Progress report

Sodium content of oral rehydration solutions: a reappraisal

The proliferation of commercial oral rehydration solutions (ORS), with widely varying compositions has left general practitioners and paediatricians in the United Kingdom in a state of confusion. Few remain unaware of the widespread use of oral rehydration therapy and its proven efficacy in preventing and treating dehydration associated with acute gastroenteritis.¹ Recommendations for the appropriate choice of oral rehydration solution particularly with regard to sodium content, however, are conflicting. The World Health Organization (WHO) continues to recommend an oral rehydration solution containing 90 mmol/l sodium regardless of the aetiology or severity of the diarrhoea or the age of the child.² WHO-ORS is used predominantly in the developing world but there has recently been some support for its use in the United Kingdom.³ In contrast, the oral rehydration solution included in the British National Formulary contains only 35 mmol/l sodium.⁴ Oral rehydration solutions containing 45, 50, 60, and 75 mmol/l sodium are also being promoted commercially (Table 1) which further complicates the issue. The purpose of this review is to consider the evidence available and define the most appropriate sodium concentration for use in the United Kingdom and other developed communities. In order to determine the appropriate concentration of a particular solute in an oral rehydration solution one must first establish its physiological function and then examine its effect in a defined clinical setting. The current rationale for the inclusion of sodium in oral rehydration solutions is two-fold: (i) to replace sodium lost in diarrhoeal stools, and (ii) to promote water absorption through glucose stimulated sodium transport. The amount of sodium required for these purposes, however, is controversial, and probably varies according to the aetiology of the diarrhoea and the age and nutritional status of the patient.

Table 1 *Composition of oral rehydration solutions available in the UK*

Product	BNF-ORS	Dioralyte	Dextrolyte	Paedialyte (maintenance)	Rehidrat	Electrolade	Nutricia* ORS	Paedialyte (rehydration)	WHO-ORS
Composition (mmol/l)									
Sodium	35	35	35	45	50	50	60	75	90
Chloride	37	37	30.5	35	50	40	63	65	80
Potassium	20	20	13.4	20	20	20	25	20	20
Lactate	0	0	17.7	0	0	0	0	0	0
Citrate	0	0	0	11.3	9	0	10	11.3	10
Bicarbonate	18	18	0	0	20	29.8	0	0	0
Glucose	200	200	200	139	91	111	111	139	111
Other ingredients	None	None	None	None	Sucrose fructose	Saccharin	None	None	None
Osmolality	310	310	297	250	336	251	289	310	331
Manufacturer	—	Rorer	Cow & Gate	Ross	Searle	Nicholas	Nutricia	Ross	—

*Available in Europe.

Historical perspective

Although parenteral fluid therapy for cholera was first suggested in 1832,⁵ oral therapy to prevent and treat dehydration was not introduced until the 1940's. Daniel Darrow, an early protagonist of oral rehydration, recommended a sodium content of 86 mmol/l on the basis of balance studies carried out in children with diarrhoea.⁶ Harrison reported the use of a solution containing 64 mmol/l sodium for mild dehydration in Baltimore City Hospital in the 1940's and this was subsequently revised to contain 50 mmol/l sodium and was produced commercially.⁷ After a spate of hypernatraemic dehydration in the USA in the 1950's, however, the sodium content was further reduced to 25–30 mmol/l.⁸ In retrospect, the high incidence of hypernatraemia in children probably related to the use of high solute feeds⁹ and to the high carbohydrate content of the oral rehydration solution, which resulted in osmotic diarrhoea thus perpetuating dehydration.¹ In 1953 in adult cholera patients in Calcutta, Chatterjee showed that an oral rehydration solution containing 68 mmol/l sodium was effective when given by mouth or *per rectum*.¹⁰ When studying the effect of infused intragastric glucose electrolyte solutions on stool output and water and electrolyte balance in adults with cholera, Hirschhorn *et al*¹¹ and Pierce *et al*¹² successfully used solutions containing between 101–133 mmol/l sodium, which approximated to the sodium concentration of adult cholera stools.

On the basis of balance studies in moderate to severe dehydration in children with cholera and other infantile diarrhoeas,¹³ the WHO recommended a solution containing 90 mmol/l sodium.¹⁴ Balance studies give a more reliable estimate of deficit than the electrolyte composition of the stool alone, as the latter fails to take into account losses in the vomitus, urine or through the respiratory tract, or the previous nutritional status. These estimates, however, may not be relevant to children in the UK with mild dehydration and diarrhoea of predominantly viral aetiology, in which the stool sodium concentration^{13 15–17} and stool volume differ considerably from those of bacterial diarrhoeas including cholera. The net sodium deficit is relatively greater for the degree of dehydration (water deficit) in cholera than in non-cholera diarrhoeas because of the higher stool sodium concentration in cholera. Stool losses in acute diarrhoea relate closely to the purging rate, which when high reduces ileal and colonic salvage of sodium. A further consideration is that pre-existing chronic malnutrition may result in reduced total body sodium and thus greater tolerance of a sodium load. It should also be stressed that the complete WHO-ORS is recommended for initial rehydration only. The addition of free water to the WHO-ORS in a ratio of two parts ORS:1 part water for maintenance therapy after rehydration, results in a fall in the sodium intake to approximately 60 mmol/l¹⁴ and should minimise the risk of hypernatraemia. Undoubtedly use of the WHO-ORS in developing communities has saved the lives of millions of children of all ages¹⁸ with diarrhoea of diverse aetiologies.¹⁹ The fear of hypernatraemia, however, has deterred paediatricians in the UK and other developed communities from its use.²⁰ In such communities where dehydration is often mild to moderate, children have a better nutritional status and sodium losses are less, a lower sodium oral rehydration solution may be a simpler, safer but equally effective alternative.

