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Feed volume
hyponatremia
plasma
sodium
urine
very low birthweight infants

Late Hyponatremia in Very Low Birthweight Infants (<1.3 Kilograms)

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Extract

Late hyponatremia (plasma Na^+ <130 mEq/liter) occurred frequently (on 54 of 159 occasions) in 46 very low birthweight (VLBW) infants (<1.3 kg at birth) between 2 and 6 weeks of age while receiving a sodium intake of ≤2 mEq/kg/24 hr. To elucidate possible pathogenetic mechanisms five groups of such infants were studied while receiving a commercially available formula reconstituted to give two different volumes and two different Na^+ concentrations. Sodium intake in the nonsupplemented (NS) infants (n = 23) was less than 2 mEq/kg/24 hr. Supplemented (S) infants (n = 16) received approximately 3 mEq Na^+/kg/24 hr. A further group of seven infants given a high volume (200 ml/kg/24 hr), high caloric (100 cal/dl) formula and Na^+ supplementation (to 3 mEq/kg/24 hr) was also included. Infants were studied from age 14 days until they weighed 1.80 ± 0.05 kg at a mean age of 47 days.

At the time of start of the study, 6 of 20 NS and 6 of 19 S infants were hyponatremic. After supplementation only two episodes of hyponatremia occurred in S infants, both during the first study week, whereas the high incidence of hyponatremia in NS infants remained unchanged throughout the first 3 weeks of the study period.

During baseline urine collections all infants excreted between 80 and 100 ml/kg/24 hr urine, but those receiving 150 ml/kg/24 hr formula decreased their urinary output rapidly to 50 ml/kg/24 hr, whereas infants receiving high volume feeds (200 ml/kg/24 hr) did not decrease their urinary output until the third balance at an average age of 45 days. All infants excreted between 1.0 and 1.2 mEq/kg/24 hr of sodium in their urine during the initial collection. Nonsupplemented infants reduced their urinary Na^+ excretion more rapidly than supplemented babies (NS: from 1.03 to 0.55 mEq/kg/24 hr, first *vs* second balance; S: from 1.00 to 0.80 mEq/kg/24 hr, first *vs* third balance). Mean potassium excretion remained unchanged in NS and S infants during the study period and was not affected by the volume or caloric content of the formula.

Extracellular volume (ECV) and total body water (TBW) were measured serially, and there were no differences between S and NS infants in the distribution of body water. The percentage of TBW and ECV decreased in all groups with increasing postnatal age.

Speculation

VLBW infants are prone to hyponatremia in the first 6 weeks of life because of the combined influence of renal immaturity, which permits relatively high urinary sodium loss in the presence of low plasma [Na^+], and low intake of sodium (≤2 mEq/kg/24 hr), the amount provided by some current formulas based on breast milk. Dilutional factors are not involved, but the role of aldosterone remains unresolved. Supplementation of the formula to provide a daily total sodium intake of 3 mEq/kg/24 hr until a weight of 1.5 kg is reached is corrective.

Investigations into the nutritional requirements for the VLBW infant (<1.3 kg) are being carried out in several phases in the Hospital for Sick Children, Toronto. During earlier investigations of calcium supplementation (7), a frequent incidental finding was a low plasma sodium concentration at 2–7 weeks postnatal age (8). The present study was designed to determine in VLBW infants the appropriate Na^+ intake to prevent this hyponatremia and to investigate possible underlying factors. We examined the effect of differences in feed volume and Na^+ and caloric intakes on plasma and urinary electrolytes and on body fluid compartments.

