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Electrolyte balance, mode of delivery and plasma aldosterone levels in newborn lambs

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Summary. Plasma aldosterone, sodium (Na) and potassium (K) concentrations, daily Na and K intakes, and urinary and faecal excretion were measured during the first week of postnatal life in 9 lambs naturally born at term (145 days of gestation) and in 10 lambs delivered by caesarean section on day 145 (6 lambs) or on day 139 (4 lambs) of gestation.

Plasma aldosterone, Na and K concentrations showed no significant variation during the experimental period in any group of lambs, and there was no significant difference concerning these parameters among the three groups.

Na and K balances were always positive during the experimental period in naturally born lambs. It was negative on days 4 and 6 postdelivery in those delivered by caesarean section on days 145 and 139 of gestation, respectively. This was probably due to the lower daily Na and K intakes measured in these 10 lambs compared to the 9 control lambs : urinary output and urinary Na and K excretion were lower in the two groups of lambs delivered by caesarean section, while Na and K urinary concentrations were not different in any group.

Introduction.

It is well known that the renin-angiotensin (RA) system and plasma adrenocorticotropin (ACTH), sodium (Na) and potassium (K) concentrations are the dominant factors controlling aldosterone secretion in adult mammals. Several studies in man (Cannon, Ames and Laragh, 1966 ; Brunner *et al.*, 1970) and various animal species (Davis, 1961 ; Corvol *et al.*, 1977) have shown a close relationship between these stimuli and aldosterone production. On the contrary the regulation of plasma aldosterone concentration is still poorly understood in newborn mammals. No relationship has been demonstrated between the RA system and aldosterone concentration in human neonates (Dillon *et al.*, 1976 ; Sulyok *et al.*, 1979b).

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The ability of the adrenal cortex to secrete aldosterone has been the subject of several investigations in foetal lambs (Alexander *et al.*, 1968 ; Wintour *et al.*, 1975). Aldosterone transfer from mother to foetus is not significant, and more than 80 % of the aldosterone in foetal blood is of foetal origin in sodium-replete sheep (Moncaup *et al.*, 1980 ; Wintour *et al.*, 1980).

In the work reported here, we observed the relationships between Na and K concentrations in blood and urine and plasma aldosterone levels during the first week of postnatal life in lambs naturally born at term and in those delivered by caesarean section since, during the first postnatal hours, plasma aldosterone, Na and K concentrations differ widely between mice delivered by caesarean section and those naturally born at term (Loctin and Delost, 1982).

Material and methods

Animals. — Nineteen single male Ile de France × (Limousin × Romanov) lambs were used. Nine were naturally born (NB lambs) at term (145 days of pregnancy) and weighed 3.4 ± 0.2 kg (mean ± SEM) at birth. Ten were delivered by caesarean section (DCS lambs), 4 at term on day 145 of pregnancy (Weight : 3.4 ± 0.6 kg) and 6 on day 139 of pregnancy (weight : 2.6 ± 0.2 kg). On day 7 of postnatal life, the body weight of the groups was 5.1 ± 0.2, 4.3 ± 0.5 and 3.7 ± 0.9 kg, respectively.

Caesarean sections were performed under halothane anaesthetia. Each lamb was removed from the uterus within 4 min following the end of the induction of anaesthesia in the ewe.

All the lambs were separated from their dams immediately after birth. They were accustomed to bottle feeding, placed in individual metabolism cages in a room at 20 °C and were fed twice daily, except for the premature lambs which were fed every 4 hours (50 ml) during the 24 h following delivery ; during these 24 h, all the lambs received colostrum from a previously collected pool of ovine colostrum. On the following days they were fed *ad libitum* a milk replacer (120 g powder per kg of water) allowing 0.45 g Na and 1.25 g K per kg of milk, similar to the Na and K contents of ewe's milk (Guéguen, 1971).

