Regulation of Amiloride-Sensitive Na$^+$ Transport in Immature Rat Distal Colon by Aldosterone

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ABSTRACT

The effects of dietary changes and plasma aldosterone levels on channel-mediated electrogenic amiloride-sensitive Na$^+$ transport were examined in the distal colon of immature and adult rats. The decrease of the short-circuit current after amiloride addition (I_{SC}^{amil}) was used as a measure of electrogenic Na$^+$ absorption. Plasma aldosterone levels were six to eight times higher between d 15 and 30 than in younger suckling or prepubertal rats. In adult rats, the plasma aldosterone was approximately 30 times lower than in young animals kept on the same standard diet. I_{SC}^{amil} followed the developmental profile of plasma aldosterone. I_{SC}^{amil} increased between d 10 and 20, reached a plateau between d 20 and 25, then decreased and entirely disappeared after d 30. I_{SC}^{amil} was zero in adult distal colon but was induced if dietary Na$^+$ intake decreased below 100 μmol Na$^+$/ (100 g body wt · d) and plasma aldosterone increased above 200–300 pg/mL. Adrenalectomy, or high Na$^+$ intake, inhibited I_{SC}^{amil} and significantly depressed plasma aldosterone in 20- and 25-d-old rats. Premature weaning decreased I_{SC}^{amil} without appreciable changes in plasma aldosterone in 18- and 20-d-old rats, prolonged suckling inhibited I_{SC}^{amil} and caused a significant depression of plasma aldosterone. We conclude from these results that the postnatal changes of distal colonic Na$^+$ transport are regulated predominantly by circulating aldosterone and dietary Na$^+$ intake. (*Pediatr Res* **38**: 356–360, 1995)

Abbreviations
I_{SC}^{amil}, amiloride-sensitive short-circuit current

Colonic mucosal epithelium plays an important role in water and electrolyte metabolism (1). Studies from our laboratory on rat pups and work by others on some other species strongly suggest that the electrolyte transport exhibits ontogenetic changes (2–5). In adult rats, the epithelium of the distal colon transports Na$^+$ via an electroneutral Na$^+$/Cl$^-$-coupled pathway (6), but in the immature epithelium of suckling and weaning rats it is via an electrogenic amiloride-sensitive Na$^+$ transport (5). The distal colon of pigs and rabbits also exhibits high electrogenic amiloride-sensitive Na$^+$ absorption in suckling and weaning animals, and high circulating levels of aldosterone appear to account for this absorption (3, 7, 8). However, in contrast to the rat this electrogenic amiloride-sensitive pathway persists until adulthood (9). In adult rats only unphysiologic treatments such as severe Na$^+$ depletion (secondary aldosteronism) or treatment with pharmacologic doses of mineralocorticoids are able to suppress the electroneutral Na$^+$/Cl$^-$ absorption and induce the electrogenic amiloride-sensitive Na$^+$ transport (10–12).

The two states of Na$^+$ transport in rat distal colon coincide with the periods of life when the growth is either very rapid or

slow. During rapid growth, the immature animals need to expand their extracellular fluid volume and thus to accumulate Na$^+$. The presence of amiloride-sensitive Na$^+$ transport might help to maintain Na$^+$ homeostasis. Earlier data have demonstrated the induction of electrogenic amiloride-sensitive Na$^+$ transport in the distal colon of adult rats by high doses of aldosterone (12) and negative correlation between plasma aldosterone and dietary Na$^+$ intake in adulthood (13). No correlation between plasma aldosterone and Na$^+$ intake was found in the neonatal period (14). Furthermore, some data indicate that not only aldosterone and sodium but also some other dietary factors might be involved in the regulation of the electrogenic amiloride-sensitive Na$^+$ pathway. Malnutrition or starvation of adult rats sensitize the distal colon to aldosterone (15) and prolonged suckling of rat pups is associated with a significantly higher net Na$^+$ absorption in comparison with normally weaned rats (2). To resolve what factors play the decisive role in inducing electrogenic amiloride-sensitive Na$^+$ transport during the early postnatal development of rat distal colon, we have studied the correlations among amiloride-sensitive Na$^+$ transport, plasma aldosterone levels, and dietary changes. The aims of the study were: 1) to compare the developmental patterns of plasma aldosterone and electrogenic amiloride-sensitive Na$^+$ transport, 2) to determine whether the presence of electrogenic amiloride-sensitive Na$^+$ transport reflects low dietary Na$^+$ intake in suckling and weaning rats, and

3) to study the effect of premature weaning and prolonged suckling on the investigated parameters.