PATIENTS, PROCEDURES, AND METHODS

PATIENTS

Forty-six infants of birthweight <1.3 kg were studied. Table 1 shows the study groups, their mean birthweight, and their gestational age. All infants <1.3 kg birthweight admitted to the Neonatal Unit of the Hospital for Sick Children, Toronto, were

assessed for gestational age from the obstetrical history and developmental scoring (9) between *days 1* and *5* of life. Infants were allotted to one of four study groups and pertinent data of a previously studied series (8) were also included. The infants entered the study at an average age of 18 days. The study terminated when the infants' weight reached 1.80 ± 0.05 kg at an average age of 47 days. Infants were excluded if there was respiratory distress requiring intermittent positive pressure ventilation or if less than 80% of the desired formula intake was achieved by 3 weeks of age.

PROCEDURES

All infants were nursed in incubators (Isolettes (25)) to maintain standard conditions of temperature and humidity. They received a proprietary formula (26) reconstituted to either 80 or 100 cal/dl to provide caloric intakes of 150–160 or 200 cal/dl. The measured caloric and Na^+ intakes are indicated in Table 1.

Twice weekly the infants were weighed on an Air Shields, Inc. (25) balance and the plasma electrolyte concentrations and acid-base status in blood were determined. The base excess was maintained within 1 SD from normal (−1.5 to −4.9 mEq/liter) (2) by appropriate sodium bicarbonate administration. Three times during the study, three consecutive 24-hr urine collections for sodium, potassium, and chloride estimations were made; on these three occasions, body water studies were also performed after the urine collection was terminated to avoid interference by the Na^+ in the NaBr administered.

Sodium intake was measured from formula and was calculated from other exogenous sources (e.g., antibiotics (27)) in NS groups. Infants in the S groups received additional Na^+ to achieve a total Na^+ intake of approximately 3 mEq/kg/24 hr. Sodium supplements were in the form of $NaHCO_3$, unless the base excess was < −1.5 mEq/liter, when sodium was given as NaCl. Significant hyponatremia (plasma Na <125 mEq/liter) was treated with NaCl or $NaHCO_3$, depending on the base deficit.

For estimation of body fluid spaces a solution of 0.5% antipyrine in 2% NaBr was injected intravenously at a dose of 4 ml/kg after a zero time blood sample has been drawn. Because of the volume of plasma required for the antipyrine estimation (0.2 ml), only one further blood sample was obtained 3 hr after injection of tracer. The antipyrine space was then estimated from zero time dilution using the average regression line calculated by Cassady and Milstead (4) for neonates during the first 24 hr of life. For estimations of the bromide space, corrections were made for the Donnan factor and plasma water (3) as well as for intracellular water.

CHEMICAL METHODS

Plasma sodium and potassium were determined by standard flame spectrophotometric techniques and plasma chloride by coulometric-amperometric titration (5). Plasma concentrations of antipyrine were determined using Mendelsohn and Levin's (14) method and bromide estimation by neutron activation analysis (10).

RESULTS

Hyponatremia was arbitrarily defined as a plasma Na^+ concentration of less than 130 mEq/liter (7). For computation, plasma electrolyte concentrations of specimens obtained twice weekly were averaged. Values were excluded if blood was taken within 48 hr of a time when Na^+ intake exceeding the desired intake (Table I) by 1.0 mEq/kg/24 hr.

PLASMA ELECTROLYTE CONCENTRATIONS

Data were pooled for NS groups (*groups I* and *II*) since there were no differences between the two groups. Similarly, values were combined for the three S groups (*groups III–V*). Mean electrolyte concentrations are shown in Figure 1. Mean baseline values for Na^+ in plasma were similar in NS and S groups. Plasma sodium in NS groups decreased from baseline during the first study week, a difference which was statistically significant on paired *t*-testing ($P < 0.05$). Thereafter, NS infants continued to show low mean values until the fourth study week at an average age of 45 days, at which time an increase was noted ($P < 0.05$). In contrast, the S groups showed an immediate and progressive increase in mean plasma Na^+ concentrations to the normonatremic range by the first study week after Na supplementation.

For computation of "hyponatremic episodes" only the regularly obtained twice weekly Na^+ values were included with the exclusions outlined above.