Balance measurements were carried out from the second to the seventh day of postnatal life. Every day during this period the quantities of milk consumed by each lamb were measured, and the urine and feaces from each were collected (Tissier, Béchet and Molénat, 1975) and weighed. Samples of urine (10 ml) were frozen until analysis. The faeces were dried at 103 °C for 48 h. A sample of the dry matter (5 g) was ashed at 380 °C for 15 h and the ash dissolved in 3N HCl and kept at 4 °C until analysis.

Blood samples were collected in heparinzed tubes from the right jugular vein once daily at 9 a.m. just before feeding. After micro-haematocrit measurement the blood was centrifuged and the plasma frozen until analysis.

Assays. — Plasma aldosterone levels were determined by direct radioimmunoassay (Bayard *et al.*, 1970 ; Safwate *et al.*, 1982). Briefly, thawed

plasma samples were extracted with dichloromethane, defatted by freezing at − 30 °C with 70 % methanol and centrifugation at 3 000 rpm at − 20°C for 30 min. Method recovery, determined by the addition of known amounts of radioactive 1,2-^{3}H aldosterone (New England Nuclear Corporation ; specific activity 40-60 Ci/mmole), was around 70 %. Sensitivity of the method was 10 pg. Concentrations were expressed as ng/dl plasma.

Sodium and potassium concentrations in offered and refused milk, plasma, urine and faeces were measured by flame emission spectrophotometry (Perkin Elmer 400).

Plasma osmolality was measured cryoscopically on fresh samples, using a Fiske model G66 osmometer.

Means are given with the standard error. Probability and significance were calculated using the Mann-Whitney U test.

Results

— In all lambs the haematocrit values decreased gradually from birth (43 ± 1 %) to day 4 (25 ± 2 ; $p < 0.01$) then remained stable until day 7 (22 ± 2 %). The lowest haematocrit values were always measured in lambs delivered by caesarean section on day 139 of gestation ; however no significant difference concerning these values was observed among the 3 groups of lambs (fig. 1).

— Plasma osmolality in lambs naturally born at term did not vary significantly from birth to day 7 (around 300 mosm/l). Plasma osmolality in lambs delivered by caesarean section at term (311 ± 2 mosm/l) or 6 days earlier (313 ± 2 mosm/l) decreased to 291 ± 10 mosm/l and 302 ± 2 mosm/l, respectively, 4 days later ($p < 0.05$). However, during the experimental period no significant difference concerning plasma osmolality was observed among the 3 groups (fig. 1).

In NB lambs plasma Na and K concentrations did not vary significantly from birth to day 7 (Na levels : around 140 mM ; K levels : around 5 mM). No significant difference concerning plasma Na and K concentrations was observed among the 3 groups of lambs during the experimental period (fig. 1).

— Daily urinary output gradually increased in NB lambs between day 2 (402 ± 33 ml) and day 7 (684 ± 19 ml ; $p < 0.01$). It was always higher ($p < 0.05$) in NB than in DCS lambs. No difference was observed between DCS lambs delivered on day 145 and those delivered on day 139 of gestation (fig. 2).

— Daily urinary Na and K excretion was always significantly lower in DCS than in NB lambs (fig. 2). It gradually ($p < 0.01$) increased between day 2 and day 7 (fig. 2), although the urinary concentrations of Na and K were never significantly different among the 3 groups of lambs.

— Na and K intakes as well as Na and K balances are shown on figure 3 and table 1. Na and K intakes were higher in NB than in DCS lambs. NB lambs were always in positive Na and K balance during the experimental period. Negative Na and K balances appeared on day 4 in animals delivered by caesarean section at term and on day 6 in those born 6 days earlier (fig. 3).