METHODS

Animals

The experiments were performed on adult (90–120 d old), prepubertal (48 d old), weaning (20–30 d old), and suckling (10–20 d old) male Wistar rats. The day of birth was regarded as d 0. Approximately 24 h after birth, all litters were reduced to eight or nine pups, and each litter was housed with the dam until the age of 30 d. The rats were fed a normal pelleted VELAZ Rat Chow (VELAZ, Prague, Czech Republic) containing 122 μmol Na$^+$/(g food), and they drank distilled water *ad libitum*. Only one litter of 13-d-old pups was fed a high salt diet (8% NaCl) and was given 0.9% NaCl instead of drinking water for 12 d to increase Na$^+$ dietary intake and decrease the plasma levels of aldosterone. In the experimental series in which the relationship between salt intake, plasma level of aldosterone, and Na$^+$ transport in adult rats was investigated, the normal laboratory diet was replaced by a low salt rice diet for 7 d before the experiment. To increase Na$^+$ intake these rats drank distilled water or NaCl solutions of various concentrations (0.1, 0.5, 1.0, 5.0, 10.0, 25.0, 50.0, and 100.0 mmol/L), and the daily food and water consumptions were monitored. The low salt rice diet was prepared according to Edmonds and Mackenzie (10) and Edmonds and Marriott (16) and contained 1.4 μmol Na$^+$/(g food).

Adrenalectomy. Bilateral adrenalectomy was performed in 14-d-old rats under ether anesthesia. After surgery they were kept with the lactating dams until d 18, and they had free access to normal pelleted chow and tap water. The adrenalectomized rats were given no hormone therapy but received 0.6 mL of 0.9% NaCl s.c. daily to prevent volume depletion. Each litter always comprised sham-operated and adrenalectomized pups. Na$^+$ transport and plasma aldosterone were determined on d 18.

Premature weaning. Two litters of eight rats each were prematurely weaned by d 16 and were given normal chow. Na$^+$ transport and plasma levels of aldosterone were determined 2 and 4 d later.

Prolonged suckling. Young rats were not weaned and were kept with the lactating dams. The pups were allowed to drink water but were given no access to solid food on postnatal d 12–30 inclusive. Throughout this period, the dams were changed every 12 h and fed in separate cages for 12 h every day. Two lactating dams were used for every litter. The experimental litter was reduced to four pups, and the control litter to eight animals. The control pups were also kept with a lactating dam until the end of the experiment. Prevention of weaning caused a slight suppression in growth rates; on d 30, the mean body weight of nonweaned pups was 60 g, whereas the weight of controls was 73 g.

At the beginning of the experiments the rats were anesthetized with ether, blood was withdrawn from the abdominal aorta (adult rats) or from a neck incision (young rats), and the distal colon was removed to be used for the assessment of Na$^+$ transport. The segment of the distal colon just proximal to the lymph node found at the pelvic brim was used.

Assessment of Electrogenic Amiloride-Sensitive Na$^+$ Transport

Electrogenic amiloride-sensitive Na$^+$ transport was assessed by measuring the I_{SC}^{amil}. The distal colon was rinsed of the luminal content, partially stripped of the serosa and outer muscle layers, and mounted in an Ussing chamber. The surface area was 4.9 mm^2; only in the experiments with the low salt rice diet the surface area was 12.6 mm^2. The epithelium was bathed on both sides with a modified Ringer solution. The composition of the solution was (in mmol/L): 140.0 Na$^+$, 5.4 K$^+$, 1.2 Ca^{2+}, 1.2 Mg^{2+}, 123.8 Cl$^-$, 2.4 HPO$_4^{2-}$, 0.6 H$_2$PO$_4^-$, 21.0 HCO$_3^-$, 10.0 glucose, 0.5 β-hydroxybutyrate, 2.5 glutamine, and 10.0 mannitol; pH 7.4 at 37°C, oxygenation with 95% O$_2$-5% CO$_2$ (17). I_{SC} was monitored as described previously using an automatic voltage clamp which corrected for the potential asymmetry of electrodes and fluid resistance (5). Amiloride, a specific blocker of epithelial Na$^+$ channels, was added to the mucosal side of the tissue to reach a final concentration of 10^{-4} M.