The incidence of hyponatremic episodes was similar in all groups at the start of the study and averaged 31% (Table 2). Nonsupplemented infants showed a persistently high incidence of hyponatremia until the fourth study week. In S infants only two episodes of hyponatremia were observed after supplementation had started, both occurring during the week after commencement of Na^+ supplementation. The incidence of hyponatremia was highly significantly different between NS and S groups ($P < 0.001$).

Baseline plasma K^+ concentrations were similar in all groups but rose in patients of NS groups, especially in *group I*, during the period when hyponatremia was noted frequently (Table 2). Mean plasma K^+ values declined in S groups by approximately 1.5 mEq/liter after supplementation had started.

Plasma chloride concentrations were similar at the beginning of the study but then decreased in NS and increased in S infants so that a significant difference developed during most of the study period ($P < 0.01$ or <0.025) (Fig. 1). In NS infants, chloride concentrations rarely paralleled Na^+ concentrations and the incidence of hypochloremia (<100 mEq/liter) was lower than the incidence of hyponatremia.

Table 1. *Characteristics of patient groups, concentration of formula used, and caloric and sodium intakes*

Group	*n*	Birthweight, kg	Gestational age, weeks	Formula concentration, cal/dl[1]	Desired volume, ml/kg/24 hr	Measured caloric intake, cal/kg/24 hr	Measured Na^+ intake, mEq/kg/24 hr
Non-Na^+ supplement (NS)							
I	14	1.03 ± 0.05	30.5 ± 0.6	80	200	141	1.6
II	9	1.06 ± 0.05	29.3 ± 0.5	100	150	149	1.7
Na^+ supplement (S)							
III	8	1.10 ± 0.05	30.4 ± 0.8	80	200	152	2.8
IV	8	1.11 ± 0.06	30.1 ± 0.6	100	150	150	3.0
V	7	1.17 ± 0.04	29.8 ± 0.6	100	200	169	2.8

[1] Formula used (manufacturer's composition before dilution): fat 7.2%; carbohydrates 14.4%; protein 3%; calories 133/dl; Na^+ 1.3 mEq/dl; K^+ 2.86 mEq/dl; Cl 2 mEq/dl.

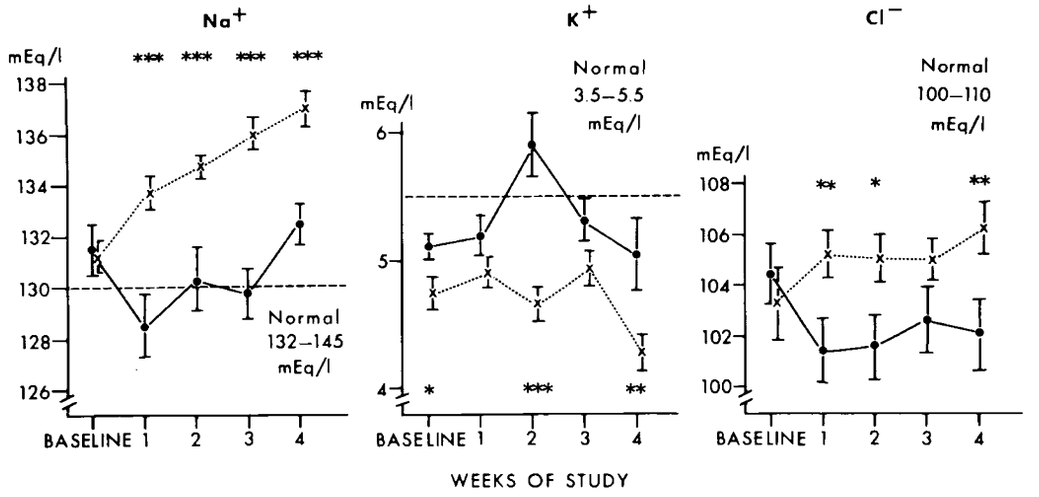

Fig. 1. Plasma electrolyte concentrations computed for weekly averages (mean ± SEM). ●——●: non-Na-supplemented infants; ×——×: Na-supplemented infants. *: $P < 0.05$; **: $P < 0.025$; ***: $P < 0.001$. "Normal" ranges for children are indicated.