Disturbances of sodium homeostasis in acute diarrhoea

Alterations to serum sodium concentrations in acute diarrhoea depend on the relative losses of water and sodium in the stools (Table 2), urine and vomitus. In the majority of children, dehydration is isonatremic. Hyponatraemic dehydration (serum sodium <130 mmol/l), which is more likely to develop in malnourished children with existing total body sodium deficit,^{1 21 22} may be exacerbated by excessive consumption of fluid with a low sodium content.²³ Hypernatraemic dehydration (serum sodium >150 mmol/l) has, historically, occurred more commonly in developed communities and was often related to a high solute load, in the form of cows' milk, consumed before and during diarrhoea.^{1 9 16} Its recent decline with the use of low solute, adapted cows' milk formulae and later introduction of solids into the diet supports this contention.^{8 24} Hypernatraemia has also been associated with carbohydrate intolerance,²³ hyperosmolar oral rehydration solutions,²⁵ incorrect reconstitution of high sodium oral rehydration solutions,²⁶ or use of high sodium oral rehydration solutions without additional water, especially in neonates.²⁷ If managed inappropriately its consequences, including stroke and convulsions, may be devastating.

Children under two years are less tolerant of high sodium oral rehydration solutions because of specific physiological factors.²¹ Immature renal function of infants is associated with a lower renal concentrating capacity and hence a lower maximal urine osmolality. In addition they have an impaired natriuretic response, which makes them less tolerant to high solute loads and more susceptible to sodium and water retention, particularly in states which lead to reduced vascular perfusion of the kidney. In contrast with well nourished infants in developed communities who usually receive a high protein diet, those in developing communities may be more tolerant of high solute loads as they are often malnourished with chronic electrolyte losses and are hyponatraemic before admission.^{22 28} In addition, stool sodium losses are greater in cholera, and in enteropathogenic and enterotoxigenic *E coli* infections which are more common in these communities, than in the viral diarrhoeas which predominate in developed communities and in

Table 2 Stool electrolyte content (mmol/l) in diarrhoea

Aetiology	Age (yr)	Na	Cl	K	HCO ₃	Reference
Cholera	<5	88	86	30	32	17
	<5	101	92	27	32	16
	5–10	107	88	26	30	13
	Adult	140	104	13	44	16
Rotavirus	<5	37	22	38	6	15
	<5	35		26		17
ETEC	<5	53	24	37	30	15
	<5	68		25		17
EPEC	<5	63		24		17
<i>Klebsiella</i> sp.	<5	72		25		17
<i>Giardia lamblia</i>	<5	36		11		17
Unknown	<5	56	25	55	14	16
(Non-cholera)	<5	68		23		17

ETEC, enterotoxigenic *E coli*; EPEC, enteropathogenic *E coli*.

which there are relatively greater losses of water than sodium in the stools.

Balance studies have further increased our understanding of sodium homeostasis in infancy. Aperia *et al.* studied sodium balance in moderately dehydrated infants given oral rehydration solutions containing 40 (ORS₄₀) or 90 (ORS₉₀) mmol/l sodium.²⁹ The majority had diarrhoea of viral aetiology and the mean stool sodium concentration was 38 mmol/l. All were in negative sodium balance on admission as shown by an increased renal fractional reabsorption of sodium. With both oral rehydration solutions sodium intake exceeded output throughout the 36 h period of rehydration. A positive sodium balance was therefore achieved with both oral rehydration solutions but was always greater with ORS₉₀. A significant increase in the urinary fractional excretion of sodium indicating that positive sodium balance had been achieved, occurred between 12–18 h with ORS₉₀ and 24–36 h with ORS₄₀. Transient slight hypernatraemia occurred in some infants who received ORS₉₀ and transient slight hyponatraemia in some who received ORS₄₀, though both groups were asymptomatic. These findings suggest that an ORS with a sodium content between the two tested might restore sodium balance while maintaining normonatraemia.

