Role of Renal Sympathetic Nerves in Lambs during the Transition from Fetal to Newborn Life

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Abstract

To determine the role of renal sympathetic nerves in influencing renal function during the transition from fetal to newborn life, studies were carried out in conscious, chronically instrumented fetal sheep with either bilateral renal denervation (n = 11) or intact renal nerves (n = 12), 3–6 d after surgery. Endocrine, renal, and cardiovascular parameters were measured before and after delivery of lambs by cesarean section. Blood pressure and heart rate were similar in intact and denervated fetuses, and increased after delivery in both groups. There was also a transient diuresis and natriuresis, in the immediate postnatal period, the response being significantly greater in denervated than intact lambs ($P < 0.05$). By 24 h postnatally, fluid and electrolyte excretions were similar in both groups, and significantly less than fetal levels. In the absence of renal nerves, the normal rise in plasma renin activity at birth was attenuated. These data provide evidence that renal sympathetic nerves play an important role during the transition from fetal to newborn life, and support the premise that birth is associated with sympathetic activation. (*J. Clin. Invest.* 1991. 88:1988–1994.) Key words: neonate • renal function • atrial natriuretic factor • plasma renin activity • birth

Introduction

In the adult animal, renal sympathetic nerves influence renin secretion, renal hemodynamics, and renal function (1), through activation of adrenergic receptors located on renal vessels and tubules. In the immature animal, stimulation of renal nerves (2) or of renal α_1-adrenergic receptors (3), results in a vasoconstriction, though to a lesser extent than later in life. Similarly, in fetal and newborn sheep, neuronal release of norepinephrine causes renin release in vitro, from renal cortical slices (4). Recent evidence indicates that stimulation of renal nerves of fetal and newborn sheep increases fractional Na^+ reabsorption (5). These data suggest that renal sympathetic nerves in the immature animal, as in the adult, may regulate renin release and influence renal hemodynamics and function.

It is well recognized that the transition from fetal to newborn life is associated with an increase in the activity of the renin-angiotensin system and a surge in plasma catecholamines, these hormonal changes being slightly attentuated in cesarean compared with vaginal delivery (6–12). In newborn lambs delivered by cesarean section, there is a marked increase in fractional Na^+ reabsorption by 24 h postnatally, from fetal levels of 93% of the filtered Na^+ load to 99% (13–15), similar to that seen later in life. This rapid rise in fractional Na^+ reabsorption soon after birth, along with elevated plasma norepinephrine (NE)[1] levels and plasma renin activity (PRA) suggests that the transition from fetal to newborn life is associated with increased sympathetic activity.

To determine whether renal sympathetic innervation influences renal and endocrine function at birth, studies were carried out in conscious, chronically instrumented fetal sheep with either bilateral renal denervation or intact renal nerves. Endocrine, renal, and cardiovascular parameters were measured before birth and after delivery of the lamb by cesarean section. Our results show that renal nerves play a major role in regulating renin release and renal function during the transition from fetal to newborn life.

Methods

Pregnant ewes of mixed breeding were obtained from a local source and housed in individual pens with free access to alfalfa pellets and water. Gestational ages were based on the induced ovulation technique (16).

Studies were carried out 3–6 d after surgery in 23 conscious, chronically instrumented fetal sheep aged 140 d, before and after delivery by cesarean section. At surgery, described in detail in the following section, either bilateral renal denervation (n = 11) or sham denervation (n = 12) was performed.

Surgical procedures. Surgery was carried out with the ewe and fetus under general anesthesia (1% halothane, 33% oxygen, 66% nitrous oxide), after induction with pentothal (500 mg sodium thiopentone, Abbott Laboratories, Irving, TX), as previously described (17). Briefly, a uterine incision was made near the fetal hindlimbs; catheters were inserted into right and left femoral arteries and veins, and into the fetal bladder. Skin incisions were sutured and an additional catheter was sutured to the fetal skin for later measurement of intraamniotic pressure.

In the 11 fetuses submitted to renal denervation, bilateral flank incisions were made and renal nerves were severed and stripped from along the aorta, renal arteries, veins, and ureters. This was followed by careful application of 10% phenol in absolute alcohol to the renal plexus and surrounding area, as previously described (18, 19). Sham-operated fetuses were submitted to the same surgical procedure except that the renal nerves were left intact, and no phenol was applied (18,

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1. *Abbreviations used in this paper:* ANF, atrial natriuretic factor; EPI, epinephrine, GFR, glomerular filtration rate; NE, norepinephrine; PRA, plasma renin activity; RBFV, renal blood flow velocity.