Analytical Techniques

Blood samples were centrifuged (3000 rpm for 20 min at 4°C), and the plasma was removed and aliquoted into appropriate tubes for the respective assays and frozen at -70°C. In the youngest rats, pooled samples of plasma were prepared; in older animals, one blood sample was from a single animal. Plasma aldosterone was measured by a commercial RIA kit (Adico Ltd., Prague) in 100-μL triplicates of the plasma. The separation of free aldosterone from aldosterone bound to the specific antibody was obtained by the addition of the second precipitate antibody (18). The validity of aldosterone determination was checked in collaboration with Dr. Mudra from Adico Ltd. by demonstration of parallelism for the dilutions of plasma and by measuring the recovery of exogenous aldosterone added to a plasma sample. Cross-reactivity for corticosterone and other steroids was less than 0.042%. Plasma Na$^+$ and K$^+$ concentrations were measured by flame photometry, Cl$^-$ by AgCl titration, and osmolality by freezing point depression. The Na$^+$ content in food was also checked by flame photometry. The food was wet-ashed with concentrated nitric acid for 48 h, then centrifuged, and the supernatant was diluted for Na$^+$ determinations.

Data Analysis

The results are expressed as means $\pm$ SEM. Statistical analysis was performed using a *t* test for paired values or one-way analysis of variance. The critical level of significance for all tests was $p \leq 0.05$. As the relationship between plasma aldosterone and I_{SC}^{amil} could not be assumed to be linear, nonlinear regression analysis was applied in this case using the BMDP3R program (19). Squared correlation R^2 was used to test the significance of the model. Parameter estimates are quoted with their asymptotic standard deviations. The follow-

ing presumption were assumed for selecting appropriate non-linear function: 1) the function should reach the finite asymptote at very high aldosterone levels and 2) the function should not pass through the origin (*i.e.* I_{SC}^{amil} is not measurable at very low aldosterone levels). The exponential function $Y = a \cdot (1 - e^{-b \cdot (X - c)})$ was used as the most simple procedure fulfilling the criteria stated above. The parameters of the model have apparent interpretation; parameter a (asymptote) denotes the maximum transport capacity of the amiloride-sensitive pathway and parameter c (x axis intercept) denotes the minimal (threshold) plasma level of aldosterone necessary for the induction of Na^+ channels.

RESULTS

The epithelia in the distal colon of suckling and weaning rats consuming maternal milk and/or a standard diet had a very active amiloride-sensitive Na^+ transport which disappeared after weaning (Fig. 1). On d 15, I_{SC}^{amil} markedly increased, having reached a peak during the weaning period. Figure 1 shows that the rise of I_{SC}^{amil} at weaning is concomitant with an increase in plasma aldosterone. The alteration of Na^+ transport seems to be primarily the result of changes in the plasma aldosterone levels because adrenalectomy suppressed I_{SC}^{amil} in 18-d-old pups (Table 1) and the developmental profile of I_{SC}^{amil} followed the profile of plasma aldosterone (Fig. 1). Plasma levels of aldosterone were 6–8-fold higher between d 15 and 30 than in younger suckling or older prepubertal animals. In adult rats, that were fed the same Chow, plasma aldosterone was approximately 30 times lower (118 ± 25 pg/mL) than in young animals. A rapid fall occurred after weaning between d 30 and 48.

To test whether the presence of amiloride-sensitive Na^+ transport is the result of insufficient dietary Na^+ intake, the relation between Na^+ intake, plasma aldosterone, and Na^+ transport was examined. When expressed per 100 g of body weight, Na^+ intake was 745 ± 24 μmol Na^+/d in adult rats,

1490 ± 45 in 7-wk-old, and 1863 ± 61 in 5-wk-old rats, respectively. The high Na^+ intake reflected a more than 2-fold higher food consumption in young rats due to a very rapid growth rate at this period of life. The estimation of Na^+ intake in younger animals was difficult because Na^+ intake was the sum of two sources, milk and food intake. The large increase of dietary Na^+ intake in the group that was fed the high salt diet and drank saline (Table 1) totally inhibited I_{SC}^{amil}. The comparison of Na^+ intake data mentioned above with the plasma aldosterone levels in Figure 1 indicates a positive relation; the higher Na^+ intakes are associated with higher plasma levels of aldosterone.

