7.37 ± 0.03</td>
<td>7.37 ± 0.01</td>
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</tr>
<tr>
<td>Hypoxemia</td>
<td></td>
<td>7.35 ± 0.01</td>
<td>7.38 ± 0.01*</td>
<td>7.41 ± 0.01*</td>
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<td>7.38 ± 0.01</td>
<td>7.36 ± 0.03</td>
</tr>
<tr>
<td>pO₂</td>
<td>Control (normoxemia)</td>
<td>25.7 ± 0.4</td>
<td>24.7 ± 0.5</td>
<td>24.6 ± 2.2</td>
<td>23.1 ± 0.5</td>
<td>24.9 ± 0.6</td>
<td>24.1 ± 0.6</td>
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<tr>
<td>Hypoxemia</td>
<td></td>
<td>25.0 ± 1.0</td>
<td>15.3 ± 1.0***</td>
<td>14.6 ± 1.5***</td>
<td>15.1 ± 1.0***</td>
<td>15.7 ± 0.8***</td>
<td>15.0 ± 1.5***</td>
</tr>
<tr>
<td>pCO₂</td>
<td>Control (normoxemia)</td>
<td>43.1 ± 0.9</td>
<td>41.5 ± 1.2</td>
<td>42.0 ± 1.6</td>
<td>44.0 ± 1.9</td>
<td>43.5 ± 0.8</td>
<td>44.8 ± 2.1</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td></td>
<td>40.7 ± 1.8</td>
<td>36.8 ± 1.3</td>
<td>37.1 ± 1.1</td>
<td>38.0 ± 1.6</td>
<td>35.3 ± 1.1</td>
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<tr>
<td>FHR</td>
<td>Control (normoxemia)</td>
<td>207 ± 5</td>
<td>204 ± 5</td>
<td>208 ± 4</td>
<td>202 ± 3</td>
<td>208 ± 4</td>
<td>208 ± 6</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td></td>
<td>201 ± 1</td>
<td>224 ± 3***</td>
<td>218 ± 2***</td>
<td>212 ± 3**</td>
<td>213 ± 3**</td>
<td>214 ± 2**</td>
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<td>m-FBP</td>
<td>Control (normoxemia)</td>
<td>35 ± 2</td>
<td>38 ± 2</td>
<td>38 ± 3</td>
<td>37 ± 2</td>
<td>35 ± 2</td>
<td>38 ± 2</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td></td>
<td>38 ± 2</td>
<td>37 ± 2</td>
<td>36 ± 2</td>
<td>38 ± 2</td>
<td>36 ± 2</td>
<td>36 ± 2</td>
</tr>
</tbody>
</table>

Data is presented as a mean ± standard error.

*p < 0.05 vs Baseline-control by Dunnett’s test, **p < 0.01 vs Baseline-control by Dunnett’s test, ***p < 0.001 vs Baseline-control by Dunnett’s test.

**FHR and mean FBP**

FHR rose and remained significantly elevated throughout the experiments (*p < 0.01*). FHR returned to control levels during the 2-h recovery period (Table 2). Mean FBP did not vary significantly during the experiment (Table 2).

![Fig. 1. Plasma level of arginine vasopressin during 24-h hypoxemia. Fetal plasma arginine vasopressin (AVP) was measured at selected intervals during prolonged hypoxemia and periods of normoxemia (control). All data are presented as mean ± standard error of the mean (S.E.M.).](image-url)

R, Recovery period (2 h after conclusion of the experiment).

Asterisk, Statistically significant difference when compared with baseline-controls (*p < 0.05*).
After 2 h of hypoxemia, fetal plasma AVP rose significantly from 0.8 ± 0.2 pg/ml to 16.6 ± 5.0 pg/ml \((p < 0.001)\), representing the peak value (Fig. 1). AVP continued to decline, but was significantly elevated at 6 h \((p < 0.005)\). Subsequently, AVP was not significantly elevated until 24 h (Fig. 1). In normoxemic controls, AVP concentrations were not significantly altered throughout the 24-h period (Fig. 1).

**Catecholamines**

Fetal plasma epinephrine levels were 0.04 ± 0.01 pg/ml at 0 time and 0.10 ± 0.03 pg/ml after 2 h of hypoxemia. There was no significant increase in the epinephrine levels throughout the experiment (Fig. 2A), although each value was higher than the control level. In contrast, fetal plasma norepinephrine significantly increased from 0.54 ± 0.15 ng/ml to 1.25 ± 0.25 ng/ml after 2 h of hypoxemia \((p < 0.001)\), and remained significantly elevated throughout the remainder of the experiment (Fig. 2B). In normoxemic controls, epinephrine and norepinephrine did not vary significantly throughout the study (Fig. 2A, B).

