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Renal Excretion of Water in Infants with Acute Gastroenteritis

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Patrick, J. (1971). *Archives of Disease in Childhood*, **46**, 641. **Renal excretion of water in infants with acute gastroenteritis.** Infants with severe gastroenteritis were given water loads of 20 ml/kg body weight during their recovery. The renal responses were correlated with changes in body weight and osmolality. A water load was not excreted until the body weight had reached a peak. It is concluded that while volume depletion persists administration of hypotonic fluids leads to a fall in osmolality which will not be corrected by renal excretion of water. The relevance of this observation to the high incidence of neurological disturbances during the treatment of hyperosmolar states is discussed.

Diarrhoeal fluid in gastroenteritis has a lower concentration of sodium than extracellular fluid (Finberg, Cheung, and Fleishman, 1960; Weil and Wallace, 1956; Darrow *et al.*, 1949; Holt, Courtney, and Fales, 1915). In the absence of sufficient and appropriate intake hypernatraemia of the extracellular fluid will result. Severe neurological complications have been associated with hypernatraemia. Dural sinus thrombosis and cerebral petechial haemorrhages have been observed in necropsy material (Finberg, Kiley, and Luttrell, 1963), and in non-fatal cases subsequent mental defect has been noted (Macaulay and Watson, 1967; Morris-Jones, Houston, and Evans, 1967). The correct therapy for hypernatraemia in this situation is not definitely established. It is known that when hypernatraemia is associated with contraction of the body fluid volume the kidney's ability to correct the hypernatraemia is impaired (Finberg, Rush, and Cheung, 1964). It has also been shown that treatment with electrolyte-free solutions is associated with a higher incidence of convulsions than treatment with electrolyte-containing solutions (Bruck, Abal, and Aceto, 1968). Animal experiments suggest that the convulsions may be caused by cerebral oedema with rapid uptake of water by the brain. The data presented here are concerned with the changing response to a water load during recovery from severe gastroenteritis.

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Patients and Methods

Eight infants with acute severe gastroenteritis were studied. Age, weight, surface area, and initial blood chemistry for each infant are shown in Table I. All the infants presented with severe salt and water defi-

TABLE I

Biochemical and Physical Details of Patients Studied

Case No.	Age (mth)	Wt. (kg)	BSA (m^2)	Na (mEq/l.)	K (mEq/l.) (ml)	Urea (mg/100 ml)	Creatinine (mg/100 ml)	POsm (mOsm/kg)
1	10	9·6	0·42	155	3·3	114	1·3	346
2	14	10·25	0·43	157	3·2	95	1·0 (7 hr)	346
3	2	5·25	0·265	151	7·0	128	2·1	350
4	21	10·8	0·48	142	2·6	32	0·5	315
5	8	7·7	0·36	—	4·8	160	1·5	324
6	7	8·7	0·38	148	3·8	80	0·9	320
7	10	7·35	0·344	152	4·7	29	0·9	305
8	6	7·9	0·42	140	4·8	—	0·9	300

Note: The weights are the final weights before discharge.
The blood chemistry results are on admission, unless the time is shown in parentheses.
BSA = Body surface area.

ciency: grades 2 or 3 of the M.R.C. criteria (*Medical Research Council Memorandum No. 26*, 1952). Treatment was designed to correct peripheral circulatory failure rapidly with intravenous isotonic fluids (0·9% saline, plasma, or dextran). Repletion of the overall deficit was attempted in 24–36 hours with ½ or ¼ strength Darrow's solution (½ strength Darrow's solution—sodium 60 mEq/l., potassium 18·1 mEq/l., chloride