The effect of Na^+ intake on plasma aldosterone and electrogenic amiloride-sensitive Na^+ transport in adult rats is shown in Figure 2. The rats had a special dietary regimen. They were fed a low salt rice diet, and tap water was replaced by NaCl solutions of different concentrations. Animals tolerated this regimen well. They gained weight throughout the whole experimental period, but the cumulative body weight gain on the low salt diet was significantly smaller than on the standard diet (5.7 ± 0.9 *versus* 10.2 ± 1.4 g/wk). Drinking of water or NaCl solution of various concentrations had no effect on weight gain, on the daily food consumption [5.5 ± 0.3 g/(100 g body wt · d)], and on plasma electrolyte chemistry. The basal dietary Na^+ intake, which reflected the Na^+ content in the consumed rice diet, was 7.6 ± 0.4 μmol Na^+/(100 g body wt · d). However, the total Na^+ intake was in the range of 7.6 to 1050 μmol Na^+/(100 g body wt · d) owing to the consumption of saline drinking fluids. Decrease of Na^+ intake stimulated I_{SC}^{amil} in the distal colon. The threshold Na^+ intake for the induction of I_{SC}^{amil} (Fig. 2) was approximately 100 μmol Na^+/(100 g body wt · d). As the daily intake of rats on the standard rat chow was 745 ± 24 μmol Na^+/(100 g body wt · d), it is obvious that amiloride-sensitive transport was not able to operate under standard conditions. Figure 2 shows that I_{SC}^{amil} correlated positively to the plasma aldosterone level. The fitted curve does not pass through the origin and the value of parameter c represents the threshold aldosterone level that is responsible for the induction of electrogenic amiloride-sensitive Na^+ transport. Despite a considerable scatter of plasma aldosterone values at zero I_{SC}^{amil}, we assume that the plasma aldosterone levels above 200–300 pg/mL are capable of inducing measurable values of I_{SC}^{amil}. Figure 2 also indicates that the rats do not possess identical sensitivity to Na^+ deprivation. The stimulation of the above mentioned intestinal and also renal (20) electrogenic amiloride-sensitive Na^+ pathway seems to compensate for the decreased dietary Na^+ intake, because the plasma Na^+ concentration and plasma osmolality were not influenced by Na^+ intake. The maximum transport capacity of this pathway was 266 ± 60 μA/cm^2 (parameter a in Fig. 2).

To assess whether different feeding patterns around the time of weaning have any influence on I_{SC}^{amil}, we studied the effect of premature weaning and prolonged suckling. Premature weaning resulted in a marked depression of I_{SC}^{amil} that did not follow plasma aldosterone levels (Table 1). In comparison with 18-d-old control pups, the plasma level of aldosterone was decreased in the prematurely weaned animals of the same age, but its value was high enough to stimulate considerable I_{SC}^{amil} (Fig. 2).
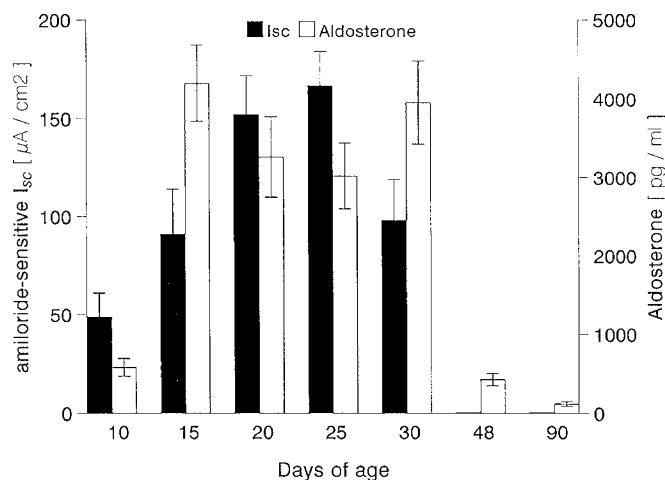

Figure 1. Developmental profile of electrogenic amiloride-sensitive Na^+ transport (I_{SC}) and plasma levels of aldosterone. The tissues and blood samples were obtained from rats fed a standard diet which were housed with the lactating dams until 30 d of life. Each group comprised 7–15 animals per group.