In two recent studies in Turkey³⁰ and Pakistan³¹ this question has been pursued further. In the first balance study of oral rehydration therapy in dehydrated infants less than two months of age, 15 infants were treated with an oral rehydration solution containing 60 mmol/l sodium.³⁰ All patients were in negative sodium balance on admission and sodium intake exceeded output throughout the period of oral rehydration therapy. Two hypernatraemic patients became normonatraemic but one remained hypernatraemic after treatment. Another patient who was normonatraemic on admission developed hypernatraemia during treatment. These infants retained more water and excreted less sodium in the urine compared with a group of infants over three months of age. It was concluded that immature renal function in young infants may predispose to salt and water retention and that an oral rehydration solution containing 60 mmol/l sodium was more appropriate than one containing 90 mmol/l. Similar conclusions were reached in a second study of 60 moderately dehydrated infants less than two years of age who received either the WHO-ORS (sodium 90 mmol/l) or an identical solution in which glucose was replaced by rice powder or dal moong (starch).³¹ Interestingly, serum sodium levels on admission were inversely correlated with age, suggesting immaturity is an important factor predisposing to hypernatraemia. Oral rehydration solutions were equally effective for rehydration, during which all patients showed a significant increase in serum sodium concentration. During maintenance therapy, however (when oral rehydration solutions and water were given using the 2:1 regimen), sodium concentrations tended to become normal reflecting the decreased sodium intake. Stool output was significantly less during maintenance therapy in those receiving the oral rehydration solution containing rice powder or dal moong, and there was a consequent increased capacity to correct serum sodium and sodium balance and increased weight gain in this group. Although no child developed hypernatraemia, it was concluded that renal immaturity was largely responsible for the electrolyte disturbances seen in infantile diarrhoea and that the decreased ability to produce concentrated urine increased the risk of hypertonicity with high sodium intake.

Role of sodium in oral rehydration solutions

The rationale for inclusion of sodium in oral rehydration solutions is to replace sodium losses and to promote water absorption. Sodium (and therefore water) absorption from oral rehydration solutions in the small intestine occurs through five main mechanisms; (i) active electrogenic sodium absorption, (ii) active co-transport with glucose, amino acids, and other organic solutes, (iii) electroneutral (coupled) sodium-chloride absorption, (iv) sodium-hydrogen exchange, and (v) solvent drag.

Active electrogenic sodium absorption is highly dependent upon luminal sodium concentration. When infusing intragastric glucose electrolyte solutions containing 101, 111, and 118 mmol/l sodium in adults with cholera, Pierce *et al* showed that despite net water absorption and effective rehydration, net sodium balance was negative.¹² Sodium loss was less, however, than in the same patients during control periods when they did not receive glucose-electrolyte solutions. Sladen and Dawson, using a human jejunal perfusion technique showed that despite net glucose and water absorption, little or no net sodium absorption occurred in the normal jejunum from glucose-electrolyte solutions containing less than 75 mmol/l sodium.³² Similarly, Fordtran noted the influence of sodium concentration on net sodium absorption.³³ Spiller *et al* observed that net sodium absorption only occurred in the jejunum when the luminal sodium concentration was above 133 mmol/l, and showed the importance of this effect on jejunal sodium absorption from enteral feeds in man.³⁴ In this study net sodium and water secretion occurred from feeds with low sodium content and net sodium absorption only occurred when initial sodium concentration was above 90 mmol/l.

Intestinal perfusion studies in animals have shown similar results. On perfusion of normal rat jejunum with a variety of oral rehydration solutions, Lifshitz and Wapnir found sodium absorption only occurred when the oral rehydration solution sodium concentration was above 60 mmol/l.³⁵ In contrast, in the cholera toxin treated secreting rat small intestine net sodium secretion occurred with all oral rehydration solutions perfused³⁶ and by extrapolation net absorption was predicted only when the oral rehydration solution sodium concentration approached 120 mmol/l. The explanation for this effect is simple. The jejunum is highly permeable, resulting in a plasma-to-lumen 'leak' of sodium and an apparent diminished ability of the jejunum to absorb sodium against a concentration gradient. Thus, its luminal contents are constantly being rendered isosmotic. The question is, does net sodium secretion in the small intestine matter? Despite net small intestinal sodium secretion, glucose and water absorption sufficient to rehydrate even patients with cholera will occur from a glucose-electrolyte solution. Sodium must therefore be absorbed even if the net flux is negative. It is important to remember that absorptive and secretory processes operate simultaneously and that net solute movement represents the sum of several transport events. An oral rehydration solution sodium concentration sufficient to result in net sodium absorption is therefore unnecessary for effective rehydration. On the other hand, both sodium and water secretion occur when solutions with low sodium concentrations (23–49 mmol/l) are perfused in normal and secreting rat small intestine.^{35–38} In addition to being ineffective in promoting water absorption there is also evidence in animals,³⁶

and from clinical trials^{18, 39} that these low sodium solutions may result in hyponatraemia. It therefore seems reasonable to contemplate an oral rehydration solution sodium concentration between these two extremes, aiming to promote adequate water absorption without adversely affecting sodium status.

