THE OSMOTIC CONCENTRATING ABILITY IN HEALTHY INFANTS AND CHILDREN

BY

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The concentrating ability of the kidney changes with age: after birth it increases (Smith, 1959), and in old age it falls (Lindeman, van Buren, and Raisz, 1960). The maximum osmolality during the newborn period is much lower than in adults (Heller, 1944; Smith, Yudkin, Young, Minkowski, and Cushman, 1949; Barnett and Vesterdal, 1953; Hansen and Smith, 1953; McCance and Widdowson, 1954; Calgagno and Rubin, 1960; Fisher, Pyle, Porter, Beard, and Panos, 1963). This smaller concentrating ability rapidly increases after birth, as shown by the significantly higher maximum osmolality of the urine in mature and some premature children in the second to fourth week of life (Pratt and Snyderman, 1953; Edelmann, Barnett, and Troupkou, 1960), and may reach 1,473 mOsm./l. at the age of 35 days (Pratt, Bienvenu, and Whyte, 1948), and 1,570 mOsm./l. at 73 days (Drescher, Barnett, and Troupkou, 1962). The osmolality of the urine of premature infants in the first month of life can be low (Calgagno, Rubin, and Weintraub, 1954), particularly in premature infants with a birth weight below 2,250 g. in comparison with that of mature infants of the same age (Vocel, Poláček, Neugebaurová, and Šebková, 1963). Results in a number of series of children investigated with various tests showed a tendency for maximum osmolality to increase after the second month of life (Winberg, 1959; Poláček and Polanská, 1962; Martínek, Janovský, and Stanincová, 1962) and even after the first year of life (Winberg, 1959; Poláček, 1962). The comparison of these data is difficult because the methods used to achieve increasing concentration of urine were diverse. For this reason it seemed desirable to investigate subjects from the early postnatal period up to adult life, using a single method. Since premature infants with a low birth

weight react to fluid restriction with lower concentration of urine, and sometimes even by haemoconcentration and raised non-protein nitrogen (Vocel *et al.*, 1963; Fisher *et al.*, 1963), only those premature infants with a birth weight over 2,250 g. were included in the series.

Material and Methods

The following 212 children were included in the investigation: 32 newborn infants from the First University Obstetric Department, 13 premature infants with a birth weight above 2,250 g. in the First University Children's Department in Prague, 79 toddlers from the Children's Home in Kunratice, and 57 pre-school and school children in the Educational Department of the First University Children's Department in Prague. Children affected with serious disease and convalescents after acute illness were excluded. The concentration test was carried out by giving the children dried milk dissolved in half the usual amount of water with sugar added, for 24 hours, in amounts corresponding to their usual calorie intake. The preparation of full-cream milk was used for older children and a half-cream milk in younger infants. The urine was collected at intervals of about three hours and stored in the refrigerator. The temperature of infants and young children was taken frequently. If it rose above 37.5°C . the experiment was stopped, but the result of this abbreviated test was also taken into the series. Osmolality was determined cryoscopically by a thermistor connected up to a Wheatstone bridge. The accuracy of the method was repeatedly checked by determining the depression of the freezing point on the same sample by the Beckmann thermometer. The difference between two measurements did not exceed 1%. Maximum osmolality was taken as the highest osmotic value attained in the urine samples. Unusually high osmolality was determined at least three times and the probability of the results confirmed by determining specific gravity and concentrations of Na, K, Cl, and urea.

FIG. 1.—Relation of maximum urine osmolality to age in healthy infants and children. Maximum urine osmolality of urine samples in course of 24-hour concentration test by means of double concentrated milk. Logarithmic scale for age.