19). In both groups, a pulsed Doppler flow probe was placed around the left renal artery (2).

Fetal skin incisions were then closed and the fetus was returned to the uterus. Uterine, maternal muscle, and maternal skin were sutured in separate layers. All catheters were exteriorized subcutaneously and placed in a cloth pouch on the ewe's flank. Ampicillin sodium was infused directly into the amniotic cavity (1 g) and administered intramuscularly (1 g) to the ewe at surgery, and at 48-h intervals thereafter. All animals were standing and eating within 1 h of completion of surgery.

Dexamethasone (5 mg) was administered intramuscularly to the ewe 18 h before experiments to ensure prevention of respiratory distress after delivery of the lamb by cesarean section.

Physiological studies. Before the start of experiments, the ewe was transferred to the laboratory in a small cart that permitted it to stand in an upright position. The fetal bladder was then drained and a priming dose of [^{14}C]-inulin (2 μCi) in 0.5 g/liter of dextrose in water was infused intravenously, followed by a constant infusion at 0.063 μCi/min, at a rate of 0.11 ml/min, for later determination of glomerular filtration rate (GFR). After this 60-min equilibration period, fetal urine was continuously collected for 30 min.

Ewes were then returned to the surgical suite, and a 20-gauge spinal needle was inserted between the lumbar/sacral intervertebral space after infiltration with local anesthetic (1% lidocaine hydrochloride). This was followed by infusion of 10 ml of 0.5% bupivicaine hydrochloride until analgesia of the lower body was achieved. The lamb was delivered by cesarean section within the ensuing 15 min, as previously described (14, 15, 20). Experiments were resumed 1 h after delivery of all lambs. During this 1-h recovery period, infusion of [^{14}C]-inulin was resumed. An additional solution containing 0.5 g/liter of dextrose, 34 mEq/liter of sodium chloride and 30 mEq/liter of potassium chloride, was infused intravenously at 0.07 ml/kg per min, during the recovery period and for the duration of the study. Urinary flow rate was continuously collected over 30-min intervals at 1, 4, 8, and 24 h after delivery.

Urinary volumes were recorded and samples stored at −70°C for later determination of electrolytes (Na^+,K^+), osmolality, and [^{14}C]-inulin concentration. At the midpoint of each urinary collection period, 2.5 ml of arterial blood were removed for immediate determination of pH, P_{O_2} and P_{CO_2}, and later determination of hematocrit, plasma electrolytes (Na^+,K^+), plasma osmolality, and [^{14}C]-inulin concentration. Additional arterial blood (9 ml) was removed at the end of each urine collection for later determination of plasma atrial natriuretic factor (ANF), aldosterone, catecholamines (NE and epinephrine [EPI]), and PRA. In lambs, blood samples were replaced with equivalent volumes of cord blood obtained at delivery, to avoid any hemodynamic effects of sampling.

During each experiment, mean arterial blood pressure (BP, corrected for intraamniotic pressure before delivery), heart rate (HR), and renal blood flow velocity (RBFV) were monitored continuously using a model P23Db pressure transducer (Statham Instruments, Schiller Park, IL), cardiotachometer, and a Doppler flowmeter. The validity of the pulsed Doppler flowmeter for measurement of RBFV in fetal and newborn sheep has previously been described (2). BP, HR, and RBFV were continuously recorded on-line to an IBM-XT computer using the software package Labtech Notebook (version 2.8; Laboratory Technology Corp., Wilmington, MA).

In 10 denervated and eight intact animals, in addition to measurements at 1, 4, 8, and 24 h after delivery, urinary flow rate, and Na^+ excretion were measured continuously for 24 h and sampled at 30-min intervals.

After completion of the study, lambs were killed with a lethal dose of sodium pentobarbitone, and upon postmortem, placement of all catheters was verified. Right and left kidneys were removed onto ice for later determination of renal tissue NE content to confirm the adequacy of renal denervation.