TABLE II

Data Showing Relations Between Changes in Osmolality, Weight, and Renal Function

Case No.	Time (hr) from Admission	Wt. (kg)	POsm (mOsm/kg)	V (ml/min)	UOsm (mOsm/kg)	CH_2O (ml/min)	UNaV (μEq/min)	CCr (ml/min)	% Water Load Excreted in 5 hr
1	0·0	8·75	346						
	15·0	9·55	299	0·14	800	−0·26	2·6	10·3	
	19·15	9·57	297	0·2	861	−0·35	6·0	19·0	
	24·0–24·30 water load of 300 ml								
	25·30	9·65	—	0·1	776	−1·2	4·4	8·0	2·3
2	0·0	7·2	350						
	10·13	7·68	321	0·4	570	−0·3	26·6	7·0	
	11·30–12·45 water load of 250 ml								
	13·38	8·83	317	0·3	283	0·0	11·6	4·0	
	15·31	9·4	—	0·4	346	−0·02	23·8	8·0	
	20·46	9·6	—	0·3	349	−0·02	21·1	9·0	
	23·55	10·0	—	0·4	332	0·0	23·1	10·5	23·2
3	0·0	4·66	350						
	7·5	4·86	340	0·1	527	−0·05	3·5	3·2	
	10·10	4·92	—	0·18	693	−0·19	8·9	8·1	
	15·45	4·98	—	0·11	801	−0·26	6·4	4·6	
	20·15	5·0	314	0·15	1000	−0·33	7·2	7·2	
	20·15–21·00 water load of 120 ml								
	23·0	5·1	309	Next urine 10 hr after water load					0·0
4	0·0	10·2	315						
	11·45	10·75	293	0·2	646	−0·2	7·5	24·3	
	15·00	10·9		0·55	425	−0·25	41·8	34·0	
	19·00	11·0	293						
	19·30–20·00 water load of 300 ml								
	22·22	10·95	291	0·71	213	+0·2	35·9	11·2	75·0
5	0·0	7·3	324						
	12·0	7·8		0·02	524	−0·02	0·3	1·8	
	15·30	7·72		0·07	515	−0·05	0·8	3·0	
	16·40–17·15 water load of 215 ml								
	16·55	—	300						
	18·00	—		0·5	212	+0·2	6·2	6·3	
	23·30	7·65		1·54	494	+2·1	17·0	13·4	55·0
6	0·0	8·08	320						
	12·30	8·7	297	0·07	1063	−1·4	0·4	4·0	
	16·45	8·94		0·3	646	−0·4	2·3	11·2	
	21·25	8·85	290	0·29	465	−0·2	16·7	12·8	
	22·00–22·45 water load of 230 ml								
	23·35			1·43	218	+0·4	47·7	21·5	
	24·03	8·8		2·2	82	+1·9	47·3	21·7	100·0
7	0·0	6·83	305						
	3·25	7·0	295	0·09	886	−0·18	11·5	7·9	
	5·35	7·23	283	0·1	866	−0·2	18·0	8·2	
	21·55	7·34	272	0·06	863	−0·13	7·5	3·5	
	23·25	7·3		0·04	742	−0·07	11·6	3·9	
	23·45–24·30 water load of 300 ml								46·0
	26·3	7·29	270	1·55	69	+1·16	21·8	15·6	in 2½ hr
8	0·0	7·14	300						
	6·30			0·04	623	−0·05	0·46	4·7	
	9·30	7·75		0·2	558	−0·18	4·0	13·5	
	12·00	7·94	284	0·21	547	−0·19	11·8	12·6	
	14·25			0·18	451	−0·11	9·8	9·5	
	14·15–14·30 water load of 240 ml								
	16·26	7·9	270	1·0	329	−0·22	18·4	17·6	
	17·21	7·9		2·1	70	+1·55	17·0	16·7	
	19·58			0·28	296	+0·03	9·4	9·0	
	22·30			0·26	538	−0·26	18·7	18·5	79·0

52·5 mEq/l., and lactate 26 mEq/l.) administered orally. The deficit was estimated clinically using the M.R.C. criteria. Approximately 150 ml water/kg per 24 hours were allowed for maintenance requirements. A high maintenance figure is required because of the high insensible water loss secondary to acidosis and fever (Kerrigan, 1963; Heeley and Talbot, 1955).

The response to an oral water load of 2 to 3% body weight given over 30 minutes, and additional to the normal fluid therapy, was studied at varying times during recovery. The infants were weighed frequently so that 5 to 9 measurements were obtained in the first 24 hours after admission. Weighings were accurate to 10–15 g.

Urine was collected in carefully timed periods with spontaneous voidings, catheterization being considered unethical. Plasma and urinary sodium, potassium, creatinine, and osmolality were measured. From these data creatinine, osmolal, and free water clearance were calculated as follows: C.Cr, creatinine clearance = $\frac{U_{Cr} \times V}{PCr}$; C. Osm, osmolal clearance = $\frac{U_{Osm} \times V}{POsm}$; CH_2O, free water clearance = V−COsm.