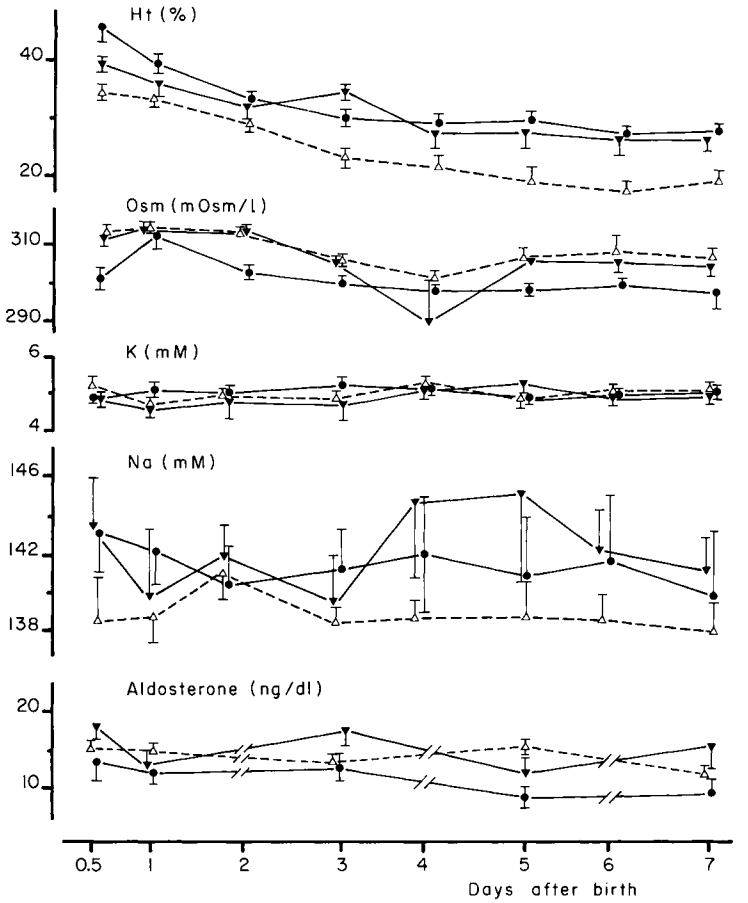

FIG. 1. — *Plasma haematocrit values* (Ht %), *osmolality* (Osm), *potassium* (K), *sodium* (Na) *and aldosterone concentrations during the first week of postnatal life in 9 lambs naturally born at 145 days of gestation* (●———●) *and in 10 lambs delivered by caesarean section at 145* (▼———▼ 4 animals) *or 139* (△----△ 6 animals) *days of gestation* (mean ± SEM).

— Immediately after delivery, plasma aldosterone concentrations (ng/dl) measured in the 9 NB and the 10 DCS lambs were 16.2 ± 2.4 and 16.7 ± 2.7, respectively. No difference was observed between lambs delivered on day 139 or on day 145. Plasma aldosterone concentrations did not vary significantly between the 12th hour and the 7th day after birth in any of the 3 groups. Simultaneously, no difference was observed concerning plasma aldosterone concentrations among the 3 groups (fig. 1). No relationships could be demonstrated in any group between plasma aldosterone concentration and any of the other measured parameters.