Analytical procedures. Arterial blood for measurement of pH, P_{CO_2} and P_{O_2} was collected anaerobically and measured immediately at 39.5°C for fetuses, or at body temperature for lambs measured before sampling (37.5–39.0°C), using an IL-1303 pH/blood gas analyzer (Laboratory Instruments). Hematocrit was determined in duplicate using a micrometer caliper. Plasma and urinary Na^+ and K^+ concentrations were determined by flame photometry (No. 430; Corning GlassWorks, Corning, NY). Plasma and urinary osmolalities were measured using a micro-osmometer (3MO; Advanced Instruments, Inc., Needham Heights, MA). Concentrations of [^{14}C]-inulin in plasma and urine were measured by liquid scintillation (LS-330; Beckman Instruments, Inc., Fullerton, CA).

Radioimmunoassays, previously established in our laboratories were used to measure plasma aldosterone (21), ANF (22), plasma and tissue catecholamines (23), and PRA (24).

Computations and data analyses. Changes in RBFV (%Δ) were calculated as previously described (2), as percent of fetal levels. GFR was calculated as the clearance of [^{14}C]-inulin. Fractional excretion of electrolytes (FE_x) was determined as the ratio of electrolyte clearance (C_x) to the clearance of [^{14}C]-inulin (C_{In}): $FE_x(\%) = (C_x/C_{In}) \times 100$. Free water clearance ($C_{H_2O}$) was calculated as the difference between urinary flow rate (V) and osmolar clearance (C_{Osm}). $C_{H_2O} = V - C_{Osm}$.

Data are expressed as mean±SEM. Changes within denervated or intact animals were determined using two-way ANOVA for repeated measures (25). Where the F value was found to be significant, newborn data were compared with fetal data using Dunnett's multiple comparison tests (25). Denervated and intact animals were compared using Student's nonpaired t tests. For all statistical tests, significance was accepted at the 95% confidence interval.

Results

Blood gas status and plasma electrolytes measured in intact and denervated lambs before and after delivery by cesarean section are shown in Table I. Arterial P_{O_2} increased in intact (F = 95.9; $P < 0.0001$) and denervated lambs (F = 28.7; $P < 0.0001$) after birth, the levels being higher in intact lambs at 4 and 8 h. There was a transient acidosis in the first hour of postnatal life in both groups (Table I). Plasma Na^+ and K^+ concentrations, and plasma osmolality remained constant after cesarean delivery in intact and denervated lambs. Hematocrit was greater in denervated than intact lambs ($P < 0.05$) before and after delivery. Hematocrit decreased after cesarean delivery in intact lambs ($F = 3.88$; $P < 0.001$) returning to fetal levels by 8 h. In denervated lambs, hematocrit showed no decrease after delivery ($F = 0.61$; $P > 0.05$).

Fig. 1 illustrates the effects of cesarean delivery on BP, HR, and RBFV (%Δ) measured in intact and denervated lambs. BP and HR were similar in intact and denervated fetuses ($P > 0.05$). BP increased after cesarean delivery in both groups ($P < 0.0001$). There was a transient increase in HR 1 h after delivery; by 24 h, HR was less than fetal values (Fig. 1). In lambs with intact renal nerves, RBFV remained constant after delivery (F = 2.22; $P > 0.05$); in denervated lambs, there was a transient decrease in RBFV at 1 h (F = 4.71; $P < 0.001$). Changes in RBFV at 1 h were significantly different when intact and denervated lambs were compared (t = 2.79; $P < 0.005$).

Renal function. GFR, urinary flow rate, electrolyte excretion rates ($U_{Na}V$, U_KV) and fractional excretion of electrolytes (FE_{Na}, FE_K) were similar in intact and denervated fetuses (Table II, Fig. 2). Birth had no effect on U_KV or FE_K in intact or denervated lambs (Table II). There was, however, a transient diuresis and natriuresis 1 h after delivery (Table II, Fig. 2), the responses being significantly greater in denervated than in intact animals ($P < 0.05$). By 24 h postnatally, FE_{Na} was significantly less than fetal levels in intact and in denervated lambs.