Table 1. *Effect of adrenalectomy, high Na$^+$ intake, premature weaning, and prolonged suckling on electrogenic amiloride-sensitive Na$^+$ transport and plasma aldosterone in rat pups*

Treatment	I_{SC}^{amil}		Plasma aldosterone	
	Controls	Experimental	Controls	Experimental
Adrenalectomy	110 ± 20 (5)	0.0* (5)	3173 ± 465 (5)	7 ± 3* (5)
High Na$^+$ intake	167 ± 13 (13)	9 ± 5* (9)	2309 ± 582 (13)	20 ± 6* (9)
Premature weaning (after 2 d)	101 ± 18 (5)	16 ± 9* (6)	3960 ± 490 (5)	1861 ± 409* (6)
Premature weaning (after 4 d)	152 ± 20 (15)	54 ± 9* (6)	3260 ± 515 (15)	4427 ± 882 (6)
Prolonged suckling	119 ± 28 (6)	3 ± 3* (6)	5026 ± 923 (6)	173 ± 47* (6)

I_{SC}^{amil} is in $\mu A/cm^2$, plasma aldosterone in pg/ml. The data are means ± SEM. Numbers in parentheses are numbers of experiments. The age of experimental and control rats was: adrenalectomy and shorter premature weaning 18 d, longer premature weaning 20 d, high Na$^+$ intake 25 d, and prolonged suckling 30 d. For further details see Methods.

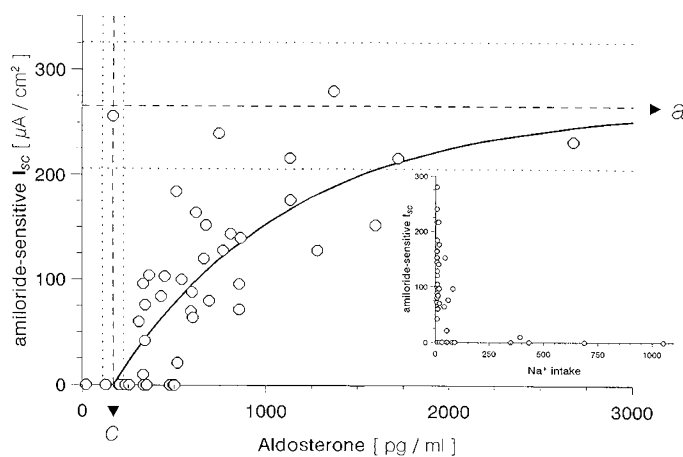* Significantly different from the controls.

Figure 2. Relation between the rate of electrogenic amiloride-sensitive Na$^+$ transport (I_{SC}) in the rat distal colon and plasma aldosterone levels. The tissues were obtained from adult rats that were fed a low salt diet and drank distilled water or NaCl solutions in the range 0.1–100.0 mM. The curve was plotted by nonlinear regression analysis according to the equation $Y = a \cdot (1 - e^{-b \cdot (X-c)})$, where $a = 265 ± 60$; $b = 0.001 ± 0.0004$; $c = 168 ± 57$; $R^2 = 0.6338$. *Inset:* Scatter plot of electrogenic amiloride-sensitive Na$^+$ transport in $\mu A/cm^2$ and Na$^+$ intake in μmol Na$^+$/(100 g body wt · d).

Plasma aldosterone levels of 20-d-old prematurely weaned rats were not significantly different from 20-d-old control pups which were housed with the dams and which had a normal feeding pattern. Mean Na$^+$ intake in prematurely weaned rats increased from 994 in 18-d-old rats to 1364 μmol Na$^+$/(100 g body wt · d) in 20-d-old animals. I_{SC}^{amil} was inhibited, and plasma aldosterone levels were considerably decreased in rats that were prevented from weaning (Table 1).