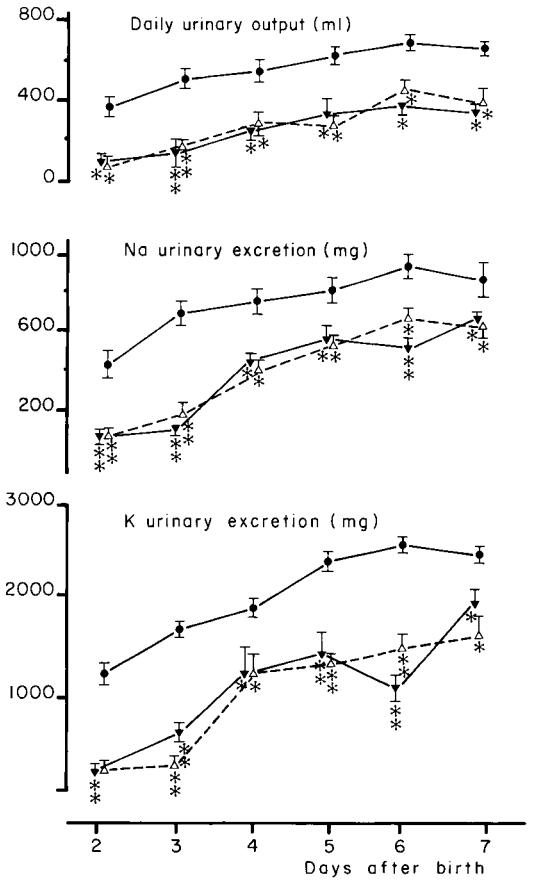

FIG. 2. — *Daily urinary output and sodium* (Na) *and potassium* (K) *urinary excretion from the second to the seventh day of postnatal life in 9 lambs naturally born at 145 days of gestation* (● ——— ●) *and in 10 lamb delivered by caesarean section at 145* (▼ ——— ▼ 4 animals) *or 139* (△----△ 6 animals) *days of gestation* (mean ± SEM) (* $p < 0.05$; ** $p < 0.01$; significance of the comparison between lambs delivered by caesarean section and those born naturally).

TABLE 1

Daily sodium (Na) *and potassium* (K) *intakes* (mg) *from the second to the seventh day of postnatal life in 9 lambs naturally born at term* (145 days of gestation ; NB 145) *and in 10 lambs delivered by caesarean section at 145* (DCS 145 ; 4 lambs) *or 139* (DCS 139 ; 6 lambs) *days of gestation* (mean ± SEM).

Lambs		Days after birth					
		2	3	4	5	6	7
NB 145	Na	1 078 ± 38	1 241 ± 117	1 168 ± 53	1 336 ± 55	1 420 ± 54	1 376 ± 39
	K	2 864 ± 70	3 137 ± 90	2 971 ± 154	3 611 ± 146	3 698 ± 135	3 710 ± 98
DCS 145	Na	450 ± 9	785 ± 169	711 ± 71	769 ± 129	1 132 ± 148	890 ± 203
	K	836 ± 197	927 ± 370	1 562 ± 130	1 627 ± 194	2 013 ± 329	2 483 ± 317
DCS 139	Na	333 ± 39	610 ± 119	759 ± 74	809 ± 80	914 ± 58	1 019 ± 83
	K	667 ± 107	1 489 ± 289	1 905 ± 28	2 048 ± 215	2 075 ± 17	2 525 ± 15

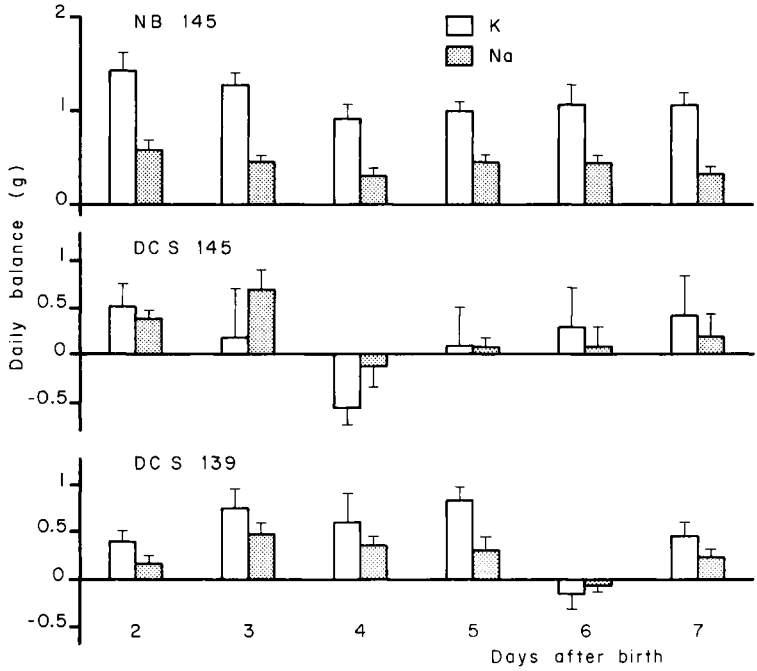

FIG. 3. — *Daily sodium* (Na) *and potassium* (K) *balances from the second to the seventh day of postnatal life in 9 lambs naturally born at 145 days of gestation* (NB 145) *and 10 lambs delivered by caesarean section at 145* (DCS 145 ; 4 lambs) *or 139* (DCS 139 ; 6 lambs) *days of gestation* (mean + SEM).