Table 2. *Incidence of hyponatremia (plasma Na^+ < 130 mEq/liter) and hyperkalemia (plasma K^+ > 5.5 mEq/liter)*

Group	Baseline[1]	Weeks of study 1	2	3	4
Hyponatremia					
I and *II*	6/20	13/32	12/29	11/28	6/31
	30%	40.6%	41.4%	39.3%	19.4%
III, *IV*, and *V*	6/19	2/33	0/38	0/30	0/26
	31.6%	6.1%			
Hyperkalemia					
I and *II*	3/21	3/17	11/19	5/14	4/13
	14.3%	17.6%	57.9%	35.7%	30.8%
III, *IV*, and *V*	1/17	2/19	1/18	3/17	0/16
	5.9%	10.5%	5.6%	17.6%	0%

[1] Results computed from blood samples drawn within 48 hr of start of the study.

URINARY EXCRETION OF WATER AND ELECTROLYTES

Urinary excretion data are shown on Table 3. In *groups II* and *IV*, receiving 150 ml/kg/24 hr of formula, urinary volumes decreased significantly between the "baseline" and the first study specimen ($P < 0.001$ on paired *t*-testing), whereas the remaining groups, receiving 200 ml/kg/24 hr, showed no such decrease ($0.1 > P > 0.05$). The differences in urinary water excretion between "normal fluid load" and "high fluid load" patients are illustrated in Figure 2. No differences in urinary volume were seen between NS and S groups, nor did the higher solute load of *group V* cause any change in urinary volume.

The urinary Na^+ excretion rate was high in all groups during the baseline collection period, particularly in view of the low mean plasma Na^+ concentrations. Between baseline and the first study specimen NS infants decreased their urinary Na^+ excretion to approximately half the initial values ($P < 0.01$, paired *t*-test), whereas urinary Na^+ remained unchanged in S infants. By the end of the study, S infants showed a slight reduction in urinary Na^+ excretion compared with baseline values ($P < 0.05$). The differences in urinary Na^+ excretion between NS and S infants are depicted in Figure 3. Analysis of results according to gestational age greater or less than 30 weeks did not show any differences.

Potassium excretion in urine was slightly but not significantly ($P < 0.10$) lower in *group I* than in the other groups only during the baseline collections. The urinary Na/K ratio reflected only the changes in urinary Na^+ excretion. The Na/K ratio was slightly lower in the NS than in S groups, but differences were not statistically significant.

Chloride excretion in urine was higher in baseline specimens in *groups I–IV* than later during the study, but did not differ significantly between NS and S infants. The decrease of chloride excretion in NS infants did not parallel the decrease in Na^+ excretion.

TBW AND EXTRACELLULAR FLUID (ECF) SPACE

The age at which these measurements were performed was similar in *groups II–V*; in babies of *group I* TBW was determined twice at an older age than in the other groups (Table 4). Baseline values for TBW were lower in *group II* than in the S groups for unknown reasons. Total body water showed no significant trend related to either different feed volume or different sodium intakes. It also did not show any specific increase in *group V* infants (Fig. 4). Measurements of extracellular volume showed lower values in the third study specimen compared to the first in all four groups; however, differences between baseline and final means were not statistically significant. All values for TBW and ECF volume were within the mean ±2 SEM of Cassady's data (3, 4) for newborn infants (Fig. 4). In one infant of *group IV*, onset of cardiac failure due to a patent ductus arteriosus was clearly associated with expansion of the ECV. After successful treatment of cardiac failure the ECV reverted to the normal range.