DISCUSSION

This study was designed to characterize the factors responsible for the developmental changes in colonic Na$^+$ transport during early postnatal life. Our data demonstrate that the presence of electrogenic amiloride-sensitive Na$^+$ transport and very high plasma levels of aldosterone in early postnatal life reflect a chronic Na$^+$ deficiency during this period of life, because excessive Na$^+$ intake during the weaning period considerably decreases plasma aldosterone and totally inhibits I_{SC}^{amil}. If we assume that the extracellular fluid represents 36% of body weight in 10-d-old and 30% in 30-d-old rats (21) and the average weight gain is usually 2–4 g daily, this means that the suckling rats expand their extracellular fluid volume by 0.7–2.2

mL and weaning animals by 0.6–1.8 mL a day, *i.e.* by 108–216 μmol Na$^+$ daily in suckling and by 90–180 μmol Na$^+$ daily in 30-d-old rats. As the body weights of 2- and 4-wk-old pups in our experiments were 26.5 and 70.1 g, respectively, the minimal Na$^+$ intake necessary for the normal development of suckling rats is 408–815 μmol Na$^+$/(100 g body wt · d), whereas they were only 129–257 μmol Na$^+$/(100 g body wt · d) after the end of weaning (30-d-old rats). In addition, it is unresolved whether all Na$^+$ is accumulated in the body due to maturation of filtration and reabsorption in immature kidney. Premature human neonates with a gestational age of less than 32 wk demonstrate high renal and intestinal losses of Na$^+$, very high plasma aldosterone and high rectal Na$^+$ absorption (22–24). If they receive only breast milk, their daily Na$^+$ excretion usually exceeds the daily Na$^-$ intake (25). In young rats (13–39 d old) the fractional Na$^+$ reabsorption is approximately the same (26), and the kidney is sensitive to aldosterone (27). This is in contrast to younger animals that were found to be essentially insensitive to aldosterone (27). Using the data published by Štolc *et al.* (28) on milk and solid food consumption in immature rats as well as those on the Na$^+$ content in milk (29, 30) and in standard solid food (this report), the calculated Na$^+$ intake is 557–895 μmol Na$^+$/(100 g body wt · d) in 2-wk-old suckling rats and 1537 μmol Na$^+$/(100 g body wt · d) in weaned 4-wk-old animals. If this reasoning is true, there is no decreased availability of dietary Na$^+$ at the end of weaning, but the younger animals may suffer from chronic Na$^+$ deficiency. In contrast to this, there is a surge of plasma aldosterone during the weaning period in the third and fourth postnatal weeks and the calculated Na$^+$ intakes in pups are much higher than the maximum Na$^+$ intake [100 μmol Na$^+$/(100 g body wt · d)] which is able to induce I_{SC}^{amil} in the adult rats. Although very high Na$^+$ intake is able to decrease plasma aldosterone and totally inhibit I_{SC}^{amil} in 25-d-old rats, we can conclude that there is not a simple correlation between plasma aldosterone and Na$^+$ intake during early postnatal life. Similar indications were reported by Raux-Eurin *et al.* (14) and Siegel *et al.* (31), who found no correlation between plasma aldosterone and Na$^+$ intake of normal preterm or full-term infants. The relatively low Na$^+$ intake during a period of rapid growth seems to contribute to the high circulating levels of aldosterone and the presence of electrogenic amiloride-sensitive Na$^+$ transport in the colon. The absence of a simple relation between plasma aldosterone and dietary Na$^+$ intake raises the question

of which other factor(s) are responsible for the presence of the amiloride-sensitive pathway.