TABLE 1
AVERAGE AND MAXIMUM URINE OSMOLALITY OF PREMATURE AND FULL-TERM INFANTS
DURING FIRST WEEK OF LIFE

Reference	Description of Infants	Diet	Urine Osmolality (mOsm./l.) on Different Days					
			1	2	3	4	5	6
Heller (1944)	23 full-term	Normal fluid intake	350-450	280-530	120-440	80-700	50-360	120-150
McCance and Widdowson (1954)	18 full-term	25 ml. water for first 48 hr.	375 ± 91.5	465 ± 51	—	—	—	—
Smith <i>et al.</i> (1949)	10 prematures (1,530-2,260 g.)	Fluid withheld 52.5-112 hr.	—	—	Maximum urine osmolality:		—	—
Hansen and Smith (1953)	3 full-term	Fluid withheld for first 72 hr.	200*-530*	350*-600*	400*-680	400-624	—	—
Calgagno and Rubin (1960)	6 prematures	Cows' milk	—	Average urine osmolality: 318		(184-449)	—	—
	4 full-term	Low osmolar milk	—	Average urine osmolality: 157		(77-492)	—	—
	12 full-term	Modified evaporated milk + carbohydrate formula	—	Average urine osmolality: 204		(114-454)	—	—
	14 full-term	Colostrum	—	Average urine osmolality: 273		(70-408)	—	—
Barnett and Vesterdal (1953)	9 full-term	Transitional milk	—	—	—	—	—	77 and 164
Fisher <i>et al.</i> (1963)	2 full-term	4 hr. after last feeding	—	—	—	—	5th to 8th day	—
	4 prematures 5-8 days	—	—	—	—	—	610	(432-778)
	60 full-term	5% glucose first 24 hr., then evaporated milk with 1½ parts water	291 (120-460)	309 (140-460)	240 (70-587)	187 (58-480)	—	—
	15 prematures	Fluid withheld 72 hr., then 5% glucose for 24 hr., then breast milk	230 ± 56	293 ± 40	441 ± 69	—	149 ± 24	94 ± 51
			Serum Na 145 mEq/l.	—	Serum Na 150 mEq/l.	—	—	Serum Na 142 mEq/l.

* Results given only in figures. Values estimated.

FIG. 2.—Regression line of maximum urine osmolality. Normal scale for age.

Results

The general results are given in Fig. 1 in which the age is expressed logarithmically, and it shows that the maximum osmolality of the urine tends to increase with age. However, the regression line does not run linearly ($F = 1.4$; $F(0.05, 200, 500) = 1.2$), but exponentially ($F = 0.955$). The unconverted course of the regression line is given in Fig. 2, which shows that the average maximum osmolality of the urine increases rapidly in the first few months of life and that subsequently the rate of increase progressively slows down.

Discussion

All authors give much lower values for the osmolality of the urine in the first week of life than at a later age. In Table 1 are set out the results of a number of investigations on the concentrating ability of premature and full-term infants during the first week of life.

In our series the average maximum osmolality of the urine was 515 mOsm./l. (S.D. 172, $n = 17$) on the 3rd day, which is in good accord with findings of Hansen and Smith (1953) who found values of 400–680 mOsm./l. in 3-day-old infants without fluid intake.

In our series the average maximum osmolality on the 6th day was 663 mOsm./l. (S.D. 133, $n = 16$),

which is significantly higher than on the third day ($p < 0.01$) and corresponds approximately to values found by Barnett and Vesterdal (1953) in premature infants aged 5–8 days (432–778 mOsm./l.), but much higher than those quoted by Heller (1944) (on the 6th day 120–150 mOsm./l.) and by Fisher *et al.* (1963) (on the 6th day 94 mOsm./l. $\pm$ 51). These considerable differences in the results can be explained by the fact that in the last two groups the infants were given a small osmotic load with adequate fluid intake. Great diversity in the osmolality of the urine has been recorded from the end of the first week to the end of the first year. For this reason comparison should be restricted to investigations in which an increased osmotic load or a restriction of fluid intake has been employed or a combination of both. In Table 2 are set out the results of investigations in infants aged over 1 week up to 3 months.

We found that at the age of 10–30 days maximum osmolality of the urine amounted to an average value of 896 mOsm./l. (S.D. 179, $n = 12$). This value is significantly higher than the average maximum osmolality in this series at 6 days ($p < 0.001$). This corresponds to the osmolality of the urine reached by infants of Edelman *et al.* (1960) fed on 8–9 g. protein/kg.

The maximum osmolality noted in our infants aged 1–2 months reached an average of 1,054 mOsm./l. and is in agreement with the average osmolality in the infants of Pratt *et al.* (1948) after the first 24 hours of water restriction.

The osmolar concentrating ability of infants aged over 2 months was investigated by Winberg (1959). He first gave an intramuscular injection of pitressin tannate in oil (0.5 pressure units per 6 kg. body weight) and then deprived the infants of all fluid for 16 hours by leaving out one or two feeds. The regression line in Winberg's series rose up to 1 to 1½ years. In children older than 3 years, Winberg recorded an average maximum osmolality of the urine of 1,069 mOsm./l. (S.D. 127, $n = 16$). Increase in urine osmolality with age in infants on a decreased fluid intake was noted by Martinek *et al.* (1962, Table 2).