DISCUSSION

The milk obtained by the young of marsupials is adapted to the varying growth requirements with increasing gestational age (18). Unfortunately, formulas available for the prematurely born human are not so adapted as has recently been pointed out by Shaw (19). To extrapolate from the requirements of full term newborns is probably inappropriate since the composition of formulas based on breast milk fails to take into account the relatively large quantities of minerals acquired by the fetus during the last trimester *in utero*. The discrepancy between mineral intake from commercially available formulas and requirements of VLBW infants have been emphasized recently by O'Donnell *et al.* (17). We agree with their statement that postnatal growth of VLBW infants should be similar to that *in utero* during the last trimester and have shown that this can be accomplished (24). From hypothetical considerations (17) and the results of our own and other studies (7, 13), we believe that mineral retention rates should parallel those *in utero* (20).

Table 3. *Urinary excretion data for each collection period expressed according to kilogram of body weight (mean ± SEM)*[1]

Group	C	Volume, ml	Na, mEq	K, mEq	Na/K	Cl, mEq
I	1	84.6 ± 5.3 (15)	0.98 ± 0.19 (12)	0.95 ± 0.12 (12)	1.10 ± 0.20 (12)	1.21 ± 0.22 (12)
	2	81.1 ± 5.8 (15)	0.64 ± 0.07 (12)	1.00 ± 0.15 (11)	0.72 ± 0.11 (11)	0.85 ± 0.10 (11)
	3	78.8 ± 3.3 (11)	0.45 ± 0.09 (11)	1.19 ± 0.10 (11)	0.30 ± 0.05 (11)	0.82 ± 0.11 (11)
II	1	76.1 ± 8.9 (8)	1.04 ± 0.22 (9)	1.24 ± 0.13 (9)	1.01 ± 0.26 (8)	1.45 ± 0.25 (8)
	2	49.8 ± 7.4 (5)	0.56 ± 0.12 (6)	1.00 ± 0.17 (6)	0.63 ± 0.13 (5)	0.85 ± 0.16 (5)
	3	66.1 ± 5.4 (8)	0.33 ± 0.07 (9)	1.39 ± 0.10 (9)	0.25 ± 0.05 (8)	0.91 ± 0.11 (8)
III	1	92.4 ± 8.6 (7)	1.11 ± 0.23 (7)	1.38 ± 0.17 (7)	0.80 ± 0.11 (7)	1.16 ± 0.20 (6)
	2	90.6 ± 3.4 (5)	1.50 ± 0.35 (5)	1.40 ± 0.14 (5)	1.08 ± 0.20 (5)	1.24 ± 0.28 (5)
	3	78.8 ± 4.6 (6)	0.92 ± 0.08 (6)	1.28 ± 0.11 (6)	0.74 ± 0.08 (6)	0.71 ± 0.05 (6)
IV	1	101.4 ± 4.7 (8)	1.54 ± 0.28 (8)	1.12 ± 0.09 (8)	1.54 ± 0.41 (8)	1.69 ± 0.30 (7)
	2	57.3 ± 4.1 (7)	0.86 ± 0.15 (7)	1.35 ± 0.06 (7)	0.64 ± 0.13 (7)	1.14 ± 0.28 (7)
	3	55.6 ± 3.2 (7)	0.83 ± 0.09 (7)	1.31 ± 0.16 (7)	0.74 ± 0.08 (7)	0.86 ± 0.16 (7)
V	1	78.1 ± 4.2 (8)	1.12 ± 0.18 (8)	1.27 ± 0.15 (8)	0.91 ± 0.16 (8)	0.88 ± 0.11 (7)
	2	88.6 ± 4.1 (5)	1.09 ± 0.13 (5)	1.50 ± 0.15 (5)	0.75 ± 0.11 (5)	0.98 ± 0.16 (4)
	3	58.5 ± 8.5 (5)	0.54 ± 0.13 (5)	1.39 ± 0.19 (5)	0.40 ± 0.09 (5)	0.78 ± 0.25 (5)

[1] C: collection period; numbers within parentheses = *n*.

