

ORIGINAL COMMUNICATION

24-h hydration status: parameters, epidemiology and recommendations

F Manz^{1*} and A Wentz¹

¹Research Institute of Child Nutrition, Dortmund, Germany

Hydration of individuals and groups is characterised by comparing actual urine osmolality (Uosm) with maximum Uosm. Data of actual, maximum and minimum Uosm in infants, children and adults and its major influencing factors are reviewed. There are remarkable ontogenetic, individual and cultural differences in Uosm. In the foetus and the breast-fed infant Uosm is much lower than plasma osmolality, whereas in children and adults it is usually much higher. Individuals and groups may show long-term differences in Uosm. In industrialised countries, the gender difference of Uosm is common. There are large intercultural differences of mean 24-h Uosm ranging from 860 mosm/kg in Germany, 649 mosm/kg in USA to 392 mosm/kg in Poland. A new physiologically based concept called 'free-water reserve' quantifies differences in 24-h euhydration. In 189 boys of the DONALD Study aged 4.0–6.9 y, median urine volume was 497 ml/24-h and median Uosm 809 mosm/kg. Considering mean \pm 2 s.d. of actual maximum 24-h Uosm of 830 mosm/kg as upper level of euhydration and physiological criterion of adequate hydration in these boys, median free-water reserve was 11 ml/24-h. Based on median total water intake of 1310 ml/24-h and the third percentile of free-water volume of -156 ml/24-h, adequate total water intake was 1466 ml/24-h or 1.01 ml/kcal. Data of Uosm in 24-h urine samples and corresponding free-water reserve values of homogeneous groups of healthy subjects from all over the world might be useful parameters in epidemiology to investigate the health effects of different levels of 24-h euhydration.

European Journal of Clinical Nutrition (2003) 57, Suppl 2, S10–S18. doi:10.1038/sj.ejcn.1601896

Keywords: water; hydration status; urine osmolality; maximum urine osmolality; free-water reserve; adequate total water intake

Introduction

Water is the most abundant compound in the body with unique physicochemical characteristics. There is increasing evidence that even mild dehydration, defined as a 1–2% loss in body mass caused by fluid loss, impairs exercise performance, affects overall health in the elderly and increases the risk of urinary stone disease (Kleiner, 1999). Nevertheless, water intake is frequently disregarded for three main reasons. Firstly, in the past the scientific interest of medicine with regard to water metabolism has mainly concentrated on the extremes, that is, severe dehydration and water intoxication. Secondly, there is no universally accepted laboratory method to characterise individual hydration status. Thirdly, water requirement depends on several factors (eg climate, physical

activity, renal solute load). It is, therefore, impossible to set general values for water requirements. In the United Kingdom, for example, water is not included in the list of dietary reference values (Department of Health, 1991) and in the USA a total water intake of 1.5 ml/kcal is recommended in infants and 1 ml/kcal in children and adults for practical purposes only (National Research Council, 1989).

Water intake is the sum of water in food and beverages plus metabolic water. Water output is the sum of water losses by the lung, skin, intestine and kidney. Water homeostasis is regulated by a multiple-loop feedback system. The most important loop includes the hypothalamus, the hypophysis and the kidney. In the hypothalamus and hypophysis plasma tonicity modulates the secretion of vasopressin. Plasma vasopressin activates the concentrating mechanisms of the kidney and therefore, plays a dominant role in the adjustment of plasma tonicity. Acute changes in the hydration status are commonly designated as dehydration or rehydration. Differences in the steady-state hydration status are called hypohydration, euhydration or hyperhydration. However, there are no universally accepted definitions

*Correspondence: F Manz, Research Institute of Child Nutrition, Heinstück11, D 44225 Dortmund, Germany.

E-mail: manz@fke-do.de

Guarantor: F Manz.

Contributors: FM designed the publication, developed the concept of free-water reserve and wrote the paper. AW carried out data analysis and assisted in compiling the data from the literature.

or laboratory methods to characterise the different forms of hydration status (Shirreffs, 2000).

In the following, differences in euhydration characterised by urine osmolality (Uosm) and a new physiologically based parameter to characterise euhydration ('free-water reserve') are presented.

Definition of euhydration

In a subject, maximum and minimum Uosm define the range of euhydration (Figure 1). Delineating the data of maximum and minimum Uosm on a logarithmic scale, the

two functional capacities are almost equidistant from plasma osmolality, allowing the kidney to overcome differences in urinary water excretion rates up to a factor of 20. If in a particular life stage and gender group values of maximum and minimum Uosm are only known in a representative subgroup of subjects, three categories of 24-h hydration can be characterised using data of Uosm: risk of hypohydration ($Uosm \geq \text{mean} - 2 \text{ s.d. value of maximum Uosm}$), euhydration ($\text{mean} - 2 \text{ s.d. value of maximum Uosm} > Uosm > \text{mean} + 2 \text{ s.d. value of minimum Uosm}$) and risk of hyperhydration ($Uosm \leq \text{mean} + 2 \text{ s.d. value of minimum Uosm}$) (Figure 1). In a subject of this life stage and gender group diagnosis of hypo(hyper)-hydration presumes, however, additional clinical or biochemical signs of hypo(hyper)-hydration. Thus, in groups of healthy subjects mean $-2 \text{ s.d. value of maximum Uosm}$ may be used as a physiologically based criterion for the 'safe' upper level of euhydration ensuring euhydration in 97.7% of the subjects (Manz *et al*, 2002).