In our series the regression line rises throughout the entire first year of life. In the children aged 10–12 months maximum urine osmolality reached an average of 1,118 (S.D. 154, $n = 7$) and was significantly higher than in infants aged 2–5 weeks ($p < 0.02$). The increase in the regression line persists, though more slowly after the first year of life. At 14–18 years the average osmolality of the urine reaches 1,362 (S.D. 109, $n = 9$), which is significantly higher than at the end of the first year ($p < 0.01$).

It is very probable that some children in our series

TABLE 2
MAXIMUM URINE OSMOLALITY OF INFANTS AGED 1 WEEK TO 3 MONTHS:
RESULTS OF INVESTIGATIONS BY VARIOUS METHODS OF CONCENTRATION

Reference	Description and Age of Infants	Description of Diet	Maximum Urine Osmolality mOsm./l.	Results After Age of 3 mth.
Calgagno <i>et al.</i> (1954)	5 prematures 5-25 dy.	12-18 hr. without fluid	617 (588-648)	
Pratt and Snydermann (1953)	6 prematures 11-23 dy.	Evaporated milk with small amounts of water for 3 dy.	637-985	
Edelmann <i>et al.</i> (1960)	Prematures 7-39 dy. No. 4 No. 5 No. 4 No. 1	Various diets for 3-7 dy. 8-9 g. protein/kg. + restricted water 8-9 g. protein/kg. + normal water intake 4 g. protein/kg. + restricted water Loaded with urea Loaded with 250 mg. NaCl/kg.	857-993 707-1,139 615-864 825 616	
Vocel <i>et al.</i> (1963)	28 prematures 26 full-term 10-90 dy.	Dried milk + $\frac{1}{2}$ water content up to 24 hr.	Full-term and prematures over 2,250 g. in 16 hr. above 700 Prematures 1,400-2,250 g.: 36% under 700 in 24 hr. 905*-1,570* Highest value in infant 73 dy. old After 24 hr.: 914-1,177 after 5-6 dy.: 973-1,473	
Drescher <i>et al.</i> (1962)	6 full-term 2 wk.-2 mth.	Various protein and urea loads with restricted water for 3 dy.	694 919 1,012 500*-960*	
Pratt <i>et al.</i> (1948)	5 infants 30-65 dy.	130 cal./kg./day: Evaporated milk with carbohydrate without added water		
Martinek <i>et al.</i> (1962)	Infants 16-19 dy. 6 wk. 2½-3 mth.	Dried breast-milk with $\frac{1}{3}$ water content for 24 hr.		
Winberg (1959)	10 infants from 1 mth. up	Fluid withheld 16 hr. + pitressin tannate in oil		4½ mth. 1,082 mOsm./l. 31 children 3-36 mth.: 580*-1,320* 16 children above 3 yr.: 1,069 (S.D.127·5)

* Results given only in figures. Values estimated.

did not reach their maximum concentrating ability in the course of 24 hours. Others perhaps did not need to reach this limiting concentration. The results of Pratt *et al.* (1948), Drescher *et al.* (1962), and Sargent and Johnson (1954, 1956) furnish evidence that some children and young men can attain higher concentrations of the urine by more prolonged water restriction combined with adequate osmotic loading. Our experience (Poláček and Polanská, 1962) shows, however, that some healthy infants do not tolerate this prolonged water restriction without greatly increased temperature and other disturbances. The method described in this paper permitted the investigation of children in the same manner from the neonatal period up to puberty while sufficiently high values of urine osmolality were obtained.

Summary

A concentrating test was carried out in 212 children aged from 3 days to 18 years by giving them dried milk made up with half amount of water for 24 hours with addition of sugar and limited to the usual intake of calories. Urine was collected at three-hour intervals, and maximum osmolality of the urine was taken as the highest value found in the separate urine samples. This maximum urine osmolality increases with age from birth to puberty.

The average maximum urine osmolality values increase rapidly in the first months of life and then the increase is slower. There are significant differences between the average values of maximum urine osmolality on the 3rd day (515 mOsm./l.), the 6th day (663 mOsm./l.), the first month excluding the first week (896 mOsm./l.), the end of the first year (1,118 mOsm./l. at 10-12 months), and at puberty (1,362 mOsm./l. at 14-18 years). The regression line has an exponential character ($Y = 1,400 \times (1 - 0.943 \times t^{-0.325})$).

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