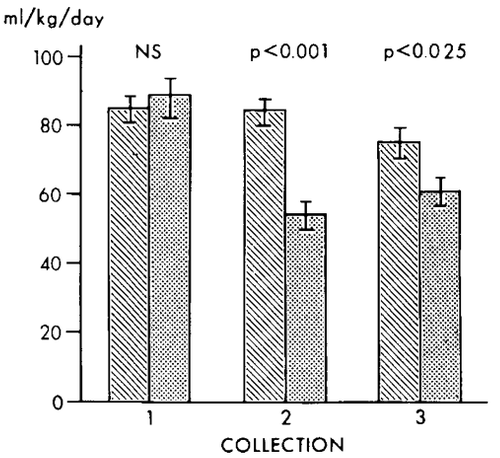

Fig. 2. Urine volume excretion (in milliliters per kg per 24 hr). Comparison between "high volume" (200 ml/kg/24 hr) ▧ and "normal volume" (150 ml/kg/24 hr) ▩ feeds. Vertical bars indicate mean ± SEM.

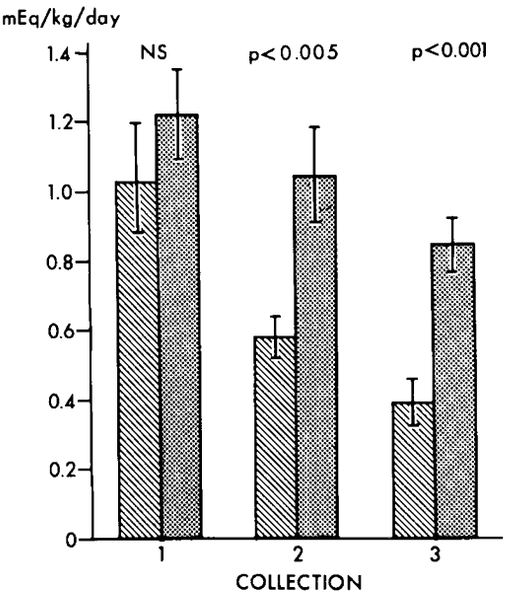

Fig. 3. Urinary Na^+ excretion (in milliequivalents per 24 hr). Comparison between non-Na-supplemented (*NS*) ▧ and Na-supplemented ▩ infants. Vertical bars indicate mean ± SEM.

The results of this study show that by feeding a formula simulating human milk and designed for full term infants such acquisition rates of Na^+ cannot be achieved and hyponatremia may develop. However, by increasing the sodium intake temporarily to 3 mEq/kg/24 hr, hyponatremia is prevented.

Although in the present study clinical symptoms, such as apnea and convulsions, did not correlate with the severity of hyponatremia, we considered it prudent to give additional Na^+ to any infant whose plasma Na^+ was less than 125 mEq/liter in view of our previous demonstration of reduced growth rates (24).

Very low birthweight infants have mean plasma Na^+ concentrations of 140 mEq/liter at birth (1, 8). Plasma Na^+ levels subsequently decline to a mean of 130 mEq/liter (8, 22, present study).

The Na^+ requirements of the VLBW infant are higher than for the full term infant for the following possible reasons. Firstly, the rate of accumulation of Na^+ in the body is proportionately and absolutely higher early during the third trimester than at term (19, 23). Secondly, Na^+ necessarily coprecipitates with calcium in bone during the process of calcification, probably contributing to the higher Na^+ requirements. Finally, there is an apparent obligatory Na^+ loss in the urine in the early postnatal period in VLBW infants (8, 22). In the present study losses of Na^+ in the urine averaged 1.2 mEq/kg/24 hr by the third week of life so that when losses in stool and through the skin are taken into consideration, a Na^+ deficit develops by the age of 2–3 weeks. Honour *et al.* (11) showed a relatively high urinary output of Na^+ coexistent with hyponatremia in VLBW twins during the second week of life. These infants were able to reduce urinary Na^+ excretion during the subsequent 4 weeks. High volume feeds in some infants apparently produced only increased urinary water excretion without concomitantly increasing urinary Na^+ output.