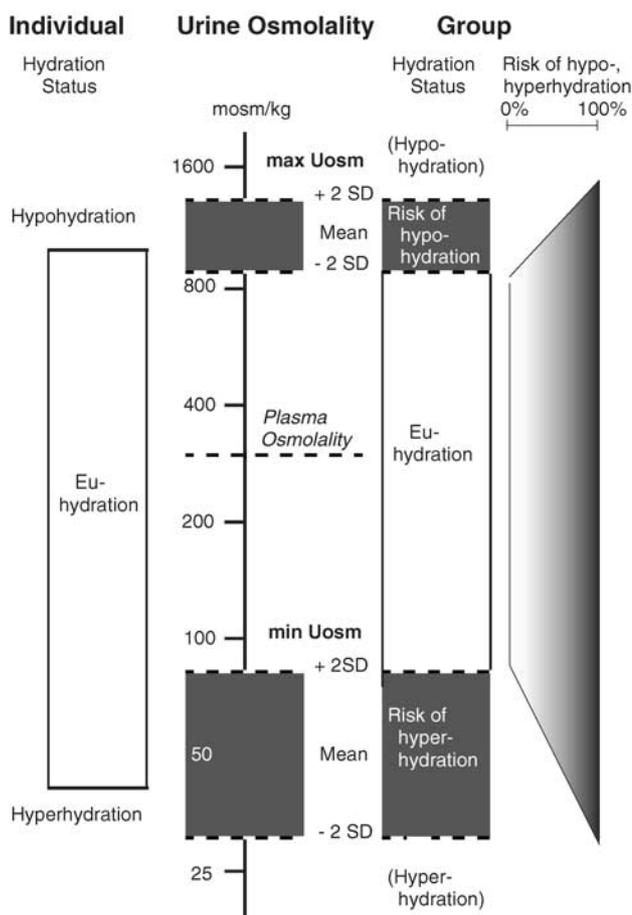


Figure 1 Definitions of 24-h hydration status: In a subject individual minimum and maximum 24-h urine osmolality characterise 24-h hydration status of hypohydration, euhydration and hyperhydration. In a group in which only mean and standard deviation values of minimum and maximum urinary osmolality of a representative subgroup of subjects are known, three categories of 24-h hydration can be characterised using data of Uosm: risk of hypohydration ($Uosm \geq \text{mean} - 2 \text{ s.d. value of maximum Uosm}$), euhydration ($\text{mean} - 2 \text{ s.d. value of maximum Uosm} > Uosm > \text{mean} + 2 \text{ s.d. value of minimum Uosm}$) and risk of hyperhydration ($Uosm \leq \text{mean} + 2 \text{ s.d. value of minimum Uosm}$). Additional clinical or biochemical signs of hypo(hyper)-hydration are necessary to diagnose hypo(hyper)-hydration in a subject of this life stage and gender group.

Maximum and minimum Uosm and age

Figure 2 shows mean values of maximum and minimum Uosm in groups of term and preterm infants fed either human milk or different infant formulas. There is a rapid increase in maximum renal concentration capacity in the first months of life. Normal levels for children were reached

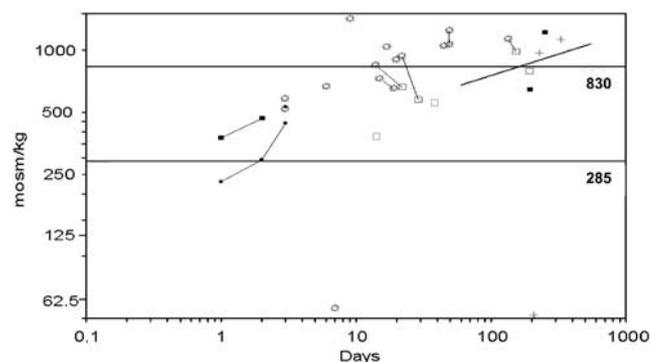


Figure 2 Mean values of maximum and minimum urine osmolality in standardised tests of renal concentrating and diluting capacity according to postnatal age, gestational age (preterm and term infants) and nutrition (human milk, cow's milk, cow's milk formula, humanised formula, beikost): (●) human milk in preterm infants (Smith *et al*, 1949; Fisher *et al*, 1963), (■) human milk in term infants (McCance and Widdowson, 1954; Janovsky *et al*, 1968; Marild *et al*, 1992), (□) humanised formula (Edelmann *et al*, 1960; Janovsky *et al*, 1968; Svenningsen and Aronson, 1974; Marild *et al*, 1992) (○) cow's milk and cow's milk formula (Pratt *et al*, 1948; Barnett *et al*, 1952; Hansen and Smith, 1953; Edelmann *et al*, 1960; Drescher *et al*, 1962; Polacek *et al*, 1965; Janovsky *et al*, 1968), (+) formula and beikost (Polacek *et al*, 1965; Rodriguez-Soriano *et al*, 1981; Assadi, 1990), (—) regression line (Winberg, 1959); (●-●; ∞-∞) repeated tests in the same infants; 830 mosm/kg: mean -2 s.d. of maximum Uosm in healthy children and adolescents consuming a typical affluent Western-type diet; 285 mosm/kg: mean plasma osmolality.

at the age of about 6 months. Minimum Uosm decreased with age. Thus, young infants showed a structurally and functionally lower renal concentrating and diluting capacity than older infants and children.

In Figure 3, mean values of maximum and minimum Uosm in healthy children and adults after fluid restriction and/or the administration of vasopressin are presented. Older adults showed lower values of maximum and higher values of minimum Uosm than children or young adults. In six groups of adults the median decrease in maximum Uosm was 3.4 mosm/kg/y (Lindeman *et al*, 1966; Rowe *et al*, 1976; Nadvornikova *et al*, 1980; Tencer, 1988; Tryding *et al*, 1988; Tan *et al*, 1991).

Functional modulation of maximum Uosm

Maximum Uosm is dependent on age and is mainly modulated by the duration of water restriction, the level of protein and sodium intake and strenuous physical activity. In young adults the prolongation of water restriction from 10–16 to 20–36 h increased mean maximum Uosm by 116 to 230 mosm/kg, respectively (Miles *et al*, 1954; Nadvornikova *et al*, 1980; Baumgarten *et al*, 2000). Fluid restriction for 3 days resulted in an additional increase in mean maximum

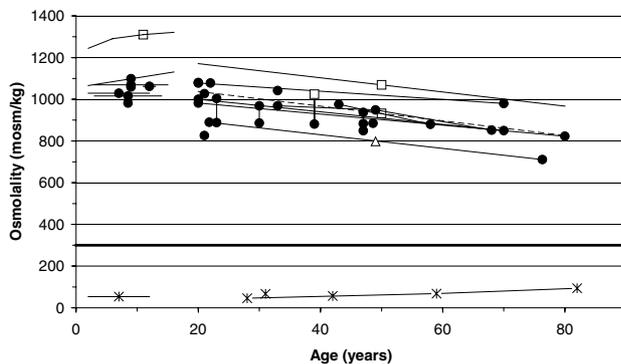


Figure 3 Mean values (Δ , \bullet , \square) and regression lines (—) of maximum urine osmolality in standardised tests of renal concentrating and diluting capacity according to age in children and adults: results of renal concentrating test with (Δ) vasopressin after high fluid intake (Bendz, 1985); (\bullet) 12–18 h fluid restriction and/or vasopressin (children: Winberg, 1959; Edelmann *et al*, 1967; Monnens, 1971; Uttley *et al*, 1972; Abyholm and Monn, 1979; Stapleton and Miller, 1988; Marild *et al*, 1992; maximum Uosm: 1054 ± 112 mosm/kg (mean \pm s.d.); 830 mosm/kg (mean -2 s.d.); adults: Miles *et al*, 1954; Isaacson, 1960; Toor *et al*, 1965; Macaronon *et al*, 1975; Rowe *et al*, 1976; Alwall, 1978; Monson and Richards 1978; Curtis and Donovan, 1979; Güllner *et al*, 1980; Askergren *et al*, 1981; Koppeschaar *et al*, 1985; Tencer, 1988; Tryding *et al*, 1988; Tan *et al*, 1991; Baumgarten *et al*, 2000; decrease in maximum Uosm at an age above 20 y: 3.4 mosm/kg/y); (\square) more than 18 h fluid restriction and/or high protein intake (Miles *et al*, 1954; Polacek *et al*, 1965; Lindeman *et al*, 1966; Nadvornikova *et al*, 1980) mean values (*) and regression lines (—) of minimum urinary osmolality in renal diluting tests in children and adults during high oral water intake or intravenous hypotonic saline (Lindeman *et al*, 1966; Klahr *et al*, 1967; Rodriguez-Soriano *et al*, 1981; DiScala and Stein, 1982).