Table I. Effects of Cesarean Delivery on Blood and Plasma Measurements

Time		Fetus	Newborn 1 h	Newborn 4 h	Newborn 8 h	Newborn 24 h
P_{O_2}	I	17.4±1.0	40.0±3.0*	71.8±3.4*‡	87.9±6.4*‡	87.4±4.9*
(*mmHg*)	D	17.0±0.8	40.0±6.4*	54.9±5.5*	65.9±6.4*	74.0±6.9*
P_{CO_2}	I	47.9±0.9	51.9±2.3	44.9±1.1	40.2±1.5	39.6±1.2
(*mmHg*)	D	48.6±1.2	52.8±2.7	46.3±2.3	45.0±2.2	44.4±2.0
pH	I	7.33±0.01	7.23±0.02*	7.32±0.01	7.36±0.01	7.39±0.01
	D	7.35±0.01	7.23±0.03*	7.33±0.01	7.36±0.01	7.37±0.01
P_{Na}	I	145±1	146±2	148±2	149±1	148±2
(*mEq/liter*)	D	146±2	146±1	147±1	149±1	148±2
P_K	I	4.4±0.2	4.2±0.1	4.1±0.1	4.1±0.1	4.31±0.1
(*mEq/liter*)	D	4.3±0.1	4.2±0.1	4.3±0.1	4.3±0.1	4.56±0.1
P_{Osm}	I	296±2	295±3	297±2	301±3	300±3
(*mOsm/kg*)	D	295±6	301±2	295±3	300±2	295±4
Hct	I	34.1±1.2‡	32.7±1.0*‡	32.1±1.2*‡	33.6±1.3‡	35.0±1.1‡
(%)	D	37.8±1.9	37.3±1.7	36.6±1.6	38.1±1.7	38.0±1.5

Values are mean±SEM measured before (fetus) and 1, 4, 8, and 24 h after delivery by cesarean section (newborn). *P*, plasma concentration; *Hct*, hematocrit. *$P < 0.05$ compared with fetus. ‡$P < 0.05$ intact (I) compared with denervated (D) animals.

Fig. 3 illustrates urinary flow rates and Na^+ excretions measured continuously during the 24 h after delivery. Urinary flow rates and Na^+ excretions were greater in denervated than intact lambs in the 4 h after cesarean delivery.

Urinary osmolality was higher and free water clearance lower in intact than in denervated lambs before and after delivery as shown in Table II. Urinary osmolality increased ($F = 4.46$; $P < 0.001$) and free water clearance decreased ($F = 3.22$; $P = 0.02$) in intact lambs 1 h postnatally; similar changes, though not significant, were also seen in denervated lambs.

Endocrine function. Effects of delivery on plasma aldosterone levels, ANF, and PRA are illustrated in Fig. 4. Plasma aldosterone levels, PRA, and ANF were similar in intact and denervated fetuses ($P > 0.05$). Plasma aldosterone increased 1 h after delivery to similar levels in both groups (Fig. 4), and remained elevated 24 h after delivery. ANF levels increased after delivery in intact ($F = 12.39$; $P < 0.0001$) and denervated lambs ($F = 9.94$; $P < 0.0001$), the levels being significantly higher in intact than in denervated newborn lambs ($P < 0.05$; Fig. 4) for up to 24 h after delivery. PRA was higher in intact than in denervated animals at 4 and 24 h after delivery (Fig. 4).

Fig. 5 shows plasma levels of NE and EPI measured before and after cesarean delivery. Plasma NE and EPI levels tended to be higher in intact than in denervated lambs before and after cesarean delivery. There was a transient increase in plasma catecholamine levels 1 h after birth in both groups, the increase being similar in intact and denervated lambs.

Renal tissue NE content was 36,044±6,134 ρg/g of cortex in intact kidneys ($n = 9$) and 950±381 ρg/g of cortex in denervated kidneys ($n = 9$). This represented a reduction in NE content of 97.4% in denervated compared with intact kidneys.