Finally, the role of the colon in salvaging sodium and water also deserves consideration. Defective colonic function has been confirmed in cholera⁴⁰ though less is known about its function in rotavirus infection. The immaturity of the infant colon may also be relevant to electrolyte conservation.⁴¹

A relationship between the absorption of sodium and sugars was first suggested in 1902.⁴² *In vitro* confirmation of the requirement of sodium ions for the active transport of glucose⁴³ was followed by numerous studies on the effect of sodium concentration on the kinetics of glucose absorption.^{44, 45} Glucose-sodium cotransport was shown *in vitro*,^{46, 47} and was subsequently confirmed *in vivo* in the rat⁴⁸ and in man.^{32, 49} Sodium is then actively pumped out of the cell at the basolateral membrane by the action of Na⁺ K⁺ ATPase. This creates a potential difference across the mucosa which promotes active sodium absorption. In addition to promoting active sodium absorption, glucose also promotes passive sodium absorption by solvent drag.⁵⁰ Evidence that glucose stimulated sodium and water absorption remains intact in diarrhoea was first shown in cholera^{11, 12, 51} which thus provided a rational basis for the inclusion of a carbohydrate in oral rehydration solutions. Coupled sodium transport occurs with other sugars and neutral amino acids.⁴⁹ Sodium (and water) absorption is also promoted by bicarbonate and certain organic anions, notably short chain fatty acids such as acetate. We have previously reviewed the role of these substances in oral rehydration solutions.⁵²

Controlled clinical trials

Despite the wide choice of oral rehydration solutions available in the United

Table 3 *Controlled trials of oral rehydration solutions with differing sodium concentrations*

Study	Ref	Location	n	ORS (Na)	Efficacy*	Complications
Chatterjee (1978)	(52)	India	39	90 v 50	Similar	Periorbital oedema/hyponatraemia with 90 mmol/l
Santosham (1982)	(53)	USA/Panama	146†	90 v 50	Similar	Periorbital oedema with 90 mmol/l
Santosham (1983)	(54)	Panama	93‡	90 v 50	Similar	None
Sunoto (1980)	(55)	Indonesia	42	90 v 51	Similar	Periorbital oedema, increased stool frequency with 90 mmol/l
Saberi (1983)	(56)	Iran	51	90‡ v 58	Similar	Periorbital oedema/hyponatraemia with 90 mmol/l
Nalin (1980)	(57)	Jamaica	58	90‡ v 60	Similar	Periorbital oedema with 90 mmol/l
Isolaure (1985)	(59)	Finland	101†	90 v 60 v 35	Similar	35 mmol/l less efficient
Bhargava (1986)	(61)	India	65	90‡ v 60	Similar	
Cutting (1988)	(58)	UK	269‡	90 v 50 v 35	Similar	Hyponatraemia with 35 and 50 mmol/l
Islam (1982)	(60)	Bangladesh	65	120 v 60	Similar	Hyponatraemia with 120 mmol/l
Listernick (1985)	(62)	USA	60†	60 v 30	Similar	Impaired rehydration with 30 mmol/l
Elliott (1989)	(72)	UK	88†	60 v 50 v 35	Similar	Carbohydrate intolerance with high glucose – 35 mmol/l oral rehydration solution

*Rehydration and correction of plasma electrolytes; †Majority rotavirus; ‡Additional water not given with WHO-ORS.

Kingdom, there are virtually no published controlled clinical trials assessing their safety or efficacy. Further, the rationale for their composition remains obscure and is empirical in most cases. Several workers in other developed and in developing communities have critically evaluated oral rehydration solution sodium content in controlled clinical trials some of which are outlined in Table 3.

HIGH SODIUM ORS (90–120 MMOL/L)

In most studies the WHO-ORS (90 mmol/l sodium) is compared with a solution with a lower sodium content. WHO guidelines for the use of WHO-ORS specify that the complete solution should be given until the child is clinically rehydrated, after which it is alternated with water (2 volumes WHO:ORS to 1 volume water) for maintenance of hydration. Using this regimen the WHO-ORS is safe and effective for rehydration and maintenance^{53–57} and corrects both hyponatraemia and hypernatraemia.^{54–57} In several studies, however, children receiving the WHO-ORS developed periorbital oedema suggesting sodium overload.^{53–57} Although there was a trend towards the development of hypernatraemia in those receiving WHO-ORS compared with a lower sodium solution, those who developed hypernatraemia were asymptomatic and the difference between groups was not statistically significant.^{53 57 58} Cutting found the WHO-ORS safe and effective in mild to moderately dehydrated children in the UK with predominantly viral diarrhoea.⁵⁹ Although the mean serum sodium was not significantly higher in children receiving oral rehydration solutions with 90 mmol/l sodium than those receiving 35 or 60 mmol/l, the urine sodium was significantly higher in the 90 mmol/l sodium group. This reflects the kidneys attempt to maintain homeostasis and suggests that an excessive amount of sodium is being provided by the WHO-ORS. In a study of a similar group in Finland, Isolauri found an ORS containing 60 mmol/l sodium and 144 mmol/l glucose was as effective for correcting dehydration and sodium deficit as the WHO-ORS.⁶⁰

In one study an oral rehydration solution with 120 mmol/l sodium was used for maintenance therapy after initial intravenous rehydration and was supplemented by diluted milk.⁶¹ Mean serum, urine and stool sodium concentrations were significantly higher than in children receiving 60 mmol/l sodium and two developed hypernatraemia. When the osmolalities of the oral rehydration solution are compared (401 and 291 mOsmol/kg respectively) it is surprising that more problems were not encountered with the hyperosmolar solution. The number of children with hyponatraemia and/or malnutrition on admission was not specified, but if high might explain the apparent 'tolerance' of such a high sodium solution.