Uosm of 400 mosm/kg (Epstein *et al*, 1957a) compared to 12 h fluid restriction after long-term high fluid intake (5000 ml/24-h for 3 days). Infants fed protein-rich cow's milk or cow's milk formulas showed higher maximum Uosm values (Figure 2). In adults, mean maximum Uosm with a high protein intake was 300 mosm/kg higher than with a low protein intake (Epstein *et al*, 1957b; Levinsky *et al*, 1959; Macaron *et al*, 1975; Koppeschaar *et al*, 1985). The difference in mean maximum Uosm between a sodium intake of 20 and 150 mmol/24-h was 74 or 94 mosm/kg (Koppeschaar *et al*, 1985). In dehydrated soldiers, heavy physical exercise transiently decreased maximum Uosm by up to 300 mosm/kg (Raisz *et al*, 1959; Schrier *et al*, 1970). If the mean Uosm of a group is to be commented on, age and functional status of the kidney should be taken into account.

Differences of euhydration characterised by urine osmolality

Many indices have been investigated to establish their potential as markers of hydration status. Current evidence and opinion tends to favour urine indices, especially osmolality as the most promising marker available (Shirreffs, 2000). Uosm above plasma osmolality implies functional water conservation, Uosm below plasma osmolality implies a functional surplus of water. Osmolality is, however, only a measure of concentration. In order to quantify individual 24-h hydration status, 24-h urine volume, 24-h urine solute excretion and maximum Uosm have to be considered additionally. In the following, an overview on available data of Uosm considering, for example, renal solute excretion, age, gender and different populations is presented.

Renal solute excretion

Renal solute excretion determines obligatory urine volume. For example, an additional intake and urine excretion of 100 mmol sodium chloride increases the obligatory urine volume by 240 ml at an assumed maximum Uosm of 830 mosm/kg.

Until the 1970s, the high renal solute load of artificially fed infants was an important risk factor in the development of hypernatremic dehydration, a complication of acute infantile diarrhoea with a high mortality rate (Finberg, 1986). Renal osmolar load in preterm and term infants fed with cow's milk was 29 mosm/kg*24-h (Pratt & Snyderman, 1953; Calcagno & Rubin, 1954; Janovsky *et al*, 1968), with cow's milk formula 17.9 mosm/kg*24-h (Pratt & Snyderman, 1953; Calcagno & Rubin, 1954; Janovsky *et al*, 1968), with humanised formula 10.4 mosm/kg*24-h (Saigal & Sinclair, 1977; Manz *et al*, 1992) and with human milk 7.4 mosm/kg*24-h (Calcagno & Rubin, 1960; Manz *et al*, 1992).

In adults urine solute excretion ranged from 1365 mosm/24-h in miners on a rest day in Australia (Cross *et al*, 1989) to about 400 mosm/24 h*1.73 m² in sweet potato eaters in Papua New Guinea (Oomen, 1967) and 362 mosm/24-h in

fasting subjects receiving 100 g glucose (Gamble, 1944). In industrialised countries, urine solute excretion is about $800 \text{ mosm}/24 \text{ h} \cdot 1.73 \text{ m}^2$ in children and adults (Chaptal *et al*, 1963; Kirkland *et al*, 1983; Höhler *et al*, 1994). Urea excretion contributes to about 40% and sodium chloride to about 35–44% of total renal solute excretion (Manz *et al*, 1984; Kanabrocki *et al*, 1988). On a diet with sweet potatoes, during fasting or in diabetic ketoacidosis the percentage of the sum of urea, sodium and chloride on the total solute excretion is only 14, 31 or 43%, respectively (Oomen, 1967; Halperin *et al*, 1988).

Individual character

Individuals may show long-term differences in hydration status. In 805 adults taking part in the international study of electrolyte excretion and blood pressure (INTERSALT) age- and sex-adjusted estimates of reliability for urine volume ranged from 0.49 to 0.57 indicating a lower intraindividual variance in 24-h urine volume than inter-individual variance (Dyer *et al*, 1994). In 630 children and adolescents from the DONALD Study with 3024 validated 24-h urine samples Uosm was $742 \pm 218 \text{ mosm}/\text{kg}$ (mean \pm s.d.). Interindividual variance explained 34% of total variance (unpublished data).

Mother and foetus

In pregnant women extracellular volume is expanded, the set point of vasopressin secretion is shifted to plasma osmolality levels which are about $10 \text{ mosm}/\text{kg}$ lower than in nonpregnant women and the metabolic clearance rate of vasopressin is four times higher (Hyttén & Thomson, 1965; Hyttén & Robertson, 1971; Agboola & Adewoye, 1978; Davison *et al*, 1993). Uosm may be unchanged during pregnancy or lower in pregnant than in non-pregnant women (Hadley *et al*, 1975; Agboola & Adewoye, 1978). In the foetal sheep plasma osmolality is about 3–5 mosm/kg lower than plasma osmolality in the ovine ewe. Furthermore, osmolality of amniotic fluid and fetal urine is constantly lower than plasma osmolality of the foetus. Finally, there is a negative correlation between the amniotic fluid volume and plasma osmolality of the ovine ewe (Schreyer *et al*, 1990; Ross *et al*, 1996a). Similar data were observed in the human foetus (Curran *et al*, 1998). In pregnant women with oligohydramnios, an additional water intake appeared to increase the amniotic fluid volume (Ross *et al*, 1996b; Kilpatrick, 1997). However, the usefulness and safety have yet to be established. Thus, the pregnant woman is in a transient functional status of 'hypo-osmolality' and the foetus with a specifically high total body water content (eg 88% at a total body mass of 200 g; 79% at 2000 g) (Diem & Lentner, 1968) and diuresis is in a physiologic status of euhydration with a steady functional surplus of water.

Neonatal period

In infants fed human milk, mean Uosm was $130 \text{ mosm}/\text{kg}$ ranging from 80 to $171 \text{ mosm}/\text{kg}$ (Calcagno & Rubin, 1954; Janovsky *et al*, 1968; Widdowson & McCance, 1970; Stevens & Savage, 1972; Armelini & Gonzalez, 1979; Manz, 1979; Goldberg & Adams, 1983). These values are just above the range of risk of hyperhydration. Mean Uosm in infants fed humanised formulas was $161 \text{ mosm}/\text{kg}$ ($104\text{--}257 \text{ mosm}/\text{kg}$) (Calcagno & Rubin, 1960; Janovsky *et al*, 1968; Saigal & Sinclair, 1977; Joppich *et al*, 1979; Manz, 1979) and in infants fed high-protein formulas $457 \text{ mosm}/\text{kg}$ ($334\text{--}658 \text{ mosm}/\text{kg}$) (Pratt *et al*, 1948; Pratt & Snyderman, 1953; Calcagno & Rubin, 1954; Janovsky *et al*, 1968). With regard to energy intake an infant fed mothers milk excreted 7.1 mosm per 100 kcal (Calcagno & Rubin, 1960; Manz *et al*, 1992), whereas an adult on a mixed diet excreted 30 mosm per 100 kcal (Höhler *et al*, 1994). Summarising, the foetus and the breast-fed infant are well euhydrated with a hydration close to the category of risk of hyperhydration. The low solute load of human milk probably is the result of an evolutionary selection of those mother-infant pairs in which the mother saved her nutrient pools without exposing her offspring to an increased risk of nutrient deficiencies. In infants with a low total body water pool related to energy turnover, the low renal solute load of human milk and the high obligatory water intake minimise the risk of dehydration in a hot climate or in acute gastroenteritis and may support a high anabolic rate.