**ACTH and cortisol**

Fetal plasma ACTH rose significantly from

![Graph A](image1)

**Fig. 2.** Plasma levels of epinephrine and norepinephrine during 24-h hypoxemia. Fetal plasma epinephrine (A) and norepinephrine (B) were measured at selected intervals during prolonged hypoxemia and periods of normoxemia (control). All data are presented as mean ± S.E.M. 

*R*, Recovery period (2 h after conclusion of the experiment).

*Asterisk,* Statistically significant difference when compared with baseline-controls \((p < 0.05)\).
8.3 ± 2.2 pg/ml to 60.2 ± 16.5 pg/ml after 2 h of hypoxemia (p < 0.05), and peaked after 6 h of hypoxemia (74.7 ± 27.7 pg/ml) (Fig. 3A). Thereafter, ACTH steadily declined up to 24 h, at which time no significant difference from baseline control measurements was apparent. Fetal plasma cortisol exhibited a gradual increase, and was significantly different from the baseline-control value by 18 h (0.88 ± 0.27 μg/ml) (Fig. 3B). In normoxemic controls, ACTH and cortisol levels did not vary significantly throughout the 24-h period (Fig. 3A, B).

**DISCUSSION**

We have previously reported that the endocrinological parameters AVP, ACTH, and epinephrine normalized during 24-h non-acidemic hypoxemia in goat fetuses at gestational day 123-131 (Fujimori et al. 1994). The present report extended our previous study to more immature goat fetuses of less than gestational day 100 to compare the responses with those of near-
term fetuses. Relatively few studies (Akagi and Challis 1990b; Carter et al. 1998; Iwamoto et al. 1989; Matsuda et al. 1992; Richardson et al. 1996) have been conducted in fetal sheep or goats at such early stages of development.

We investigated fetal responses to sustained hypoxemia with $pO_2$ values around 15 mmHg for a duration of 24 h. Continuous infusion of nitrogen through the maternal tracheal catheter allowed us to rapidly and accurately adjust fetal $pO_2$ to the desired level. Lower maternal $N_2$ infusion value was needed to maintain fetal arterial $pO_2$ level compared to the previous study (Fujimori et al. 1994). We believe this difference is related to the differences in fetal body size and fetal oxygen consumption. The decreased fetal $pCO_2$ and increased pH during prolonged hypoxemia were most likely the result of maternal hyperventilation. We were able to produce the same hypoxic condition in immature goat fetuses as achieved in near-term fetuses (Fujimori et al. 1994).

Akagi and Challis (1990a) observed no significant hormonal or biophysical changes with acute (1-h) mild hypoxemia (4.6-5.3 mmHg drop in $PO_2$) in fetal sheep (full-term, 145-150 days) at either gestational day 125-129 or 134-147. At gestational day 134-147, moderate hypoxemia (8.3-8.8 mmHg drop in $PO_2$) induced a significant increase in ACTH, but this response was less than at gestational day 125-129. AVP response resembled that at gestational day 125-129 and no significant change was seen in cortisol. Akagi and Challis (1990b) also demonstrated that a drop in fetal arterial $pO_2$ of 4.1-8.4 mmHg was necessary to elicit ACTH and AVP responses to non-acidemic hypoxemia (for 1 h) in fetal sheep at gestational day 106-117, although no changes in cortisol were induced by this degree of hypoxemia. However, the present study of fetuses at about gestational day 100 with more severe hypoxemia (a drop of about 10 mmHg) demonstrated that AVP and ACTH levels initially increased, and that the fetal arterial $pO_2$ drop and a duration of 18 h resulted in an increased cortisol level.

The present study demonstrated the dynamic changes in fetal plasma AVP, ACTH and norepinephrine levels during prolonged hypoxemia, which are similar to those seen in near-term fetuses (Fujimori et al. 1994). In contrast, epinephrine and cortisol levels were not comparable. Fetal plasma epinephrine in near-term fetuses increased after 6 h of hypoxemia, then steadily decreased and returned to baseline control values after 24 h of hypoxemia (Fujimori et al. 1994). In immature fetuses, fetal plasma epinephrine increased throughout the experiment, although this increase was not statistically significant. Fetal plasma cortisol in near-term fetuses significantly increased after 2 h of hypoxemia and remained high for the remainder of the hypoxic period (Fujimori et al. 1994). However, fetal plasma cortisol gradually increased in immature fetuses, and was significantly increased by 18 h. Carter et al. (1998) demonstrated that exogenous ACTH induced the increase in adrenal cortical blood flow and plasma cortisol in ovine fetuses at 0.7 gestation. They suggested that vascular responses to ACTH were not closely linked to adrenal metabolic activity, given the rapid blood flow response to ACTH and a delay (after 24 h) in the rise of plasma cortisol. In our study, using the same gestational age as Carter et al. (1998), we observed an initial elevation of ACTH and a delayed rise of plasma cortisol. The delayed rise in fetal plasma cortisol may derive from the long-term stimulation of the adrenal gland by fetal ACTH, while the progressive decrease in ACTH appears to be caused by the increasing negative feedback effect of elevated cortisol. With the exception of cortisol and epinephrine, endocrinological parameters (AVP, ACTH, and norepinephrine) observed in this experiment increased after the onset of hypoxic stress and subsequently normalized.

