CURRENT SURVEY

Gastro-enteritis in infancy

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Incidence

The incidence of diarrhoeal disease in infancy has greatly decreased over the last 25 years, mainly due to improvements in social, hygienic and medical standards, but diarrhoea and vomiting still remain an important cause of death during the 1st year of life especially in poorly developed countries (Heese *et al.*, 1966). Since 1958 the infant mortality rates attributed to gastro-enteritis in the U.K. are shown in Table 1.

TABLE 1. Death rate from gastro-enteritis per 100,000 live births

1958	1959	1960	1961	1962	1963	1964	1965
36.5	40.2	43.7	47.7	53.7	46.5	47.9	39.5

In Britain about 400 babies with gastro-enteritis under the age of 1 year die every year; 10,000 require hospital admissions and about 90,000 are treated at home (Registrar General, *Statistical Reviews*, 1958-66).

During the 1960s the infant mortality rates have shown a slight, but disturbing increase, which some attribute to the change in feeding habits from breast to bottle. Others (Wheatley, 1968) found 'no evidence that either the incidence of the condition or its response to treatment were influenced by the method of feeding'. This is further supported by the fact that about 30% of infants develop gastro-enteritis during the second 6 months of life and not the first (Registrar General, *Statistical Reviews*, 1958-66).

Aetiology

Aetiology varies a great deal, although the clinical features are similar in the majority of babies. Whatever the organism involved, the infectivity rate is usually high and it is particularly so when infants of the same age are grouped together (epidemic diarrhoea of the newborn, infant and children nurseries, hospitals). Pathogenic bacteria account for only about 30% of diarrhoea in children

(Cramblett & Siewers, 1965; Connor & Barrett-Connor, 1967; Moffet, Shulenberger & Burkholder, 1968). The most important are enteropathogenic *Escherichia coli*, *Shigellae* and *Salmonellae*. Viruses probably account for 10% of diarrhoea in children (Cramblett & Siewers, 1965; Moffet *et al.*, 1968). The most commonly isolated are enteroviruses (Ramos-Alvarez & Olarte, 1964), adenoviruses, Coxsackie and ECHO viruses type 14 and 18 (Duncan & Hutchison, 1961; Sterner, 1962; Cramblett & Siewers, 1965). Other viruses have been incriminated, but mainly during epidemics.

Escherichia coli

Diarrhoea due to *E. coli* most often occurs in newly-born-baby nurseries, is highly infectious and may result in a high mortality especially when premature babies are affected (Sabin, 1963). Although about 150 sub-groups of *E. coli* have been detected only about 10% have been associated with diarrhoea in infants (Olarte & Ramos-Alvarez, 1965; Moffet *et al.*, 1968), more especially the sero-types O-111, O-55, O-26 (Thomson, Watkins & Gray, 1956), O-128 and O-119 (Teeside Epidemic, 1968; Anderson, 1968).

Shigella

Sporadic infections may occur at any age, most commonly under 2 years of age. *Shigella sonnei* and *Shigella flexner* are the most common organisms isolated from the stools (Mosley, Adams & Lyman, 1962).

Salmonella

Occur at any age and usually spread from contamination. Most commonly isolated are *Salmonella typhimurium* (Bate & James, 1958).

Monilia

Some reports suggest *Candida albicans* as the sole cause of infantile diarrhoea (Kozim & Taschdjian,

1962; Moffet *et al.*, 1968), but these observations are not generally accepted.

Other causes

Diarrhoea due to other pathogens such as *Proteus* and *Pseudomonas* is infrequent and may be due to prolonged antibiotic use, cystic fibrosis or hypogammaglobulinaemia.

It is important to exclude other conditions which may present with diarrhoea and/or vomiting. The more common include cystic fibrosis, gluten-induced enteropathy, disaccharide intolerance, metabolic diseases, feeding mismanagement, parenteral infections, intolerance to drugs, milk allergy and any surgical conditions, e.g. Hirschprung's disease.

Clinical features and pathology

The clinical features and pathology are well known and will be described only briefly. Signs of dehydration will not be present until an infant has lost more than 60 ml of fluid per kilogram body weight. Dehydrated infants fall into three groups: those who have isotonic dehydration (50%), hypotonic dehydration (30%) and hypertonic dehydration (20%) (Cooke, 1955; Brusiler & Cooke, 1964).

These authors have estimated that the possible deficits of water and electrolytes in moderate dehydration (per kilogram body weight) were as shown in Table 2.

Losses in excess of 150 ml/kg body weight are usually associated with complete circulatory collapse and death.

Treatment

Antibiotics

Antibiotics, generally speaking, are rarely indicated in the treatment of gastro-enteritis. *Shigella* infections are as a rule self-limited diseases lasting up to 1 week and in the majority of children correction of fluid and electrolyte losses is all that is required.