Infants consuming supplementary food had higher values of Uosm ($580 \text{ mosm}/\text{kg}$; Widdowson & McCance, 1970) than infants fed only on human milk or humanised formulas.

Childhood, adult state and old age

In many countries, Uosm increased during the second and third year of life up to the very specific common level of children, adolescents and young adults (Chaptal *et al*, 1963; Widdowson & McCance, 1970; Werner *et al*, 1990; Phillip *et al*, 1993; Kawauchi *et al*, 1996; Frenzke *et al*, 1998). In cross-sectional studies in healthy adolescents and adults ranging in age from 15 y to about 65 y, mean Uosm decreased by $3.5 \text{ mosm}/\text{kg} \cdot \text{y}$ in the USA (Kutz *et al*, 1992) and $4.4\text{--}4.9 \text{ mosm}/\text{kg} \cdot \text{y}$ in the UK (Waters *et al*, 1967). This decrease is very similar to the age decrease in maximum Uosm of about $3.6 \text{ mosm}/\text{kg} \cdot \text{y}$ (Figure 3). Whereas the hydration of the foetus and the breast-fed infant is close to the category of risk of hyperhydration, in many countries of the world, the hydration of children, adults and seniors is close to the category of risk of hypohydration. Toddlers were in between.

Gender

In the USA, geometric mean of Uosm in spontaneous urine samples of a subsample of the Second National Health and Nutrition Examination Survey was $649 \text{ mosm}/\text{kg}$ in males and $540 \text{ mosm}/\text{kg}$ in females ($P < 0.01$, Kutz *et al*, 1992).

Higher urine osmolalities in males than females were also demonstrated in Germany (2.5–17.5 y-old: 801 vs 729 mosm/kg, Robers & Manz, 1996; 7.0–11.9 y-old: 810 vs 706 mosm/kg, Ebner & Manz, 2002; 50–76 y-old: 713 vs 610 mosm/kg, Singhof & Manz, 2001) and the UK (15–65 y-old: 749 vs 643 mosm/kg, Waters *et al*, 1967; 3- to 18-y-old: 896 vs 781 mosm/kg, Skinner *et al*, 1996). However, no significant sex difference was observed in Italy (3-month- to 12-y-old: 663 mosm/kg, Riva *et al*, 1984), Israel (2- to 6-y-old: 806 vs 760 mosm/kg, Phillip *et al*, 1993) and Poland (402 vs 380 mosm/kg, Fydryk J, personal communication). Thus, in industrialised countries the gender difference of Uosm is common, however, not obligatory.

Different populations

Representative data of Uosm from different countries are rare. However, in adults taking part in the INTERSALT Study ($n=10079$) large differences of mean 24-h urine volume between 52 centres all over the world hint to differences in hydration (Intersalt Cooperative Research Group, 1988). Mean 24-h urine volume in industrialised countries ranged from 1870 ml in Canada to 850 ml in a black population in the USA. There was a large scattering of mean values in all

continents even between different centres of one country, for example, in the US or in Germany or between blacks and whites of the same town.

In Table 1, mean data of Uosm from different countries are listed according to the mean value of the most sophisticated study. Furthermore, sampling procedure, sample size, method of urine collection and age class are given. There are large intercultural differences ranging from China and Japan with a mean Uosm of about 900 mosm/kg in spontaneous urine samples to Poland and Kenya with a mean Uosm of about 400 mosm/kg.

In Germany, a long-term trend of increasing total water intake has been documented as an indirect sign of a change in the hydration status of the population (Sichert-Hellert *et al*, 2001). Starting about 1900 and stretching over three generations the German population were advised by scientists in paediatrics, internal medicine, nutrition, physiology or industrial medicine to keep their total fluid intake low. These recommendations may explain some aspects of the ascetic attitude of the German population against a high fluid intake. The observations of the scientists were usually correct. Their conclusions and recommendations, however, turned out to be wrong or overstated. For example, Czerny, a great German paediatrician, recommended a limited total

Table 1 Mean urine osmolality in healthy subjects from different countries

Urine osmolality mean (mosm/kg)	Country	Subjects			Urine sampling		References
		Age (y)	Sex	Number	Quality	24-h/Spontaneous (Sp)	
909	China	50	m, f	16		Sp, night ^a	Liqaing <i>et al</i> (1997)
900	Japan	3–12	m, f	1453	Repr ^b	Sp, night	Kawauchi <i>et al</i> (1996)
880	Tunisia	20–41	m	15		Sp, morning	Zebidi <i>et al</i> (1990)
841	Sweden	12–17	m, f	20		18-h	Läckgren <i>et al</i> (1997)
801	Germany	3–18	m, f	231	Repr.	24-h	Robers and Manz (1996)
729		3–18		238	Repr.	24-h	Robers and Manz (1996)
659		50–76	m, f	566	Repr.	Sp, day, night	Singhof and Manz (2001)
860		5	m, f	25		24-h	Stolley and Schlage (1977)
791	Israel	2–6	m, f	200		Sp, 12:00	Phillip <i>et al</i> (1993)
1028		Adult	m	132		Sp, 9:00	Berlyne <i>et al</i> (1976)
776	Russia	6–14	m, f	23		Sp, 9:00	Kutznetsova <i>et al</i> (2000)
755	France	3–14	m, f	46		24-h	Chaptal <i>et al</i> (1963)
752	Switzerland	Children	m, f	200		Sp, day	Guignard and Torrado (1978)
723	Nigeria	Adult	f	125		Sp, 9:30	Agboola and Adewoye (1978)
699	UK	15–65	m, f	394	Repr.	Sp, night	Waters <i>et al</i> (1967)
845		3–18	m, f	322	(Repr.)	Sp, night	Skinner <i>et al</i> (1996)
536		44	m, f	10		24-h	Fogarty (1971)
696		>3	m, f	11		Sp, day	Widdowsen and McCance (1970)
676	Denmark	Children	m, f	22		24-h	Rittig <i>et al</i> (1989)
672	Australia	20	m, f	13		24-h	Cross <i>et al</i> (1989)
658	Italy	3–12	m, f	75		Sp, 12:00	Riva <i>et al</i> (1984)
649 ^c	USA	12–74	f	6990	Repr.	24-h	Kutz <i>et al</i> (1992)
540							
572		12	m, f	36		24-h	Miller and Stapleton (1989)
560	Belgium	Children	m, f	24		24-h	Vande Walle <i>et al</i> (2000)
416	Uganda	>3	m, f	3		Sp, day	Widdowsen and McCance (1970)
392	Poland	5–18	m, f	52		24-h	Fydryk (pers. communicat)
392	Kenya	4–5	m, f	15		3-h	Simmons and Korte (1972)

^aFirst morning urine sample.