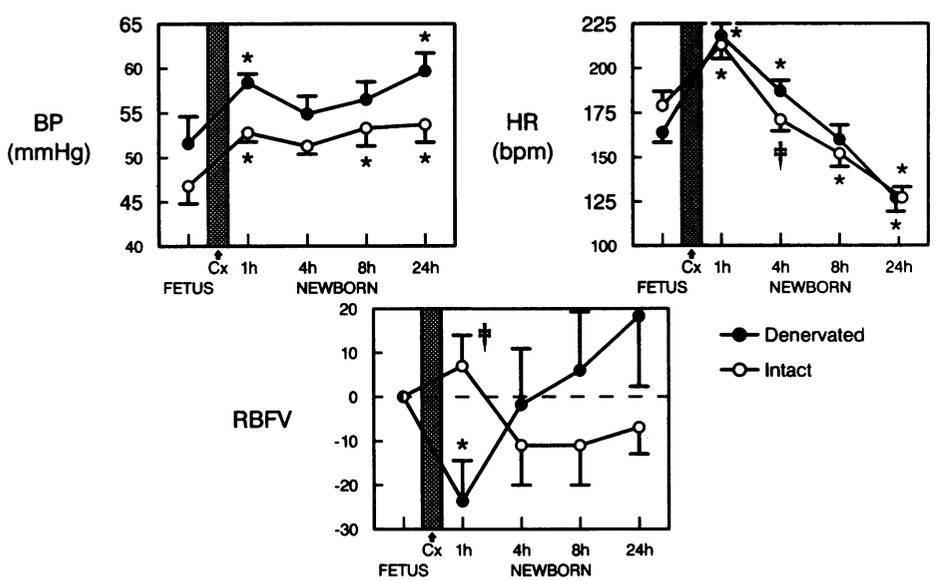

Figure 1. Effects of cesarean delivery on systemic and renal hemodynamics in intact and denervated lambs. *BP*, blood pressure; *HR*, heart rate; *RBFV*, renal blood flow velocity (%Δ), before (fetus) and 1, 4, 8, and 24 h after cesarean delivery (newborn). *$P < 0.05$ newborn compared with fetus; ‡$P < 0.05$ intact compared with denervated lambs.

Table II. Effects of Cesarean Delivery on Renal Function

Time		Fetus	Newborn 1 h	Newborn 4 h	Newborn 8 h	Newborn 24 h
GFR	I	4.7±0.6	5.6±0.9	4.9±0.9	6.1±1.0	6.4±0.6
(*ml/min*)	D	5.8±0.4	7.0±0.7	6.4±1.1	6.5±0.6	6.7±0.6
V	I	0.61±0.14	0.60±0.17‡	0.45±0.14	0.34±0.05*	0.29±0.06*
(*ml/min*)	D	0.7±0.1	1.1±0.2*	0.5±0.1	0.5±0.1	0.3±0.04*
$U_{Na}V$	I	31±10	64±20*‡	21±7‡	14±4*	14±5*
(*μEq/min*)	D	45±6	127±25*	38±6	23±6*	15±3*
$U_K V$	I	17±5	18±5	12±3	10±2	9±1
(*μEq/min*)	D	11±2	14±3	10±1	11±1	11±1
FE_{Na}	I	4.5±1.4	7.8±1.4*‡	3.1±0.8	2.0±0.5*	1.8±0.6*
(%)	D	5.6±0.7	12.3±2.0*	4.5±0.8	2.4±0.6*	1.6±0.3*
FE_K	I	75±17	69±19	59±8‡	42±4	35±3*
(%)	D	46±8	60±19	41±7	40±4	35±3
U_{Osm}	I	280±37	373±23*‡	266±41	228±25	252±23
(*mOsm/kg*)	D	252±39	293±29	278±42	198±21	283±33
C_{H_2O}	I	0.16±0.10	−0.08±0.02*‡	0.14±0.07	0.12±0.05	0.06±0.03
(*ml/min*)	D	0.22±0.12	0.19±0.12	0.13±0.08	0.22±0.09	0.04±0.03

Values are mean±SEM measured before (fetus) and 1, 4, 8, and 24 h after delivery by cesarean section (newborn). GFR, glomerular filtration rate; V, urinary flow rate; $U_X V$, excretion rate; FE_X, fractional excretion. *$P < 0.05$ compared with fetus; ‡$P < 0.05$ intact (I) compared with denervated (D) animals.

Discussion

The present study provides the first evidence that the transition from fetal to newborn life is associated with stimulation of renal sympathetic nerves. In the absence of renal nerves, the normal rise in renin release at birth is attenuated, and a greater diuresis and natriuresis occurs in the immediate postnatal period. Renal nerves therefore modulate both renal function and renin release at birth.