WHO-ORS IN NEONATES

The safety of the WHO-ORS in neonates has been questioned. In a controlled trial Bhargava *et al* compared the use of WHO-ORS and a 60 mmol/l ORS in neonates and concluded that when used for rehydration without additional water the WHO-ORS carries a significantly higher risk of hypernatraemia.²⁷ Sodium intake, mean serum sodium at 8, 24, and 48 h after admission and urinary sodium excretion were significantly higher in this group. Further, 50% developed hypernatraemia and pedal oedema, and

4.5% showed excessive irritability and had convulsions. Serum sodium concentrations were normal throughout treatment in the group receiving oral rehydration solution with 60 mmol/l sodium. In a subsequent trial he compared the same two oral rehydration solutions but used the WHO-ORS in the 2:1 regimen for rehydration. Both oral rehydration solutions were effective but it was concluded that it was safe to recommend a solution containing 60 mmol/l sodium for this age group.⁶²

MID-SODIUM ORS (50–60 MMOL/L)

Oral rehydration solutions containing between 50–60 mmol/l sodium are safe, effective treatment for the dehydration and electrolyte abnormalities associated with gastroenteritis of varied aetiology^{53–57 63} and in all age groups including neonates.^{27 62} Asymptomatic hypernatraemia and periorbital oedema observed in many studies during treatment with the higher sodium solution did not occur. Mild asymptomatic hyponatraemia was observed in several children, however.^{57 58} In one study weight gain was significantly greater and diarrhoea less in children receiving an oral rehydration solution containing 58 mmol/l sodium which may reflect the increased palatability of this oral rehydration solution compared with one containing more sodium.⁵⁶

LOW SODIUM ORS (30–35 MMOL/L)

Although solutions with low sodium and high glucose content are the most commonly used in the UK, they have only recently been subjected to controlled clinical trial.^{39 59} Results suggest that they effectively rehydrate children hospitalised with acute gastroenteritis, however, hyponatraemia may develop during treatment^{39 57} and they may fail to correct hyponatraemia. Carbohydrate intolerance may be exacerbated by the high glucose content required to render these oral rehydration solution isotonic and the osmotic effect of unabsorbed glucose may exacerbate diarrhoea.⁶³

In summary, clinical trials suggest that when used correctly oral rehydration solutions with a sodium content of between 30–90 mmol/l are safe and effective. Exceptions include the potential for hypernatraemia if the complete WHO-ORS is used in neonates and for symptomatic hyponatraemia with prolonged use of low sodium oral rehydration solutions, particularly in malnourished children. The combination of high sodium and high glucose concentrations in oral rehydration solutions, particularly when associated with monosaccharide intolerance, is potentially very dangerous and may exacerbate dehydration and hypernatraemia. The need to alternate the WHO-ORS with water after rehydration complicates its use, particularly in the home, and the risks of incorrectly reconstituting oral rehydration solutions are probably greater with high sodium solutions.

Several uncontrolled studies also give information relating to sodium content of oral rehydration solutions.^{23 26 28 64–69} The conclusions which can be drawn from these reports are generally similar to those from the controlled studies described above.

Conclusions

Evidence accumulated worldwide over decades leaves no doubt that oral glucose-electrolyte solutions are invaluable for rehydrating, maintaining hydration and preventing dehydration in acute diarrhoea in childhood

regardless of its aetiology and severity. Commercial production of a large variety of oral rehydration solutions whose composition cannot always be justified scientifically has caused confusion among practitioners. Introduction of the WHO-ORS to developing communities has saved millions of lives and its use in accordance with WHO recommendations should be encouraged. In developed communities such as the United Kingdom, however, where the aetiology of acute diarrhoea differs and its consequences are usually less severe, we suggest that use of the 90 mmol/l sodium solution is inappropriate and that one containing approximately 50–60 mmol/l sodium with 90–111 mmol/l glucose should be recommended.

Oral rehydration solutions containing 50–60 mmol/l sodium will safely and effectively rehydrate and maintain hydration eliminating the need for additional free water as recommended by the WHO for maintenance therapy. Hyponatraemia and hypernatraemia can both be successfully corrected and normonatreaemia maintained. The sodium content is adequate to replace stool losses resulting from both viral and bacterial diarrhoeas. Unlike oral rehydration solutions with low (30–35) or high (90 mmol/l) sodium concentration, however, iatrogenic hyponatraemia and hypernatraemia respectively are unlikely to occur. In particular, the safety of the oral rehydration solution containing 50–60 mmol/l sodium in neonates and young infants with immature renal function, who are incapable of coping with increased sodium loads should be stressed. The glucose concentration needed to render the oral rehydration solution containing 50–60 mmol/l isotonic or slightly hypotonic is similar to that in WHO-ORS but approximately half that in solutions containing 30–35 mmol/l sodium. This decreases the likelihood of their causing osmotic diarrhoea with dehydration and electrolyte disturbances, especially when there is accompanying monosaccharide intolerance. Oral rehydration solutions containing 50–60 mmol/l sodium have been proven safe and effective in controlled clinical trials in which they performed favourably with the WHO-ORS, both for rehydration and correction of acidosis. In addition, perfusion studies of both the normal and secreting rat small intestine⁷⁰ and the human jejunum⁷¹ suggest an oral rehydration solution containing 60 mmol/l sodium is superior with regard to water absorption than other oral rehydration solutions tested.