^bRepresentative sample.

^cGeometric mean.

fluid intake of up to 800 ml per day in infants and the early introduction of solid foods to promote chemical development and improve immunity. He connected three observations: a decrease of total water content from newborns (75%) to toddlers (70%) and adults (65 to 60%); a decreasing susceptibility to infections during the first years of life (Czerny, 1939) and a high susceptibility in infections together with a high total body water content in infants who received a low amount of fat and a high amount of carbohydrates (Czerny, 1942).

Further factors

Several other causes of differences in Uosm between groups have been specified. In the USA, white population showed a lower Uosm than black population (Kutz *et al*, 1992: 581 vs 677 mosm/kg). In four settlements of Israel mean Uosm ranged from 875 to 1205 mosm/kg and indoor workers showed a lower mean Uosm of 852 mosm/kg than outdoor workers of 952 mosm/kg (Berlyne *et al*, 1976). Rural populations had a lower mean Uosm than suburban or urban populations (UK: Waters *et al*, 1967; Thailand: Van Reen *et al*, 1970). Athletes in nonweight category sports showed a lower mean morning Uosm of 627 mosm/kg than boxers of 775 mosm/kg and wrestlers of 777 mosm/kg in weight category sports (Shirreffs & Maughan, 1998).

Adequate total water intake

Unfortunately, there is no way to describe the natural drinking behaviour or natural range of Uosm in man, as fluid intake is always influenced by the cultural context. In an environment with easy access to water, a Uosm in the range of plasma osmolality would show the highest functional flexibility to adapt to a water deficit or surplus. A Uosm in the range of plasma osmolality therefore may be adequate. In pigs with a similar mean plasma osmolality and mean maximum renal concentrating capacity (1000 mosm/kg) as man, mean Uosm is 370 mosm/kg during free access to water and feed (Schiavon and Emmans, 2000).

Concept of dietary reference intakes

The actual concept of dietary reference intakes of the National Academy of Sciences 'goes beyond criteria needed to prevent classical nutrient deficiencies, and includes a review of data related to the risk of chronic diseases, developmental disorders, and other related problems' (Yates *et al*, 1998). Based on the pathophysiology or physiologic functions of a nutrient, criteria of adequacy were defined and biomarkers registering the criteria were adopted. The recommended dietary allowance of a nutrient 'is the intake at which the risk of inadequacy is very small — only 2–3%'. It corresponds to 'the average daily intake level that is sufficient to meet the nutrient requirement of nearly all (97% to 98%) healthy individuals in a particular life stage

and gender group' (Yates *et al*, 1998). If sufficient scientific evidence is not available to define recommended dietary allowances of a nutrient, adequate intakes are provided. 'The adequate intake is based on observed or experimentally determined estimates of nutrient intake of a group of healthy people' (Yates *et al*, 1998).

Criterion of water requirement

As a physiological criterion for the limit between long-term euhydration and the range of risk of long-term hypohydration, the value of the 24-h Uosm was used which corresponds to the mean -2 s.d. value of maximum Uosm of renal concentrating tests of healthy subjects of the respective age group. In children and young adults consuming a typical affluent Western-type diet with a high intake of protein, fat and sodium chloride and a relatively low intake of complex carbohydrates from starch and fibre containing foods, this value is approximately 830 mosm/kg (Manz *et al*, 2002).

Free water reserve

Osmolality is a measure of concentration. Thus, a new term representing a volume, the 'free water reserve (ml/24-h)', has been defined as a quantitative measure of individual 24-h euhydration (Manz *et al*, 2002). Free water reserve corresponds to the difference between the measured urine volume (ml/24-h) and the ideal urine volume (ml/24-h = $\text{mosm} \cdot 1000 \text{ ml/24-h} / \text{mosm}$) necessary to excrete the actual 24-h urine solutes (mosm/24-h) at the mean -2 s.d. value of maximum Uosm (eg 830 mosm/1000 g water in subjects consuming a typical affluent Western type diet) assuming 1 g water equals 1 ml urine. If almost all subjects (mean $+2$ s.d. or 97.7%) of a population show 24-h Uosm below the criterion of water requirement (eg 830 mosm/kg) or positive free-water reserve values, then the population can be classified as adequately hydrated. In a group with functionally lower maximum Uosm values, for example, in sweet potato eaters (Oomen, 1967) calculation of the ideal volume must take the specific lower mean -2 s.d. value of maximum Uosm into account.

Calculation of adequate total water intake

If in a particular life stage and gender group, both individual total water intake and free water reserve values are known, an adequate total daily water intake value can be calculated. It corresponds to the difference in the observed median total water intake and the third percentile free water reserve value of the particular group. In 189 boys aged 4.0–6.9 y taking part in the DONALD (Dortmund Nutritional and Anthropometric Longitudinally Designed) Study with a median weight of 21.1 kg, median energy intake was 1495 kcal/24-h, median total water intake 1310 ml/24-h, median urine volume 497 ml/24-h, median Uosm 809 mosm/kg, median free water reserve 11 ml/24-h, (third percentile: -156 ml/24-h) and

adequate total water intake 1466 ml/24-h or 1.01 ml/kcal (Manz *et al*, 2002). Thus, in this age and gender group a general additional water intake of 156 ml/24-h is necessary to ensure euhydration in 97.7% of these children and would result in a predicted median Uosm of 598 mosm/kg (Manz *et al*, 2002).

The presented procedure to analyse water metabolism may prove to be a valuable tool to help characterise 24-h hydration status, to investigate the effect on health of different levels of hydration in euhydrated subjects and to calculate the adequate total daily water intake values in homogeneous population groups.

Summary

Young infants show a structurally and functionally lower renal concentrating and diluting capacity than older infants, children and young adults. Maximum Uosm decreases and minimum Uosm increases with age starting at 20 y. The renal concentrating capacity is modulated by the duration of water restriction, the level of protein and sodium intake and the amount of strenuous physical activity. There are remarkable differences in 24-h Uosm between subjects and groups mainly caused by age, individual character, renal solute excretion, gender and cultural context.

Free water reserve seems to be a new suitable parameter to quantify individual 24-h euhydration. By accepting mean -2 s.d. of maximum Uosm of specific groups of healthy subjects as a physiological criterion of water requirement, AI values of total water intake can be calculated. Data of Uosm in 24-h urine samples and the free water reserve of homogeneous groups of healthy subjects all over the world might be useful parameters in epidemiology to investigate the health effects of different levels of euhydration.

Acknowledgements

This work was supported by the 'Ministerium für Schule, Wissenschaft und Forschung' of North-Rhine-Westphalia and by the 'Bundesministerium für Gesundheit'.

References

Abyholm G & Monn E (1979): Intranasal DDAVP-test in the study of renal concentrating capacity in children with recurrent urinary tract infections. *Eur. J. Pediatr.* **130**, 149–154.

Agboola A & Adewoye HO (1978): A study of serum and urine osmolality values in pregnant Nigerian women. *Int. J. Gynaecol. Obstet.* **16**, 56–57.