In the adult animal, renin release from the kidney occurs through renal vascular baroreceptors, *macula densa* receptors and renal sympathetic nerves (1). In fetal and newborn animals, renin release can also be promoted by stimulation of renal vascular baroreceptors, and *macula densa* receptors (26–28). Stimulation of neural norepinephrine release by veratridine also results in renin release in vitro from renal cortical slices of fetal and newborn sheep (4, 29). In vivo, renin release

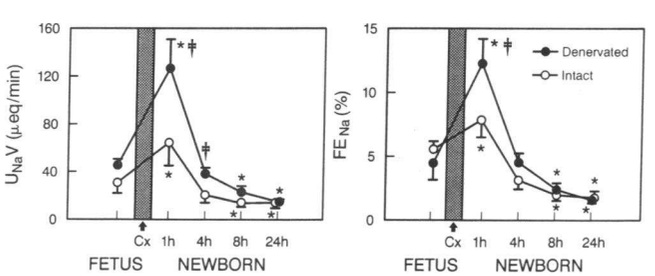

Figure 2. Effects of cesarean delivery on renal function in intact and denervated lambs. Sodium excretion ($U_{Na}V$) and fractional excretion of Na^+ (FE_{Na}) before (fetus) and 1, 4, 8, and 24 h after cesarean delivery (newborn). *$P < 0.05$ newborn compared with fetus; ‡$P < 0.05$ intact compared with denervated lambs.

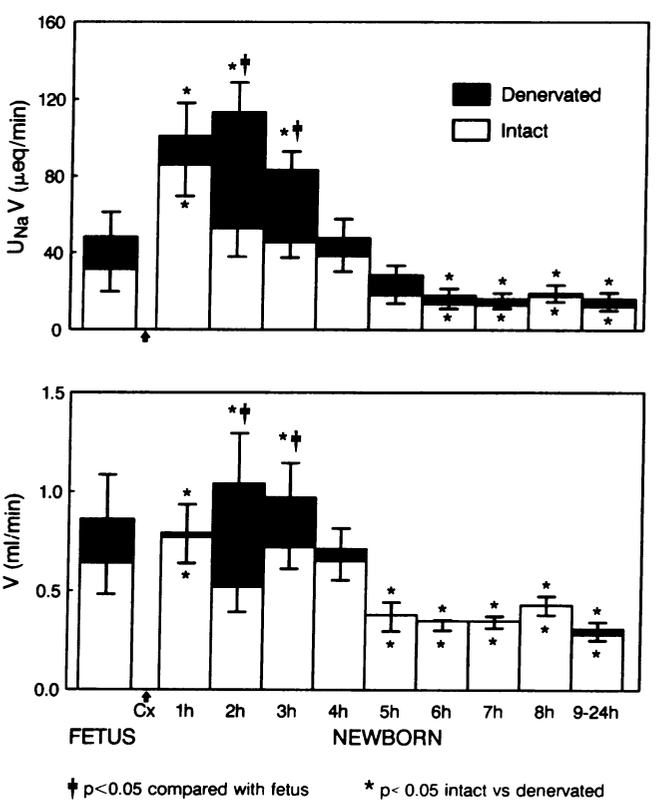

Figure 3. Continuous renal function measurements in the 24 h after cesarean delivery in intact and denervated lambs. Urinary flow rate (V), and Na^+ excretion ($U_{Na}V$) measured continuously before (fetus) and for 24 h after cesarean delivery (newborn). *$P < 0.05$ newborn compared with fetus; ‡$P < 0.05$ intact compared with denervated lambs.