Discussion

The different parameters of aldosterone metabolism are well documented in the chronic foetal lamb preparation. The RA system is functional during the perinatal period : an acute infusion of furosemide stimulates an increase in renin concentration in the foetal kidney on day 110 of gestation (Trimper and Lumbers, 1972) as well as an increase in plasma renin activity on day 124 (Siegel and Fisher, 1980). During gestation, foetal renin originates principally from the foetal kidney since renin activity is very low in the amniotic fluid (Siegel, 1981). Angiotensin II levels increase in reponse to hypoxaemia (Pipkin *et al.,* 1974a) or hemorrhage (Pipkin, Lumbers and Mott, 1974b).

It has been suggested that plasma aldosterone concentration in foetal lambs is maintained via placental transfer from the ewe (Siegel and Fisher, 1980 ; Siegel, 1981). However transplacental transfer from the ewe to its foetuses was found to be negligible (Moncaup *et al.,* 1980 ; Wintour *et al.,* 1980). No relationship could be demonstrated between plasma Na and K concentrations and plasma aldosterone levels in lambs either before or after birth (Moncaup *et al.,* 1980). Similar results have been observed during the first week of postnatal life in guinea

pigs (Giry and Delost, 1977) as well as in human infants (Sparano *et al.*, 1978), foals (Giry *et al.*, 1979), mice (Loctin, 1980) and calves (Safwate *et al.*, 1982). Under our experimental conditions as in lambs kept with their dams after birth (Moncaup *et al.*, 1980), no increase in plasma aldosterone concentration was observed between birth and day 7 in either the 9 NB lambs or the 10 DCS lambs (fig. 1).

High plasma aldosterone levels measured in newborn pigs (Ferguson *et al.*, 1979) and calves (Safwate *et al.*, 1980) may be responsible for the decrease in the faecal excretion of Na observed in these animals during the first week of postnatal life. This may be due to aldosterone-induced Na reabsorption from the colon (Cremashi *et al.*, 1979 ; Safwate *et al.*, 1982). Loctin (1980) has suggested that aldosterone hypersecretion observed 6 h after birth in premature mice delivered by caesarean section at 19 days of pregnancy may contribute to renal Na as well as water reabsorption.

Infusion of furosemide in 24-48 h old lambs induced a twofold increase in plasma aldosterone concentration (Siegel and Fisher, 1977).

The plasma renin activity and aldosterone concentration following furosemide infusion were not accompanied by a change in haematocrit values or Na concentration (Siegel and Fisher, 1980). Plasma aldosterone values during blood withdrawal in newborn infants could not be correlated with plasma electrolyte concentrations or osmolality (Dillon *et al.*, 1978). The high plasma aldosterone concentrations measured in newborn guinea pigs were related to intense adrenal activity (Giry and Delost, 1977), as observed in mice (Dalle *et al.*, 1978 ; Loctin, 1980).

The effect of an intravenous infusion of K on plasma aldosterone concentration differs before and after birth : the ovine foetus (during the last days of gestation) cannot accommodate high levels of plasma K by an increase in blood aldosterone levels (Wintour *et al.*, 1979). Siegel (1979) demonstrated that in 5-10 day-old-lambs, a rise in plasma K concentration (following KCl intravenous infusion) from 5 mM to 7 mM induced an increase in plasma aldosterone concentration from 160 pg/ml to 220 pg/ml.