Alwall N (1978): Population studies on non-obstructive urinary tract infection in non-pregnant women: importance of method and material. *Acta Med. Scand.* **203**, 95–105.

Armellini PA & Gonzalez CF (1979): Breast feeding and fluid intake in a hot climate. *Clin. Pediatr.* **18**, 424–425.

Askergren A, Allgen LG & Bergström J (1981): Studies on kidney function in subjects exposed to organic solvents. *Acta Med. Scand.* **209**, 485–488.

Assadi KF (1990): Renal tubular dysfunction in fetal alcohol syndrome. *Pediatr. Nephrol.* **4**, 48–51.

Barnett HL, Vesterdal J, McNamara H & Lauson HD (1952): Renal water excretion in premature infants. *J. Clin. Invest.* **31**, 1069–1073.

Baumgarten R, van de Pol MHJ, Deen PMT, van Os CH & Wetzels JFM (2000): Dissociation between urine osmolality and urinary excretion of aquaporin-2 in healthy volunteers. *Nephrol. Dial. Transplant.* **15**, 1155–1161.

Bendz H (1985): Kidney function in a selected lithium population. *Acta Psychiatr. Scand.* **72**, 451–463.

Berlyne GM, Yagil R, Goodwin S & Morag M (1976): Drinking habits and urine concentration of man in southern Israel. *Israel J. Med. Sci.* **12**, 765–769.

Calcagno PL & Rubin MI (1954): Effect of added carbohydrate on growth, nitrogen retention and renal water excretion in premature infants. *Pediatrics* **13**, 193–201.

Calcagno PL & Rubin MI (1960): Water requirement for renal excretion in full-term newborn infants and premature infants fed a variety of formulas. *J. Pediatr.* **56**, 717–727.

Chaptal J, Jean R, Guillaumot R & Morel G (1963): Etude statistique de l'élimination urinaire des électrolytes chez l'enfant normal à différents âges. *Arch. Franc. Pediatr.* **20**, 905–931.

Cross RB, Galton-Fenzi B & Jordan L (1989): A simple field test for assessing salt balance in heat-stressed miners. *J. Occupat. Med.* **31**, 668–673.

Curran MA, Nijland MJM, Mann SE & Ross (1998): Human amniotic fluid mathematical model: determination and effect of intramembranous sodium flux. *Am. J. Obstet. Gynecol.* **178**, 484–490.

Curtis JR & Donovan BA (1979): Assessment of renal concentrating ability. *Br. Med. J.* **1** 304–305.

Czerny A (1939): *Die Pädiatrie meiner Zeit*. pp 52–54. Berlin: Springer.

Czerny A (1942): *Sammlung klinischer Vorlesungen über Kinderheilkunde*. p 20. Leipzig: Thieme.

Davison JM, Sheills EA, Philips PR, Barron WM & Lindheimer MD (1993): Metabolic clearance of vasopressin and an analogue resistant to vasopressinase in human pregnancy. *Am. J. Physiol.* **264**, F348–F353.

Department of Health (1991): *Dietary Reference Values for Food, Energy and Nutrients for the United Kingdom*. pp 1–212. London: The Stationery Office.

Diem K & Lentner C (1968): *Documenta Geigy, Wissenschaftliche Tabellen*. p 513 7th edition. Basel: Geigy.

DiScala VA & Stein RM (1982): Effects of chronic sodium depletion on renal tubular sodium and water reabsorption in man. *Nephron* **31**, 151–158.

Drescher AN, Barnett HL & Troupkou V (1962): Water balance in infants during water deprivation. *Am. J. Dis. Child.* **104**, 80–93.

Dyer AR, Shipley M, Elliott P & INTERSALT Cooperative Research Group (1994): Urinary electrolyte excretion in 24 hours and blood pressure in the INTERSALT Study: estimates of reliability. *Am. J. Epidemiol.* **139**, 927–939.

Ebner A & Manz F (2002): Sex difference of urinary osmolality in German children. *Am. J. Nephrol.* **22**, 352–355.

Edelmann CM, Barnett HL & Troupkou V (1960): Renal concentrating mechanisms in newborn infants. Effect of dietary protein and water content, role of urea, and responsiveness to antidiuretic hormone. *J. Clin. Invest.* **39**, 1062–1069.

Edelmann CM, Barnett HL, Stark H, Boichis H & Rodriguez-Soriano J (1967): A standardized test of renal concentrating capacity in children. *Am. J. Dis. Child.* **114**, 639–644.

Epstein FH, Kleeman CR & Hendriks A (1957a): The influence of bodily hydration on the renal concentrating process. *J. Clin. Invest.* **36**, 629–634.

Epstein FH, Kleeman CR, Pursel S & Hendriks A (1957b): Effect of feeding protein and urea on the renal concentrating process. *J. Clin. Invest.* **36**, 635–640.

Finberg L (1986): Too little water has become too much. *Am. J. Dis. Child.* **140**, 524.

Fisher DA, Pyle HR, Porter JC, Beard AG & Panos TC (1963): Control of water balance in the newborn. *Am. J. Dis. Child.* **106**, 51–60.