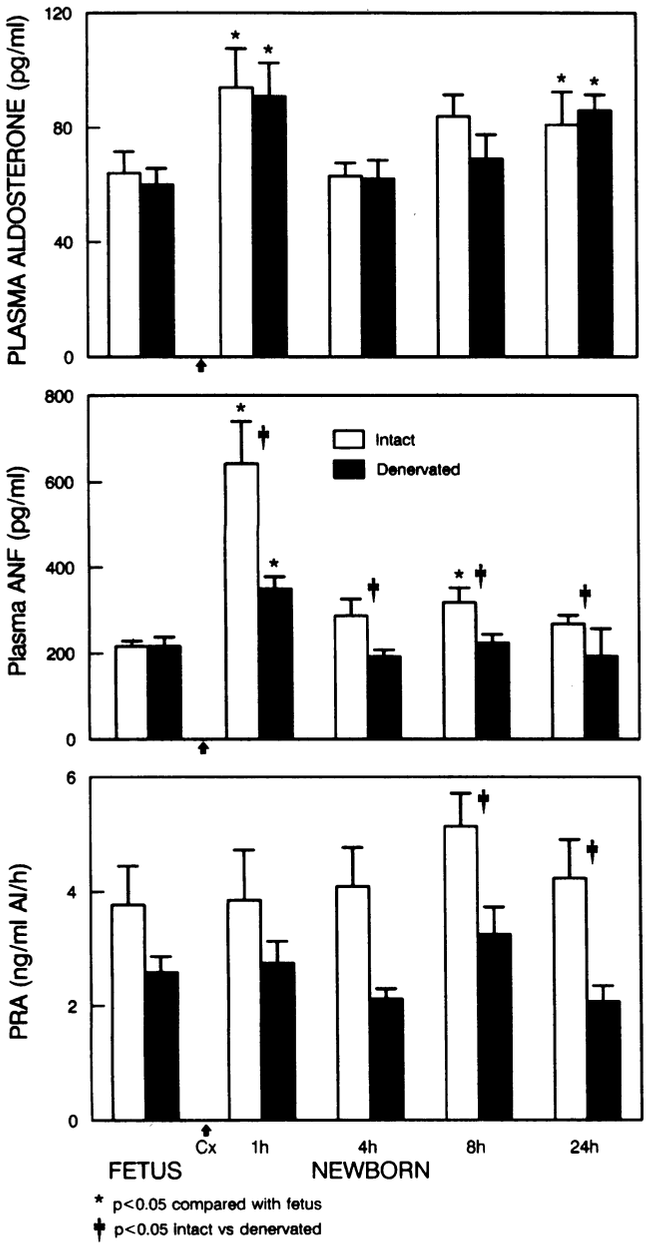

Figure 4. Effects of cesarean delivery on endocrine function. Plasma aldosterone levels, plasma renin activity (PRA), and plasma atrial natriuretic factor (ANF) measured before (fetus) and 1, 4, 8, and 24 h after cesarean delivery (newborn). $*P < 0.05$ newborn compared with fetus; $‡P < 0.05$ intact compared with denervated lambs.

can also be stimulated in preweanling Sprague-Dawley rats (30) by activation of β_1-adrenoceptors. In the present study, renal denervation did not alter basal renin release, confirming the previous studies of Smith et al. (18, 31) in fetal and newborn sheep. Basal renal sympathetic tone in the fetus and newborn, therefore, does not appear to modulate renin release during resting conditions.

Birth, however, results in significant stimulation of the renin-angiotensin system (6, 7, 14). Our data demonstrate that the normal rise in PRA at birth is attenuated in the absence of renal nerves. These data confirm that renal sympathetic nerves can modulate renin release during the perinatal period, and demonstrate that an intact renal sympathetic system is necessary for stimulation of the renin-angiotensin system which occurs at birth. This increase in renin and angiotensin II, is thought to be important in influencing some of the circulatory adaptations which occur postnatally, including the rapid decrease in pulmonary vascular resistance (7, 32, 33). The attenuated rise in PRA in denervated lambs may help to explain the lower arterial oxygen tension seen 4–8 h after cesarean delivery (Table I). Support for this hypothesis is the reduced arterial oxygen tension seen in newborn lambs in which angiotensin II formation or receptor occupancy were blocked by administration of saralasin or captopril, respectively, before birth (7).

In addition to the role of renal nerves in influencing renin release at birth, the present study illustrates that renal denervation alters renal function in the immediate postnatal period. In adult animals, stimulation of renal sympathetic nerves is associated with a significant increase in tubular reabsorption of a number of electrolytes, with predominant effects on Na^+ and water reabsorption (1, 34). In intact and denervated fetuses, Na^+ excretion and the fractional excretion of Na^+ were similar, as was urinary flow rate and glomerular filtration, in agreement with our recent studies in near-term fetal sheep (18). During the immediate postnatal period, however, denervated lambs exhibited a greater diuresis and natriuresis than intact lambs. This increased water and Na^+ excretion in the absence of renal sympathetic nerves occurred despite a transient decrease in renal blood flow velocity in the immediate postnatal period (Fig. 1), resulting probably from a denervation hypersensitivity of the renal vasculature to circulating catecholamines, maximal during this first hour (Fig. 5), and despite similar changes in GFR in the two groups. The slightly, though not significantly higher GFRs seen in denervated lambs (Table I) could account for part of these effects on Na^+ excretion, through a glomerulotubular imbalance. These small differences in GFR between intact and denervated lambs are, however, not sufficient to account for the greater rise in Na^+ excretion and fractional Na^+ excretion in the first 4 h after birth.