Where U_{cr} = urinary creatinine concentration mg/100 ml; U_{osm} = urinary osmolality mOsm/kg; P_{cr} = plasma creatinine mg/100 ml; P_{osm} = plasma osmolality mOsm/kg; and V = urine flow ml/min.

Free water clearance was used as the index of renal ability to excrete a water load. It represents the rate at which the kidneys remove 'pure' (i.e. solute-free) water from the plasma. Sodium and potassium were estimated by flame photometry, osmolality by freezing point depression with an 'advanced' osmometer, and creatinine by the Technicon modification of the Folin and Wu method.

All clearances are expressed as means of two or three consecutive periods.

Results

Plasma osmolality was initially high in all the infants though not all were hypernatraemic. At the time of the water load, 4 infants were still hyperosmolar. Weight changes in all the infants followed a similar pattern, with an initial rapid gain followed by a peak or plateau before normal growth was resumed.

It was found that when the water load was given after the peak weight during recovery there was an appropriate rise in urine flow and free water clearance with a sharp fall in urinary osmolality. However, when the water load was given before the peak weight had been reached the renal response was minimal or absent (Table II, Fig. 1–3). Sodium excretion rose and creatinine clearance increased in association with water loading after the peak weight had been reached.

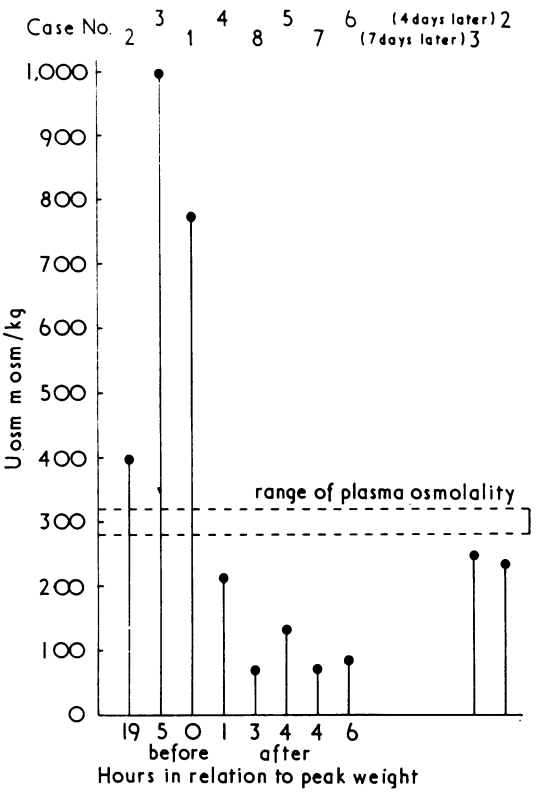

FIG. 1.—*Plot of lowest U_{Osm} achieved after H_2O load against time relative to peak weight.*

Discussion

It has been shown that when infants with gastroenteritis and hypernatraemia are treated with electrolyte-free solutions there is a high incidence of convulsions (Bruck *et al.*, 1968). The present results show that these infants retain all administered water for several hours after the beginning of fluid therapy. If fluid therapy is very hypotonic this will cause retention of water with dilution of the body fluids. Studies of experimental animals in comparable states have shown an increase in brain water leading to neurological disturbances and ultimately to death (Hogan *et al.*, 1969). It seems likely that the convulsions occurring during treatment of children with gastroenteritis with hypotonic solutions are also related to water retention, and an understanding of the changes in renal water excretion at this time is therefore important.

During fluid therapy the weight change of these children followed a characteristic pattern, rising steeply to a peak then falling slightly before rising again more slowly. A normal renal response to a

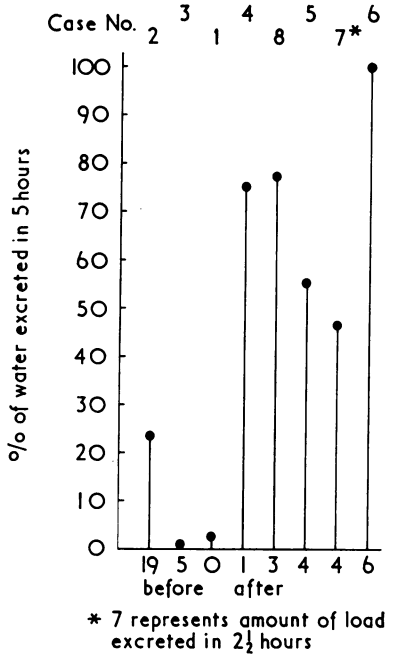

FIG. 2.—*Plot of percentage of water load excreted against time relative to peak weight.*