Errors in reconstituting oral rehydration solutions are common but are less likely to result in dangerous hypernatraemia when the original oral rehydration solution sodium concentration is below 90 mmol/l. Finally, in a community such as the UK where the fall in mortality caused by gastroenteritis has been dramatic, but where it remains an important cause of morbidity and hospital admission, the aim of treatment should be simplicity and economy. Production of a single 'all purpose' physiological oral rehydration solution for rehydration and maintenance would make oral rehydration therapy in developed communities cheaper, simpler and safer and the choice for the clinician infinitely easier.

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ELIZABETH J ELLIOTT, R CUNHA-FERREIRA, J A WALKER-SMITH,
AND M J G FARTHING

*Depts of Gastroenterology and Child Health,
St Bartholomew's Hospital,
London.*

Address for correspondence: Dr M J G Farthing, Department of Gastroenterology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.

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References

- 1 Hirschhorn N. The treatment of acute diarrhea in children. An historical and physiological perspective. *Am J Clin Nutr* 1980; **33**: 637–63.
- 2 World Health Organization/UNICEF. *Oral rehydration salts. Planning, establishment and operation of production facilities*. WHO/CDD/SER 1985; **85**: 1–136.
- 3 Candy DCA. Rehydration in gastrointestinal infections. In: Black JA, ed. *Paediatric emergencies*. London: Butterworths & Co, 1987: 403–11.
- 4 *British National Formulary*. A joint publication of the British Medical Association and the Pharmaceutical Society of Great Britain. 1986; **11**: 290.
- 5 Latta T. Malignant cholera. Documents communicated by the Central Board of Health, London, relative to the treatment of cholera by the copious injection of aqueous and saline fluids into the veins. *Lancet* 1832; **ii**: 274–7.
- 6 Darrow DC. The retention of electrolyte during recovery from severe dehydration due to diarrhea. *J Pediatr* 1946; **28**: 515–40.
- 7 Harrison HE. The treatment of diarrhea in infancy. *Pediatr Clin North Am* 1954; **1**: 335–48.
- 8 Finberg L. Editorial. Oral therapy for dehydration in diarrheal diseases as a global problem. *J Pediatr Gastroenterol Nutr* 1982; **1**: 3–5.
- 9 Colle E, Ayoub E, Raile R. Hypertonic dehydration (hypernatremia): the role of feedings high in solute. *Pediatrics* 1958; **22**: 5–12.
- 10 Chatterjee HN. Control of vomiting in cholera and oral replacement of fluid. *Lancet* 1953; **ii**: 1063.
- 11 Hirschhorn N, Kinzie JL, Sachar DB, et al. Decrease in net stool output in cholera during intestinal perfusion with glucose-containing solutions. *N Engl J Med* 1968; **279**: 176–81.
- 12 Pierce NF, Banwell JG, Mitra RC, et al. Effect of intragastric glucose-electrolyte infusion upon water and electrolyte balance in Asiatic cholera. *Gastroenterology* 1968; **55**: 333–43.
- 13 Mahalanabis D, Wallace CK, Kallen RJ, Mondal A, Pierce NF. Water and electrolyte losses due to cholera in infants and small children: a recovery balance study. *Pediatrics* 1970; **45**: 374–85.
- 14 WHO. *A manual for the treatment of acute diarrhoea – for use by physicians and other senior health workers*. WHO/CDD/SER 80; **2**: Rev 1. Geneva: WHO 1984.
- 15 Molla AM, Rahman M, Sarker SA, Sack DA, Molla A. Stool electrolyte purging rates in cholera caused by rotavirus, enterotoxigenic *E coli* and *V cholerae* in children. *J Pediatr* 1981; **98**: 835–8.
- 16 Pierce NF, Hirschhorn N. Oral fluid – a simple weapon against dehydration in diarrhoea. *WHO Chronicle* 1977; **31**: 87–93.
- 17 Deorari AK, Bhan MK, Arora NK, et al. Stool electrolyte composition in relation to etiology in acute gastroenteritis. *Indian Pediatric J* 1982; **19**: 217–20.
- 18 Finberg L. The role of oral electrolyte-glucose solutions in hydration for children – international and domestic aspects. *J Pediatr* 1980; **96**: 51–4.
- 19 Pizarro D, Posada G, Mohs E, Levine MM, Nalin DR. Evaluation of oral therapy for infant diarrhoea in an emergency room setting: the acute episode as an opportunity for instructing mothers in home treatment. *Bull WHO* 1979; **57**: 983–6.
- 20 Harrison HE, Finberg L. Hypernatremic dehydration. *Pediatr Clin North Am* 1964; **11**: 955–61.
- 21 Bart KJ, Finberg L. Single solution for oral therapy of diarrhoea. *Lancet* 1976; **ii**: 633–4.
- 22 Patra FC, Mahalanabis D, Jalan KN, Sen A, Banerjee P. Is oral rice electrolyte solution superior to glucose electrolyte solution in infantile diarrhoea? *Arch Dis Child* 1982; **57**: 910–2.
- 23 Hirschhorn N, McCarthy BJ, Ranney B, et al. Ad libitum oral glucose electrolyte therapy for acute diarrhea in Apache children. *J Pediatr* 1973; **83**: 562–71.
- 24 Manuel PD, Walker-Smith JA. Decline of hypernatraemia as a problem in gastroenteritis. *Arch Dis Child* 1980; **55**: 124–7.