The greater natriuresis in denervated lambs could also not be explained by differences in plasma aldosterone, because the levels were similar in intact and denervated lambs (Fig. 4). Nor could these differences in renal function be attributed to differences in plasma levels of the natriuretic hormone, ANF. On the

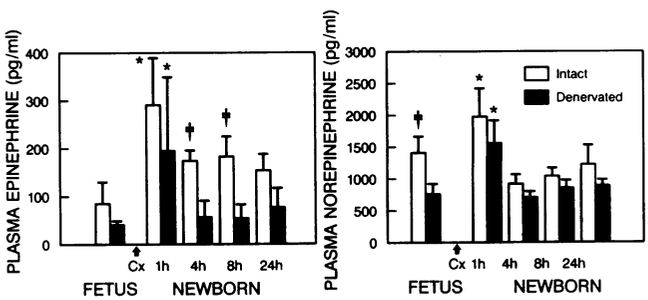

Figure 5. Effects of cesarean delivery on plasma catecholamines. Plasma norepinephrine (NE) and epinephrine (EPI) measured before (fetus) and 1, 4, 8, and 24 h after cesarean delivery (newborn). $*P < 0.05$ newborn compared with fetus; $‡P < 0.05$ intact compared with denervated lambs.

contrary, plasma levels of ANF were much lower in denervated than in intact lambs (Fig. 4).

The reason for the greater ANF levels in intact lambs after birth is not clear. In recent studies by our group (18, 31), ANF was elevated after volume expansion in fetal sheep and newborn lambs, the levels again being lower in denervated animals. It is plausible to suggest from these observations that there is normally an interaction between the renal sympathetic system and ANF release. Recent studies in adult WKY rats (35) and in humans (36) have purported that ANF activates vagal afferents, thereby inhibiting renal sympathetic activity (35). It is also possible that elevated ANF in intact lambs represents a control factor for fluid and electrolyte homeostasis at birth, which is disturbed in denervated animals in which a greater amount of Na^+ is lost at birth. Evidence for this is the decrease in hematocrit seen at birth in intact but not in denervated lambs. Further studies are needed to determine the interaction between ANF and the renal sympathetic system in the perinatal period.

The greater natriuresis and diuresis seen in the immediate postnatal period in denervated lambs therefore appears to be attributed to lack of renal sympathetic innervation, and indicates that renal sympathetic nerves play an important role in the adaptation of the kidney to postnatal life. By 24 h after delivery, however, the effect of renal denervation on water and Na^+ excretion at birth was absent. Hence, renal sympathetic nerves do not appear to influence basal renal function in newborn lambs beyond the initial transition phase, as previously suggested (18, 31). The normal increase in fractional Na^+ excretion which occurs by 24 h after cesarean delivery (13–15), was seen in both intact and denervated lambs. Such an effect is not surprising because, in the adult, it is now generally accepted that renal sympathetic nerves are important in influencing Na^+ homeostasis during stressful conditions, with a minimal role in influencing basal renal hemodynamics and function (1).

The increased urinary osmolality and decreased free water clearance seen in intact lambs in the immediate postnatal period is in agreement with previous observations (13, 15), and probably reflects the increased levels of arginine vasopressin during this time (37). The lack of urinary concentrating capacity after birth in denervated lambs is consistent with the hypothesis of Kurkus et al. (38) who found that denervated kidneys had an elevated tissue water content due probably to disruptions in the medullary gradient. Such a disruption in medullary gradient could prevent the antidiuretic effects of vasopressin. An alternative explanation is that central vasopressin release may be inhibited in renally denervated lambs through loss of renal afferent input, because, at least in the adult, neurosecretion of vasopressin is increased by afferent renal nerve stimulation (39, 40). Although there is presently no evidence that afferent renal nerve activity is increased at birth, circulating bradykinin, a substance known to stimulate afferent renal nerves (41), is elevated in the immediate postnatal period (32, 33, 42). In the present study, however, neither plasma vasopressin nor bradykinin levels were measured.

In conclusion, the present study shows that renal sympathetic nerves play an important physiological role during the transition from fetal to newborn life. In the absence of renal nerves, the normal increase in PRA at birth is attenuated, and there is a greater diuresis and natriuresis in the immediate postnatal period. These data indicate that renal sympathetic nerves regulate fluid and electrolyte homeostasis during the adaptation of the kidney to postnatal demand, and provide the first evidence that birth is associated with stimulation of the sympathetic system.

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