In our animals, no relationship could be established between haematocrit values or plasma osmolality and plasma aldosterone concentrations (fig. 1). In calves, the age of the animal accounted for 57 % (multiple regression analysis ; $r = 0.76$; $p < 0.01$) of the changes in the plasma aldosterone concentrations observed during the first week of postnatal life (Safwate *et al.*, 1982). In the present experiment, haematocrit and plasma Na concentrations were similar in NB and DCS lambs (fig. 1). Daily urinary output was greater in NB than in DCS lambs (fig. 2). This probably resulted from the greater mean daily milk intake in NB (1 151 $\pm$ 44 g) than in DCS (DCS 139 : 657 $\pm$ 62 g ; $P < 0.01$; DCS 145 : 578 $\pm$ 79 ; $P < 0.01$) lambs from the second to the 7th day. Thus daily Na and K urinary excretion was more elevated in NB than in DCS lambs (fig. 2), in spite of similar urinary Na and K concentrations. Lambs delivered by caesarean section at 145 days of gestation showed negative Na and K balances on the 4th day after birth, whereas premature lambs obtained at 139 days of gestation demonstrated negative Na and K balances on the 6th day after birth. NB lambs always showed

a positive Na and K balance (fig. 3). This might also be explained by the fact that daily Na and K intakes in DCS lambs were lower ($p < 0.05$) than in naturally born lambs (table 1).

In young lambs of two different age groups (5-28 and 48-57 days) glomerular filtration rate (GFR) did not significantly change during saline infusion (Aperia, Broberger and Herin, 1975). In foetal sheep (122-138 days of gestation) there was a direct relationship between GFR and the amount of reabsorbed Na ; the correlations between GFR and urinary Na excretion were found to be positive (Stevens and Lumbers, 1981). Aldosterone infusion to chronically catheterized foetal lambs altered the renal excretion of Na and K (Lingwood *et al.,* 1978). In our experimental conditions, no relationship was observed between Na and K urinary excretion and plasma aldosterone concentration in any group of lambs. Premature infants born at (or before) 33-35 weeks of gestation can increase their plasma renin activity above values found in full-term babies in response to renal salt loss and subsequent negative Na balance (Sulyok *et al.,* 1979a). Their adrenal glands however fail to respond adequately to this stimulation (Sulyok *et al.,* 1979a). Plasma aldosterone concentration measured between 24 and 48 h after birth in premature and fullterm infants is significantly altered by the duration of pregnancy (Godard *et al.,* 1979 ; Sulyok *et al.,* 1979a) and cannot be correlated with renal Na excretion or urinary Na/K ratio (Sulyok *et al.,* 1979b).

In conclusion, no significant variation in plasma Na, K and aldosterone concentrations during the first week of postnatal life was observed either in naturally born lambs (145 days of gestation) or in those delivered by caesarean section at term (145 days) or 6 days earlier. Thus in lambs during the last 6 days of gestation, the mode of delivery does not seem to have a major influence on aldosterone secretion.

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Résumé. *Balance électrolytique, mode de délivrance et aldostéronémie de l'agneau nouveau-né.*

L'aldostéronémie, la natrémie, la kaliémie, l'ingestion et l'excrétion urinaire et fécale de sodium et de potassium ont été mesurées pendant la première semaine postnatale chez 9 agneaux nés spontanément à terme (145 jours de gestation) et chez 10 agneaux délivrés par césarienne, dont 6 au 145e jour et 4 au 139e jour de gestation.

L'aldostéronémie, la natrémie et la kaliémie n'ont pas présenté de variations significatives pendant la période expérimentale. Il n'y avait pas de différences concernant ces trois paramètres entre les trois lots d'agneaux.

Les balances sodée et potassique étaient toujours positives chez les agneaux nés spontanément, alors qu'elles étaient négatives le 4e et le 6e jour postnatal chez ceux nés par césarienne au 145e et au 139e jour de gestation respectivement. Ces balances négatives résultaient probablement d'une ingestion plus faible de lait (donc de sodium et de potassium) chez les 10 agneaux nés par césarienne que chez les 9 témoins. En effet, la

diurèse et l'excrétion urinaire de ces éléments étaient plus faibles chez les premiers que chez les seconds, alors que la natriurie et la kaliurie n'étaient pas différentes chez les 3 lots. Nous n'avons pu mettre en évidence aucune relation entre l'aldostéronémie et les paramètres du métabolisme du sodium et du potassium que nous avons étudiés.

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