We have shown that the ability to retain Na^+ improves with postnatal rather than postconceptional age. This finding is in agreement with the concept of Nash and Edelmann (16) that renal function matures in response to a stimulus, in this case, hyponatremia. Steichen and Kleinman (21) found that increased dietary

Table 4. *Body fluid spaces (in milliliters per kilogram of body weight) (mean ± SEM)*[1]

Group	Period	Average age, days	Body weight, kg	TBW	ECV
I	1	35	1,223 ± 64	788 ± 16 (5)	
	2	64	2,038 ± 124	735 ± 38 (5)	
II	1	19	1,077 ± 55	779 ± 14 (5)	433 ± 54 (5)
	2	31	1,434 ± 54	796 ± 48 (6)	334 ± 36 (4)
	3	55	1,738 ± 29	824 ± 39 (4)	379 ± 13 (5)
III	1	19	1,167 ± 75	883 ± 36 (4)	397 ± 34 (5)
	2	30	1,458 ± 92	833 ± 45 (3)	346 (2)
	3	41	1,803 ± 17	795 ± 27 (6)	360 ± 15 (4)
IV	1	18	1,058 ± 40	852 ± 32 (6)	410 ± 22 (7)
	2	28	1,371 ± 60	801 ± 71 (3)	422 ± 19 (4)
	3	44	1,795 ± 53	892 ± 37 (5)	363 ± 13 (6)
V	1	24	1,107 ± 150	862 ± 65 (3)	501 ± 51 (3)
	2	33	1,337 ± 179	816 ± 54 (3)	399 ± 11 (3)
	3	42	1,847 ± 77	783 ± 27 (5)	369 ± 8 (5)

[1] TBW: total body water; ECV: extracellular fluid volume. Numbers within parentheses = *n*.

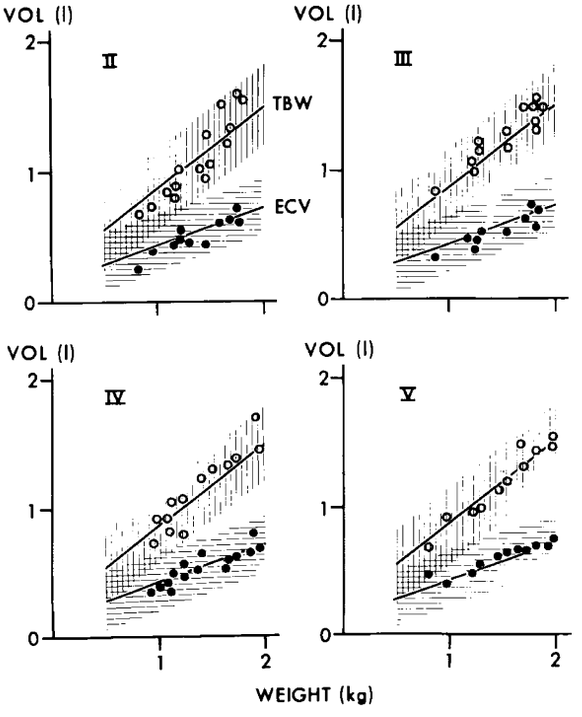

Fig. 4. Total body water (antipyrine space) and extracellular volume (bromide space) for *groups II–V*. Shaded areas indicate mean ± SEM of Cassady's data (3, 4).

salt intake improved the response of the kidney of newborn puppies to an acute salt stress, but did not affect other maturational functions in their animals.

Factors involved in the relatively high renal losses of Na^+ in the premature infant after birth have been reviewed by Metcoff (15). We have been unable to clarify the role of the renin-angiotensin-aldosterone system in this phenomenon in our study infants. The decreased Na^+/K^+ ratio in the urine is due almost entirely to a decreased urinary content of Na^+, since the urinary K^+ excretion rises only slightly, if at all, despite a constant rather high plasma K^+ in NS infants. This finding suggests that maturation of the aldosterone response to hyponatremia is present in VLBW infants, an aspect which is discussed in the preceding paper (8).