The fetal endocrinological responses suggest that certain differences may exist in sensitivities to hypoxemia in immature fetuses. Persistent hypoxemia produces a redistribution of fetal cardiac output, which in turn is thought to result in asymmetrical fetal growth patterns. Richardson et al. (1996) reported that redistribution effects in response to a sustained hypoxic insult (8 h) were qualitatively similar for both preterm and near-term ovine fetuses. To sustain this redistribution,
peripheral vasoconstriction in the fetus must be essentially maintained by sustaining hormonal effects. Both AVP and norepinephrine have been shown to be vasoactive. AVP (Iwamoto et al. 1979) and norepinephrine (Reuss et al. 1982) cause redistribution effects in near-term fetal lambs. In both our previous study (Fujimori et al. 1994) and the present investigation, AVP concentrations decreased by the end of the experiment. It is unlikely that AVP and norepinephrine could maintain fetal redistribution of blood flow during chronic hypoxemia, given their tachyphylaxic effects (Miyake et al. 1991). Iwamoto et al. (1989) reported that in younger sheep fetuses, as in older fetuses, cerebral, myocardial, and adrenal blood flow increased, while pulmonary blood flow decreased with acute hypoxemia. These responses mature early and probably represent local vascular responses to decreased oxygen content. Unlike the response of fetuses older than gestational day 120, acute hypoxemia did not decrease blood flow to musculoskeletal, cutaneous, gastrointestinal, or renal circulations. Umbilical-placental blood flow is usually maintained in sheep fetuses older than gestational day 120, whereas blood flow to the fetal body decreases; conversely, the umbilical-placental circulation decreases by 33% in sheep fetuses at gestational day 80-100 (Iwamoto et al. 1989). These developmental differences in responses to acute hypoxemia may be related to the rate at which chemoreceptor function, the cardiovascular system, autonomic nervous system, or adrenergic or vasopressin receptor-effector mechanisms mature. Riquelme et al. (1998) reported that transection of the carotid sinus nerves, which are related to chemoreceptor function, in llama fetuses completely prevented the cortisol response to acute hypoxemia from affecting the increase in fetal plasma ACTH concentrations, the increase in fetal combined adrenal blood flow, and plasma ACTH delivery to the fetal adrenals. These findings suggested the existence of an important carotid chemoreflex component to cortisol release during acute hypoxemia in the llama fetus, which is well developed by 0.6 to 0.7 gestation. Significant fetal tachycardia occurred, but blood pressure was unchanged throughout the study.

Matsuda et al. (1992) reported that the cardiovascular and biophysical responses of the preterm sheep fetus to sustained hypoxemia were much less pronounced than those of more mature fetuses, and suggested that these differences might impact both survival and precision of antenatal assessment protocols. Boddy et al. (1974) reported fetal tachycardia in response to induced hypoxemia in preterm fetuses (gestational day 100), as did Iwamoto et al. (1989), Matsuda et al. (1992), and Gleason et al. (1990). These findings may relate to a predominance of sympathetic cardiac effects at earlier gestational ages. In near-term fetuses, an increase in arterial blood pressure represents a well-described cardiovascular response to hypoxemia mediated through aortic chemoreceptor stimulation and α-adrenergic receptor-induced vasoconstriction. In this study, fetal arterial blood pressure remained unchanged throughout the period of sustained hypoxemia, as previously reported for the preterm fetus with relatively short-term hypoxemia.

The present study has shown that preterm fetuses could respond to acute hypoxic stress by increasing the plasma levels of AVP, norepinephrine and ACTH. The changes in AVP, ACTH and norepinephrine levels are essentially similar to those seen in near-term fetuses (Fujimori et al. 1994). However, despite the rapid increase in ACTH, the level of cortisol in the fetal plasma was significantly elevated only after 18 h of hypoxemia. The stress hormone responses seen in preterm fetuses (0.7 gestation) suggest that the fetal chemoreceptors, which regulate the release of cortisol, may be less sensitive to hypoxic insults.

References
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