- Fogarty AJ (1971): The significance of sodium in renal stone formation. *Br. J. Urol.* **43**, 403–405.
- Frenzke H, Rudloff S & Manz F (1998): Flüssigkeitsversorgung von Dortmunder Kleinkindern. *Monatsschr. Kinderheilkd.* **146**, 777–783.
- Gamble JL (1944): The water requirements of castaways. *Proc. Am. Phil. Soc.* **88**, 151–158.
- Goldberg NM & Adams E (1983): Supplementary water for breast-fed babies in a hot and dry climate not really a necessity. *Arch. Dis. Child.* **58**, 73–74.
- Guignard JP & Torrado A (1978): Nitrite indicator strip test for bacteriuria. *Lancet* **1**, 47.
- Güllner HG, Gill JR, Bartter FC & Düsing R (1980): The role of the prostaglandin system in the regulation of renal function in normal women. *Am. J. Med.* **69**, 718–724.
- Hadley R, Bernard HO & Stinson JM (1975): Serial urinary osmolality in pregnancy. *J. Nat. Med. Assoc.* **67**, 373–374.
- Halperin ML, Margolis BL, Robinson LA, Halperin RM, West ML & Bear RA (1988): The urine osmolal gap: a clue to estimate urine ammonium in “hybrid” types of metabolic acidosis. *Clin. Investig. Med.* **11**, 198–202.
- Hansen JDL & Smith CA (1953): Effects of withholding fluid in the immediate postnatal period. *Pediatrics* **12**, 99–113.
- Höhler M, Decher-Splithoff E, Kersting K, Ternes ML & Manz F (1994): Funktionsbelastung des Stoffwechsels und der Niere bei Kraftsportlern mit eiweißreicher Kost. *Deutsche Z. Sportmed.* **45**, 92–103.
- Hyttén FE & Robertson EG (1971): Maternal water metabolism in pregnancy. *Proc. Roy. Soc. Med.* **64**, 46.
- Hyttén FE & Thomson AM (1965): Pregnancy, childbirth and lactation. In *The Physiology of Human Survival*, eds OG Edhohn, AL Bacharach, pp 327–350. London: Academic Press.
- Intersalt Cooperative Research Group (1988): Intersalt: an international study of electrolyte and blood pressure Results for 24 hour urinary sodium and potassium excretion. *Br Med J* **297**, 319–328.
- Isaacson LC (1960): Urine osmolality in thirsting normal subjects. *Lancet* **I**, 467–468.
- Janovsky M, Martinek J & Slechtova R (1968): The effect of different diets on the economy of water and electrolytes during restricted water intake in human infants. *Phys. Bohemoslovaca.* **17**, 143–152.
- Joppich R, Scherer B & Weber PC (1979): Renal prostaglandins: relationship to the development of blood pressure and concentrating capacity in pre-term and full term healthy infants. *Eur. J. Pediatr.* **132**, 253–259.
- Kanabrocki EL, Snedeker PW, Zieher SJ, Raymond R, Gordey J, Bird T, Sothorn RB, Hrushesky WJM, Marks G, Olwin JH & Kaplan E (1988): Circadian characteristics of dialyzable and non-dialyzable human urinary electrolytes, trace elements and total solids. *Chronobiol. Int.* **5**, 175–184.
- Kawauchi A, Watanabe H & Miyoshi K (1996): Early morning urine osmolality in non-enuretic and enuretic children. *Pediatr. Nephrol.* **10**, 696–698.
- Kilpatrick SJ (1997): Therapeutic interventions for oligohydramnios: amnioinfusion and maternal hydration. *Clin. Obstetr. Gynecol.* **40**, 328–336.
- Kirkland JL, Lye M, Levy DW & Banerjee AK (1983): Patterns of urine flow and electrolyte excretion in healthy elderly people. *Br. Med. J.* **287**, 1665–1667.
- Klahr S, Tripathy K, Garcia FT, Mayoral LG, Ghitis J & Bolanos O (1967): In the nature of renal concentrating defect in malnutrition. *Am. J. Med.* **43**, 84–96.
- Kleiner SM (1999): Water: an essential but overlooked nutrient. *J. Am. Diet. Assoc.* **99**, 200–206.
- Koppeschaar HPF, Meinders AE & Schwarz F (1985): Renal concentrating ability in obesity, effect of modified fasting and the supplementation of T3, sodium chloride and carbohydrate. *Metabolism* **34**, 1066–1072.
- Kutz FW, Cook BT, Carter-Pokras OD, Brody D & Murphy RS (1992): Selected pesticide residues and metabolites in urine from a survey of the U. S. general population. *J. Toxicol. Environ. Health.* **37**, 277–291.
- Kuznetsova AA, Shakhmatova EI, Prutskova NP & Natchin YV (2000): Possible role of prostaglandins in pathogenesis of nocturnal enuresis in children. *Scand. J. Urol. Nephrol.* **34**, 27–31.
- Läckgren G, Neveus T & Stenberg A (1997): Diurnal plasma vasopressin and urinary output in adolescents with monosymptomatic nocturnal diuresis. *Acta Paediatr.* **86**, 385–390.
- Levinsky NG, Berliner RW & Preston AS (1959): The role of urea in the urine concentrating mechanism. *J. Clin. Invest.* **38**, 741–748.
- Lindeman RD, Lee TD, Yiengst MJ & Shock NW (1966): Influence of age, renal disease, hypertension, diuretics and calcium on the antidiuretic responses to suboptimal infusion of vasopressin. *J. Lab. Clin. Med.* **68**, 206–223.
- Liqiang Z, Xizhen H, Xuewang L & Quanyou W (1997): Alterations in renal function in patients with obstructive sleep apnea syndrome and effects of continuous positive airway pressure. *Chin. Med. J.* **110**, 915–918.
- Macaron C, Schneider G & Ertel NH (1975): The starved kidney: a defect in renal concentrating ability. *Metabolism* **24**, 457–458.
- Manz F (1979): *Säure-Basen-Haushalt bei Ernährung mit synthetischen Diätpräparaten und bei Ernährung mit Frühgeborenen- und Säuglingsmilchnahrungen*, pp 178–213. Heidelberg: Ruprecht-Karl-Universität, Habilitationsschrift.
- Manz F, Vecsei P & Wesch H (1984): Renale Säureausscheidung und renale Molenlast bei gesunden Kindern und Erwachsenen. *Monatsschr. Kinderheilkd.* **132**, 163–167.
- Manz F, Diekmann L, Kalhoff H, Stock GJ & Kunz C (1992): Low renal net acid excretion, high calciuria and biochemical signs of sodium deficiency in low-birth-weight infants fed a new low-phosphorus formula. *Acta Paediatr.* **81**, 969–973.
- Manz F, Wentz A & Sichert-Hellert W (2002): The most essential nutrient: defining the adequate intake of water. *J. Pediatr.* **141**, 587–592.
- Marild S, Jodal U, Jonasson G, Mangelus L, Oden A & Persson NG (1992): Reference values for renal concentrating capacity in children by the desmopressin test. *Pediatr. Nephrol.* **6**, 254–257.
- McCance RA & Widdowson EM (1954): Normal renal function in the first two days of life. *Arch. Dis. Child.* **29**, 488–494.
- Miles BE, Paton A & de Wardener HE (1954): Maximum urine concentration. *Br. Med. J.* **II**, 901–905.
- Miller LA & Stapleton FB (1989): Urinary volume in children with urolithiasis. *J. Urol.* **141**, 918–920.
- Monnens LAH. (1971): *De ontwikkeling van het concentrerend — en zuurvormend vermogen van de nier bij het kind*, pp 1–189. Nijmegen: Schippers.
- Monson JP & Richards P (1978): Desmopressin urine concentration test. *Br. Med. J.* **I**, 24.
- Nadvornikova H, Schück O & Cort JH (1980): A standardized desmopressin test of renal concentrating ability. *Clin. Nephrol.* **14**, 142–147.
- National Research Council (1989): *Recommended Dietary Allowances*, 10th Edition, pp 247–250. Washington: National Academy Press.
- Oomen HAPC (1967): Nitrogen compounds and electrolytes in the urine of New Guinean sweet potato eaters: a study of normal values. *Trop. Geogr. Med.* **19**, 31–47.
- Phillip M, Singer A, Chaimovitz C & Golinsky D (1993): Urine osmolality in nursery school children in a hot climate. *Isr. J. Med. Sci.* **29**, 104–106.
- Polacek L, Vocel J, Neugebauerova L, Sebkova M & Vechetova E (1965): The osmotic concentrating ability in healthy infants and children. *Arch. Dis. Child.* **40**, 291–295.
- Pratt EL & Snyderman SE (1953): Renal water requirement of infants fed evaporated milk with and without added carbohydrate. *Pediatrics* **11**, 65–69.
- Pratt EL, Bienvenu B & Whyte MM (1948): Concentration of urine solutes by young infants. *Pediatrics* **1**, 181–187.