The immediate response of plasma Na^+ concentrations to increased Na^+ intake showed that the late hyponatremia of the VLBW infant can be readily corrected and that the dietary Na^+ requirement of these infants is higher than the presumed intrauterine accretion rates. The formulas used for feeding VLBW infants contain less Na^+ than necessary for their growth because their electrolyte content is adjusted to the requirements of the full term infant and to the composition of human milk (12).

Of potential adverse effects of supplemental Na^+ administration we have excluded expansion of TBW and ECV, because in S infants, there was neither deviation from normal nor change with supplementation. The hyponatremia in NS infants was not a dilutional phenomenon since hyponatremic episodes were not associated with expansion of ECV. There was also no inappropriate weight gain or increase in skinfold thickness indicating edema during the episodes of hyponatremia in NS infants.

The role of dietary Na^+ in potentiating any tendency to future development of hypertension is still in question (6). We recommend small doses of Na^+ distributed throughout the day at the end of each feed or mixed with feeds so that the osmotic load of the added Na^+ does not become an adverse factor. Our recommendations for increased Na^+ intake are for infants of birthweight $<$ 1.3 kg at a time of high urinary Na^+ excretion and become unnecessary for such infants of postnatal age greater than 45 days or body weight greater than 1,500 g, about which time sodium retention improves, presumably because of maturing renal function.

SUMMARY

Hyponatremia (plasma Na^+ $<$130 mEq/liter) was found in approximately one-third of "healthy" VLBW infants ($<$1.3 kg birthweight) fed formulas providing less than 2 mEq/kg/24 hr of Na^+ between the second and sixth week of life. This hyponatremia can be corrected and adequate sodium retention achieved by supplementing the formula to provide a total daily sodium intake of 3 mEq/kg until the postnatal age of 6–7 weeks.

The major factor causing inadequate Na^+ retention is high urinary Na^+ loss relative to plasma Na^+ levels, probably because of immature renal function. There was no significant dilutional effect contributing to the hyponatremia.

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25. Air Shields (Canada), Ltd., 22 Lepage Court, Downsview, Ontario.
26. SMA-S26, Wyeth Ltd., 4455 Chesswood Drive, P. O. Box 10, Downsview, 461, Ontario.
27. Ampicillin, 200 mg/kg/24 hr iv, supplying 0.66 mEq/kg/24 hr of Na^+. Gentamicin, 3 mg/kg/24 hr im, supplying 0.02 mEq/kg/24 hr of Na^+.
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Cystic fibrosis spermidine
fibroblasts spermine
polyamines

The Effect of Spermidine and Spermine on Proliferation *in Vitro* of Fibroblasts from Normal and Cystic Fibrosis Patients

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Extract

The effects of spermidine and spermine at varying concentrations upon the replicative ability of human fibroblasts in cell culture have been studied. The average concentrations of spermidine causing a 50% inhibition of proliferation (ID_{50}) after 3 days of growth for three normal cell strains and three strains derived from patients with cystic fibrosis (CF) were $4.4 \times 10^{-6} \pm 1.2$ M and $6.2 \times 10^{-6} \pm 2.1$ M, respectively. The values for spermine were $2.0 \times 10^{-6} \pm 0.5$ M for normal and $2.2 \times 10^{-6} \pm 0.1$ M for fibroblasts from cystic fibrosis patients. No significant difference between the replicative ability of normal and CF cell strains was seen over a wide range of polyamine concentrations employed for a period of up to 3 days.

Speculation

This work shows no difference in the replicative ability of fibroblasts obtained from normal or CF patients when exposed to spermidine or spermine. We cannot relate the results of this study to recent reports of increased blood cell polyamine levels in cystic fibrosis, but examination of cellular uptake and metabolism of polyamines may allow us to do so in the future.