The experiments with premature weaning suggest that additional factors might be responsible for the induction of I_{SC}^{amil}, because 4 d after premature weaning I_{SC}^{amil} was significantly reduced even though plasma aldosterone levels were still very high. Several factors can be proposed as candidates responsible for this reduction. Stress, undernutrition, thirst, changes of food composition, and hormones or other factors in maternal milk appear to be essential. At present, there is no evidence that stress coupled to the premature weaning might be responsible for the decrease of I_{SC}^{amil}. The combination of separation from the mother and solid food is a major stress for the pups, and not only mineralocorticoids but also glucocorticoids are able to induce I_{SC}^{amil} in the distal colon of immature and adult rats (12, 32). However, premature weaning decreases I_{SC}^{amil} (Table 1) and plasma corticosterone concentration in rats 4 d after premature weaning is not significantly changed in control rats of the same age (33, 34). According to Buts *et al.*, plasma corticosterone is 18 μg/dl on d 17 (33) and 21 μg/dl 4 d after premature weaning (34). Similarly, undernutrition is not a good candidate for the inhibition of I_{SC}^{amil}. Colonic weight is not significantly changed 4 d after premature weaning (33, 34), and Nzegwu and Levine (15) demonstrated recently that starvation or undernutrition induce I_{SC}^{amil} in the distal colon of adult rats. Premature weaning is associated with an abrupt change from a relatively high fat, low carbohydrate diet (milk) to relatively low fat, high carbohydrate diet (solid food). It cannot therefore be excluded that the composition of the diet or some factors in the milk, including corticosteroid hormones, have a permissive effect on electrogenic amiloride-sensitive transport. Prolonged suckling provides a striking contrast with the effect of premature weaning. This dietary manipulation inhibited I_{SC}^{amil} and significantly depressed plasma aldosterone to levels found in adult animals. Thus, during normal development, suckling may play a temporary permissive role for electrogenic amiloride-sensitive Na^+ transport before d 20, but could cause an inhibition later. This inhibition is a secondary effect of very low plasma aldosterone, which is below the threshold level for inducing of I_{SC}^{amil}. Further investigations should be undertaken to shed light on the effect of prolonged suckling on the aldosterone system.

In summary, this study shows that the electrogenic amiloride-sensitive Na^+ transport is induced in the rat distal colon if Na^+ intake falls below 100 μmol Na^+/(100 g body wt · d). The corresponding plasma level of aldosterone, which is essential for the induction of this pathway, is at least 200 pg/mL. The presence of this amiloride-sensitive transport in suckling and weaning rats (but not in adult animals kept on the same standard diet) is induced predominantly by high plasma levels of aldosterone. The high plasma levels of aldosterone during early postnatal life indicate that at this period of life the growing animals are threatened by a relative Na^+ deficiency.