- 25 Sandhu BK, Jones BJM, Brook CGD, Silk DBA. Oral rehydration in acute infantile diarrhoea with a glucose-polymer electrolyte solution. *Arch Dis Child* 1982; **57**: 152–60.
- 26 Cleary TG, Cleary KR, Dupont HL, *et al*. The relationship of oral rehydration solution to hypernatraemia in infantile diarrhoea. *J Pediatr* 1981; **99**: 739–41.
- 27 Bhargava SK, Sachdev HPS, Das Gupta B, Daral TS, Singh HP, Mohan M. Oral rehydration of neonates and young infants with dehydrating diarrhoea: comparison of low and standard sodium content in oral rehydration solutions. *J Pediatr Gastroenterol Nutr* 1984; **3**: 500–5.
- 28 Hirschhorn N, Cash RA, Woodward WE, Spivey GH. Oral fluid therapy of Apache children with acute infectious diarrhoea. *Lancet* 1972; **ii**: 15–8.
- 29 Aperia A, Marin L, Zetterstrom R, *et al*. Salt and water homeostasis during oral rehydration therapy. *J Pediatr* 1983; **103**: 364–9.
- 30 Marin L, Saner G, Sokucu S, Gunoz H, Neyzi O, Zetterstrom R. Oral rehydration therapy in neonates and young infants with infectious diarrhoea. *Acta Paediatr Scand* 1987; **76**: 431–7.
- 31 Murtaza A, Zulfiqar I, Khan SR, Lindblad BS, Aperia A. Regulation of serum sodium in dehydrated and orally rehydrated infants. Influence of age and of purging rates. *Acta Paediatr Scand* 1987; **76**: 424–30.
- 32 Sladen GE, Dawson AM. Interrelationships between the absorptions of glucose, sodium and water by the normal human jejunum. *J Clin Invest* 1975; **55**: 728–37.
- 33 Fordtran JS. The mechanism of sodium absorption in the human small intestine. *J Clin Invest* 1968; **47**: 884–900.
- 34 Spiller RC, Jones BJM, Silk DBA. Jejunal water and electrolyte absorption from two proprietary enteral feeds in man: importance of sodium content. *Gut* 1987; **28**: 681–7.
- 35 Lifshitz F, Wapnir RA. Oral hydration solutions: experimental optimization of water and sodium absorption. *J Pediatr* 1985; **106**: 388–9.
- 36 Rolston DDK, Borodo MM, Kelly MJ, Dawson AM, Farthing MJG. Efficacy of oral rehydration solutions in a rat model of secretory diarrhoea. *J Pediatr Gastroenterol Nutr* 1987; **6**: 624–30.
- 37 Elliott EJ, Watson AJM, Walker-Smith JA, Farthing MJG. Effect of bicarbonate on efficacy of oral rehydration therapy: studies in an experimental model of secretory diarrhoea. *Gut* 1988; **29**: 1052–7.
- 38 Wapnir RA, Lifshitz F. Osmolality and solute concentration – their relationship with oral hydration solution effectiveness: an experimental assessment. *Pediatr Res* 1985; **19**: 894–8.
- 39 Elliott EJ, Armitstead JCM, Farthing MJG, Walker-Smith JA. Oral rehydration therapy without bicarbonate for prevention and treatment of dehydration: a double-blind controlled trial. *Aliment Pharmacol Therapy* 1988; **2**: 253–63.
- 40 Speelman P, Butler T, Kabir I, Ali A, Banwell J. Colonic dysfunction during cholera infection. *Gastroenterology* 1986; **91**: 1164–70.
- 41 Jenkins HR, Milla PJ. The development of colonic transport mechanisms in early life: evidence for reduced anion exchange. *Early Hum Dev* 1988; **16**: 213–8.
- 42 Reid EW. Intestinal absorption of solutions. *J Physiol* 1902; **28**: 241–56.
- 43 Riklis E, Quastel JH. Effects of cations on sugar absorption by isolated surviving guinea pig intestine. *Can J Biochem Physiol* 1958; **36**: 347–62.
- 44 Csaky TS. A possible link between active transport of electrolytes and non-electrolytes. *Fed Proc (Baltimore)* 1963; **22**: 3–7.
- 45 Crane RK. Sodium-dependent transport in the intestine and other animal tissues. *Fed Proc* 1965; **24**: 1000–6.
- 46 Schultz SG, Zalusky R. Ion transport in isolated rabbit ileum II. The interaction between active sodium and active sugar transport. *J Gen Physiol* 1964; **47**: 1043–59.
- 47 Barry RJC, Smyth DH, Wright EM. Short circuit current and solute transport by rat jejunum. *J Physiol* 1965; **181**: 410–31.
- 48 Levinson RA, Scheld HP. Absorption of sodium chloride, water and simple sugars in rat small intestine. *Am J Physiol* 1966; **211**: 939–42.
- 49 Schultz SG. Sodium-coupled solute transport of small intestine: a status report. *Am J Physiol* 1977; **223**: 249–54.
- 50 Fordtran JS. Stimulation of active and passive sodium absorption by sugars in the human jejunum. *J Clin Invest* 1975; **55**: 728–37.
- 51 Phillips RA. Water and electrolyte losses in cholera. *Fed Proc (Balti)* 1964; **23**: 705–9.
- 52 Elliott EJ, Walker-Smith JA, Farthing MJG. The role of bicarbonate and base precursors in the treatment of acute gastroenteritis. *Arch Dis Child* 1987; **62**: 91–5.
- 53 Chatterjee A, Mahalanabis D, Jalan KN, *et al*. Oral rehydration in infantile diarrhoea. *Arch Dis Child* 1978; **53**: 284–9.