- Raisz LG, Au WYW & Scheer RL (1959): Studies on the renal concentrating mechanism III. *Effect of heavy exercise. J. Clin. Invest.* **38**, 8–13.
- Rittig S, Knudsen UB, Norgaard JP, Pedersen EB & Djurhuus JC (1989): Abnormal diurnal rhythm of plasma vasopressin and urinary output in patients with enuresis. *Am. J. Physiol.* **256**, F664–F671.
- Riva E, Rottoli A, Castelli L, Magno F, Paccanelli S & Giovanni M (1984): Valutazione di alcuni parametri del metabolismo idrosalinico in età pediatrica. *Min. Ped.* **36**, 667–672.
- Robers F & Manz F (1996): Zur Flüssigkeitsversorgung im Kindesalter. *Sozialpäd. KiPrax.* **18**, 85–89.
- Rodriguez-Soriano J, Vallo A, Castillo G & Oliveros R (1981): Renal handling of water and sodium in infancy and childhood: a study using clearance methods during hypotonic saline diuresis. *Kidney Int.* **20**, 700–704.
- Ross MG, Nijland MJM & Kullama LK (1996a): 1-Deamino-[8-D-arginine] vasopressin-induced maternal plasma hypoosmolality increases ovine amniotic fluid volume. *Am. J. Obstet. Gynecol.* **174**, 1118–1127.
- Ross MG, Cedars L, Nijland MJM & Ogundipe A (1996b): Treatment of oligohydramnios with maternal 1-deamino-[8-D-arginine] vasopressin-induced plasma hypoosmolality. *Am. J. Obstet. Gynecol.* **174**, 1608–1613.
- Rowe JW, Shock NW & DeFronzo RA (1976): The influence of age on the renal response to water deprivation in man. *Nephron* **17**, 270–278.
- Saigal S & Sinclair JC (1977): Urine solute excretion in growing low-birth-weight infants. *J. Pediatr.* **90**, 934–938.
- Schiavon S & Emmans GC (2000): A model to predict water intake of a pig growing in a known environment on a known diet. *Br. J. Nutr.* **84**, 873–883.
- Schreyer P, Sherman DJ, Ervin MG, Day L & Ross MG (1990): Maternal dehydration: impact on ovine amniotic fluid volume and composition. *J. Dev. Physiol.* **13**, 283–287.
- Schrier RW, Hano J, Keller HI, Finkel RM, Gilliland PE, Cirksena WJ & Teschan PE (1970): Renal, metabolic and circulatory responses to heat and exercise. *Ann. Intern. Med.* **73**, 213–223.
- Shirreffs SM (2000): Markers of hydration status. *J. Sports Med. Phys. Fitness* **40**, 80–84.
- Shirreffs SM & Maughan RJ (1998): Urine osmolality and conductivity as indices of hydration status in athletes in the heat. *Med. Sci. Sports Exerc.* **30**, 1598–1602.
- Sichert-Hellert W, Kersting M & Manz F (2001): Fifteen year trends in water intake in German children and adolescents: results of the DONALD Study. *Acta Paediatr.* **90**, 732–737.
- Simmons WK & Korte R (1972): The excretion of urea in relation to protein intake and diuresis. *Arch. Latinoamericanas Nutr.* **22**, 33–40.
- Singhof S & Manz F (2001): Flüssigkeitsversorgung der Senioren in Deutschland. *Aktuel. Ernähr. Med.* **26**, 102–106.
- Skinner R, Cole M, Pearson ADJ, Coulthard MG & Craft AW (1996): Specificity of pH and osmolality of early morning urine sample in assessing distal renal tubular function in children: results in healthy children. *Br. Med. J.* **312**, 1337–1338.
- Smith CA, Yudkin S, Young W, Minkowski A & Cushman M (1949): Adjustment of electrolytes and water following premature birth. *Pediatrics* **3**, 34–47.
- Stapleton FB & Miller LA (1988): Renal function in children with idiopathic hypercalcaemia. *Pediatr. Nephrol.* **2**, 229–235.
- Stevens LH & Savage DCL (1972): Neonatal homeostasis. *Aust. Paediatr. J.* **8**, 16–29.
- Stolley H & Schlage C (1977): Water balance and water requirement of preschool children. *Nutr. Metab.* **21**(Suppl 1), 15–17.
- Svenningsen NW & Aronson AS (1974): Postnatal development of renal concentration capacity as estimated by DDAVP-test in normal and asphyxiated neonates. *Biol. Neonate* **25**, 230–241.
- Tan ACITL, Hoefnagels WHL, Gerritsen AAJ, Jansen RWMM, Kloppenborg PWC & Benraad TJ (1991): Mild dehydration and atrial natriuretic peptide in young and elderly subjects. *Horm. Metab. Res.* **23**, 435–437.
- Tencer J (1988): Asymptomatic bacteriuria — a long term study. *Scand. J. Urol. Nephrol.* **22**, 31–34.
- Toor M, Katz AI, Massry S, Agmon J & Rosenfeld J (1965): Concentration and dilution of urine in man living in a hot climate. *Isr. J. Med. Sci.* **1**, 157 (abstract).
- Tryding N, Berg B, Ekman S, Nilsson JE, Sterner G & Harris A (1988): DDAVP test for renal concentration capacity. *Scand. J. Urol. Nephrol.* **22**, 141–145.
- Uttley WS, Paxton J & Thistlethwaite D (1972): Urinary concentrating ability and growth failure in urinary tract disorders. *Arch. Dis. Child.* **47**, 436–441.
- VandeWalle J, Thijs J, VanLaecke E & Hoebeke P (2000): Nocturnal enuresis related to the abnormalities of the nycthemeral rhythm of diuresis on renal function and salt handling and bladder dysfunction. *Pediatr. Nephrol.* **14**, C61 (abstract).
- Van Reen R, Valyasevi A & Dhanamitta S (1970): The effect of methionine and pyridoxine supplements on urinary sulfate. *Am. J. Clin. Nutr.* **23**, 940–947.
- Waters WE, Sussmann M & Asscher AW (1967): Community study of urinary pH and osmolality. *Br. J. Prev. Soc. Med.* **21**, 129–132.
- Werner M, Kersting M & Manz F (1990): Untersuchung des Wasserhaushalts bei 19 Kleinkindern in häuslicher Umgebung. *Monatsschr. Kinderheilkd.* **138**, 528 (abstract).
- Widdowson EM & McCance RA (1970): Use of random specimens of urine to compare dietary intakes of African and British children. *Arch. Dis. Childh.* **45**, 547–552.
- Winberg J (1959): Determination of renal concentration capacity in infants and children without renal disease. *Acta Paediatr.* **48**, 318–328.
- Yates AA, Schlicker SA & Suitor CW (1998): Dietary Reference Intakes: the new basis for recommendations for calcium and related nutrients, B vitamins, and choline. *J. Am. Diet. Assoc.* **98**, 699–706.
- Zebidi A, Rached S, Dhidah M, Sadraoui M, Tabka Z, Dogui M, Sfar H, Chaieb M & Chaieb A (1990): Effets du jeûne de Ramadan sur certains paramètres plasmatiques et urinaires. *La Tunisie Méd.* **68**, 367–372.