REFERENCES

1. Binder HJ, Sandle GI, Rajendran VM 1991 Colonic fluid and electrolyte transport in health and disease. In: Phillips SF (ed) The Large Intestine: Physiology, Pathophysiology and Disease. Raven Press, New York, pp 141–168
2. Finkel Y, Aperia A, Eklöf A-C 1985 Development of colonic fluid and electrolyte transport: Influence of weaning pattern. J Pediatr Gastroenterol Nutr 4:457–462
3. O'Loughlin, Hunt DM, Kreutzmann D 1990 Postnatal development of colonic electrolyte transport in rabbits. Am J Physiol 258:G447–G453
4. Pácha J 1993 Epithelial ion transport in the developing intestine. Physiol Res 42:365–372
5. Pácha J, Popp M, Čapek K 1987 Amiloride-sensitive sodium transport of the rat distal colon during early postnatal development. Pflugers Arch 409:194–199
6. Perrone RD, Jenks SL 1984 Suppression of coupled Na-Cl absorption by aldosterone and dexamethasone in rat distal colon *in vitro*. Am J Physiol 246:F785–F793
7. Cremaschi D, Ferguson DR, Henin S, James PS, Meyer G, Smith MW 1979 Postnatal development of amiloride sensitive sodium transport in pig distal colon. J Physiol 292:481–494
8. Ferguson DR, James PS, Paterson JYF, Saunders JC, Smith MW 1979 Aldosterone induced changes in colonic sodium transport occurring naturally during development in the neonatal pig. J Physiol 292:495–504
9. Hoffman B, Clauss W 1989 Time-dependent effects of aldosterone on sodium transport and cell membrane resistances in rabbit distal colon. Pflugers Arch 415:156–164
10. Edmonds CJ, Mackenzie J 1984 Amiloride sensitive and insensitive sodium pathways and the cellular sodium transport pool of the colonic epithelium in rats. J Physiol 346:61–71
11. Foster ES, Zimmerman TW, Hayslett JP, Binder HJ 1983 Corticosteroid alteration of active electrolyte transport in rat distal colon. Am J Physiol 245:G668–G675
12. Will PC, Cortright RN, DeLisle RC, Douglas JG, Hopfer U 1985 Regulation of amiloride-sensitive electrogenic sodium transport in the rat colon by steroid hormones. Am J Physiol 248:G124–G132
13. Douglas J, Hansen J, Catt KJ 1978 Relationship between plasma renin activity and plasma aldosterone in the rat after dietary electrolyte changes. Endocrinology 103:60–65
14. Raux-Eurin MC, Pham-Huu-Trung MT, Marrec D, Girard F 1977 Plasma aldosterone concentrations during the neonatal period. Pediatr Res 11:182–185
15. Nzegwu HC, Levin RJ 1992 Dietary restriction sensitizes the rat distal colon to aldosterone. J Physiol 447:501–512
16. Edmonds CJ, Marriott J 1970 Sodium transport and short-circuit current in rat colon *in vivo* and the effect of aldosterone. J Physiol 210:1021–1039
17. Hegel U, Fromm M 1990 Electrical measurements in large intestine (including caecum, colon, rectum). Methods Enzymol 192:459–484
18. Cook B, Beanstall GH 1987 Measurement of steroid hormone concentrations in blood, urine and tissues. In: Green B, Leake RE (eds) Steroid Hormones. A Practical Approach. IRL Press, Oxford, pp 1–65
19. Dixon WJ 1992 BMDP Statistical Software Manual, Vol. 2. University of California Press, Berkeley, CA, pp 1007–1048
20. Pácha J, Frindt G, Antonian L, Silver, RB, Palmer LG 1993 Regulation of Na channels of the rat cortical collecting tubule by aldosterone. J Gen Physiol 102:25–42
21. Jelínek J 1961 The development of the regulation of water metabolism. VI. Changes in the volume of cellular and extracellular fluid in the body of the rat during development. Physiol Bohemoslov 10:259–266
22. Sulyok E, Nemeth M, Tenyi I, Csaba J, Gyory EK, Erlt T, Varga R 1979 Postnatal development of renin angiotensin-aldosterone system (RAAS) in relation to electrolyte balance in premature infants. Pediatr Res 13:817–820
23. Verma R, John E, Fornell L, Vidyasagar D 1989 Stool K/Na ratio as a measure of K homeostasis in preterm infants. Pediatr Res 25:299A(abstr)
24. Jenkins HR, Fenton TR, McIntosh N, Dillon MJ, Milla PJ 1990 Development of colonic sodium transport in early childhood and its regulation by aldosterone. Gut 31:194–197
25. Aperia A, Broberger O, Thodenius K, Zetterström R 1972 Renal response to an oral sodium load in newborn full-term infants. Acta Pediatr Scand 61:670–676
26. Lelievre-Pegorier M, Merlet-Benichou C, Roinel N, DeRouffignac C 1983 Developmental pattern of water and electrolyte transport in rat superficial nephrons. Am J Physiol 245:F15–F21
27. Stephenson G, Hammet M, Hadaway G, Funder JW 1984 Ontogeny of renal mineralocorticoid receptors and urinary electrolyte responses in the rat. Am J Physiol 247:F665–F671
28. Štolc V, Knopp J, Štolcová E. 1966 Iodine, solid diet, water and milk intake by lactating rats and their offsprings. Physiol Bohemoslov 15:219–225
29. Hazon N, Parker C, Leonard R, Henderson IW 1988 Influence of an enriched dietary sodium chloride regime during gestation and suckling and postnatally on the ontogeny of hypertension in the rat. J Hypertens 6:517–524
30. Yagil R, Etzion Z, Berlyne GM 1973 The effect of D-aldosterone and spironolactone on the concentration of sodium and potassium in the milk of rats. J Endocrinol 59:633–636
31. Siegel SR, Fisher DA, Oh W 1974 Serum aldosterone concentrations related to sodium balance in the newborn infant. Pediatrics 53:410–414
32. Pácha J, Popp M, Čapek K 1988 Corticosteroid regulation of Na^+ and K^+ transport in the rat distal colon during postnatal development. J Dev Physiol 10:531–540
33. Buts J-P, DeMeyer R, Kolanowski J 1983 Ontogeny of cell proliferation and DNA synthesis in rat colon: Role of glucocorticoids. Am J Physiol 244:G469–G474
34. Buts J-P, Nyakabasa M 1985 Role of dietary protein adaptation at weaning in the development of the rat gastrointestinal tract. Pediatr Res 19:857–862