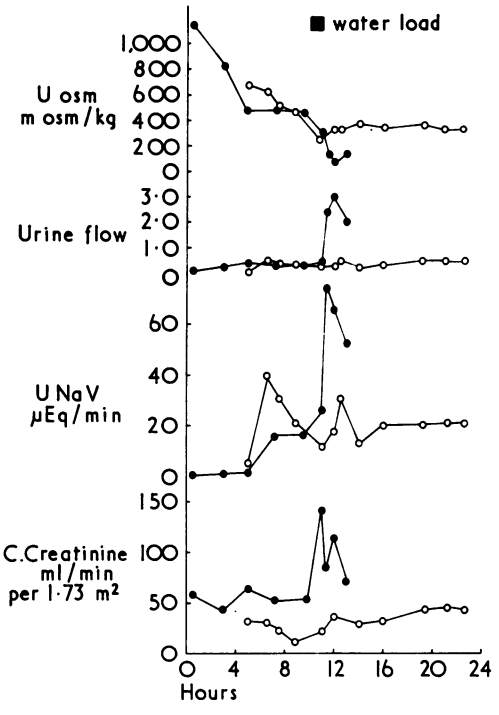

FIG. 3. *Plot of changes in U_{Osm}, urine flow, sodium excretion, and creatinine clearance in relation to a water load. Open circles indicate a subject loaded before peak weight was reached. Closed circles indicate a subject loaded after peak weight was reached.*

water load was not seen before the first peak in body weight, but water loads given after the peak were excreted more normally. This pattern of weight change corresponds with the initial salt retention in excess of salt deficit observed by Darrow (Darrow, 1946). The drop in weight corresponds with the excretion of the excess sodium. Natriuresis does not follow a water load (Metzger *et al.*, 1969) but is a well-documented response to volume expansion. Similar over-retention of sodium has been reported in experimental salt depletion (McCance, 1936). It is also known that salt depletion impairs the renal response to a water load in the dog (Cizek and Huang, 1951; Coxon and Ramsay, 1968) and in man (McCance and Widdowson, 1937). The recovery of the renal ability to excrete a water load after the body weight peaked during treatment suggests that the initial defect in water excretion was related to the salt deficiency and consequent deficiency of extracellular volume.

Although salt deficiency thus appears to be a likely cause for the change in water excretion, other possible causes are present. Potassium depletion is also usually present in infants with gastroenteritis (Darrow *et al.*, 1949), but the renal ability to form a dilute urine is well maintained in potassium deficient animals and man until the deficit is large (Levitin, Manitius, and Epstein, 1960; Holliday *et al.*, 1960; Rubini, 1961).

The fluid losses in gastroenteritis also lead to a fall in glomerular filtration rate (Calcagno and Rubin, 1951), and this may impair the response to a water load. The creatinine clearances in these infants must be interpreted with caution in view of the difficulties of accurate measurement. However, they suggest that the glomerular filtration rate was reduced initially and returned to normal only slowly. Physicians caring for such infants will be familiar with the tendency for the blood urea to remain high for several days after correction of the fluid deficit. This slow recovery of the glomerular filtration rate contrasts with the rapid recovery of the water excretory ability after peak weight and suggests that salt deficiency may impair the mechanism for urinary dilution independently of the glomerular filtration rate. Whatever the precise mechanism, the anomaly in water excretion present in infants with gastroenteritis must be appreciated

when planning fluid replacement and underlines the dangers of rapidly administered hypotonic fluids in the presence of an extracellular volume deficit. In these circumstances dangerous dilutional hyponatraemia can develop very rapidly since the normal water diuretic response is inhibited. We were careful to avoid rapid administration of large quantities of hypotonic fluids while a deficiency of extracellular fluid was still present, and it is interesting that no neurological abnormalities or sequelae were seen in these children.

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