- 54 Santosham M, Daum RS, Dillman L, *et al*. Oral rehydration therapy of infantile diarrhea. *N Engl J Med* 1982; **306**: 1070–6.
- 55 Santosham M, Carrera E, Sack B. Oral rehydration therapy in well nourished ambulatory children. *Am J Trop Med Hyg* 1983; **32**: 804–8.
- 56 Sunoto, Suharyono, Suryono Wibowo, Sumarso. Oral rehydration solution. An appropriate formula for acute infantile diarrhea. *Pediatr Indones* 1980; **20**: 205–15.
- 57 Saberi MS, Assacc M. Oral hydration of diarrhoeal dehydration. Comparison of high and low sodium concentration in rehydration solutions. *Acta Paediatr Scand* 1983; **72**: 167–70.
- 58 Nalin DR, Harland E, Ramlal A, *et al*. Comparison of low and high sodium and potassium content in oral rehydration solutions. *J Pediatr* 1980; **97**: 848–53.
- 59 Cutting WAM, Belton NR, Gray JA, *et al*. The safety and efficacy of three oral rehydration solutions for children with diarrhoea. *Acta Paediatr Scand* 1989; **78**: 253–8.
- 60 Isolauri E. Evaluation of an oral rehydration solution with Na+ 60 mmol/l in infants hospitalized for acute diarrhoea or treated as outpatients. *Acta Paediatr Scand* 1985; **74**: 643–9.
- 61 Islam MR, Bardhan PK, Rahman MM. A comparison of oral replacement solutions containing sodium in concentrations of 120 mmol/l and 60 mmol/l in paediatric diarrhoea. *Indian J Pediatr* 1982; **49**: 349–95.
- 62 Bhargava SK, Sachdev HPS, Das Gupta B, Man Mohan, Singh HP, Daral TS. Oral therapy of neonates and young infants with World Health Organization Rehydration Packets: a controlled trial of two sets of instructions. *J Pediatr Gastroenterol Nutr* 1986; **5**: 416–22.
- 63 Listernick R, Zieserl E, Davis AT. Oral glucose-electrolyte solutions as maintenance therapy of acute diarrhea. *Am J Dis Child* 1985; **139**: 571–4.
- 64 Abdalla S, Henry N, El Essaily M, Nasser S, Hirschhorn N. Oral rehydration for the low-birthweight baby with diarrhoea. *Lancet* 1984; **ii**: 818–9.
- 65 Sack DA, Islam R, Brown KH, *et al*. Oral therapy in children with cholera: a comparison of sucrose and glucose electrolyte solutions. *J Pediatr* 1980; **96**: 20–5.
- 66 Pizarro D, Posada G, Mata L, Nalin D. Oral rehydration of neonates with dehydrating diarrhoeas. *Lancet* 1979; **ii**: 1209–10.
- 67 Pizarro D, Posada G, Mata L. Treatment of 242 neonates with dehydrating diarrhea with an oral glucose-electrolyte solution. *J Pediatr* 1983; **102**: 153–6.
- 68 Blum D, Brasseur V, Kahn A, Brachet E. Safe oral rehydration of hypertonic dehydration. *J Pediatr Gastroenterol Nutr* 1986; **5**: 232–5.
- 69 Hutchins P, Wilson C, Manly JAE, Walker-Smith HA. Oral solutions for infantile gastroenteritis – variations in composition. *Arch Dis Child* 1980; **55**: 616–8.
- 70 Elliott EJ, Walker-Smith JA, Farthing MJG. Relationship between glucose and sodium in oral rehydration solutions: studies in a model of secretory diarrhoea. *Pediatr Res* 1986; **20**: 690.
- 71 Elliott EJ, Hunt JB, Watson AJM, Walker-Smith JA, Farthing MJG. Oral rehydration solutions: assessment in human and animal models of intestinal perfusion. *Pediatr Res* 1987; **22**: 108.
- 72 Elliott EJ, Da Cunha Ferreira RMC, Cameron D, Farthing MJG, Walker-Smith JA. Evaluation of three oral rehydration solutions designed for use in developed countries. *Aliment Pharmacol Therap* 1989; **3**: 233–43.