Antibiotics should be reserved for the very ill child. Ampicillin has been found to be most effective (Haltalin *et al.*, 1967). Enteritis due to *Salmonellae* is in a majority of infants a short and self-limited condition and no treatment is required (Dixon, 1965; Rosenstein, 1967) but should there be evidence of bacteraemic spread chloramphenicol or ampicillin

should be used. There is some evidence that ampicillin may be more effective in eradicating the carrier state of *S. typhi* (Simon & Miller, 1966). Gastro-enteritis due to pathogenic *E. coli* assumes great significance in the first few weeks of life as it often occurs in epidemic form and carries a high mortality (Rosansky *et al.*, 1964). Antibiotics are recommended while awaiting the results of stool culture. Various antibiotics have been used but the most effective at present are oral colomycin and neomycin although many strains have been found to be resistant to neomycin (Murray, Kheder & Wheeler, 1964).

Fluid and electrolytes

Infants who manifest clinical features of dehydration will as a rule require intravenous treatment, but many infants today are diagnosed before signs of dehydration occur and can be effectively managed by replacing fluid and electrolytes orally. Treatment consists of stopping all oral feeding and replacing it with 10% dextrose in 1/5 N saline feeds for 12–24 hr and then gradually re-introducing dilute milk feeds according to the infant's progress.

The majority of infants who require i.v. treatment have moderate deficits in intravascular volume and thus reduction in blood flow to vital structures. It is imperative, therefore, to restore the blood volume to normal before anything else is considered. Clinical features of peripheral circulatory failure such as hypotension, elevated packed cell volume and haemoglobin and concentrated urine with specific gravity greater than 1.030 are ominous signs. It is sound practice to start treatment with plasma or half strength plasma (allowing about 20 ml/kg) or low molecular weight Dextran (Rheomacrodex) which is considered by some to be superior to plasma in restoring the peripheral circulation (Lillehei *et al.*, 1964). It is claimed that there is less tendency to thrombosis as Dextran decreases the blood viscosity which is increased in all conditions where blood flow is sluggish. Use of Dextran solutions may, therefore, be particularly useful in infants with hypernatraemic dehydration (see below). Normal saline should not be used to restore the blood volume as only 25% is retained in the vascular compartment within 2 hr of infusion and it is a poor expanding-solution.

TABLE 2

	Water (ml)	mEq		
		Sodium	Potassium	Chloride
Isotonic dehydration	100–120	8–10	8–10	8–10
Hypotonic dehydration	100–120	10–12	8–10	+0 to +2
Hypertonic dehydration	100–120	2–4	0–4	–4 to –6

Once the intravascular volume is restored fluid and electrolyte replacement can start, as well as partial correction of the metabolic acidosis which is almost always present. Only in rare instances does diarrhoea lead to metabolic alkalosis (Tucker *et al.*, 1964).

Treatment of isotonic and hypotonic dehydration consists of infusion of either half-normal saline or dextrose or 1/5 N saline and dextrose. The results are satisfactory whichever solution is used. Once the intravascular volume has been restored it does not really matter what is infused afterwards, i.e. 1/2 or 1/5 N dextrose-saline in all infants except newborns in which 1/5 N saline is preferred. A practical and safe method of estimating fluid losses in infants over 2 weeks of age is to allow 150 ml/kg body weight and adding to this 5% of the weight loss (earliest signs of dehydration) or 10% of the weight loss (early circulatory failure)—the amounts being calculated for each 24-hr period. Neonates who are not dehydrated require only 60 ml/kg (Rickham, 1957).

It should also be stressed that these infants have moderate potassium losses (see Table 2) which should be replaced concurrently. Some (Barness & Young, 1964) prefer not to use potassium early in cases of hypertonic dehydration as losses in these cases are small or none at all. Provided urine formation is satisfactory, potassium losses can be replaced by allowing 3 mEq/kg (potassium chloride solution 1 g = 13 mEq/l of potassium) and the best practical way is to estimate requirements for each 24-hr period.

It is important to correct the metabolic acidosis, at least partially, as well as replace fluid and electrolyte losses. Acidosis causes cardiac arrhythmia, especially fibrillation, and may lead to impairment of cardiac function (Stewart, 1965); it inhibits various enzymes (Thrower, Darby & Aldinger, 1961; Coleman & Glariano, 1963) and a stage may be reached whereby fluid and electrolyte losses are corrected but death still ensues.

Lactate has no place in the correction of metabolic acidosis. It was used in the days before satisfactory solutions were prepared for the intravenous route, e.g. Hartmann's solution (Ringer's solution + lactate; Hartmann & Senn, 1932). Although Hartmann reported a large series of children who improved after lactate he also had some who did not (Hartmann *et al.*, 1938). He postulated a congenital cause for this defect. We now know that in all states in which circulatory insufficiency is present lactic acid is produced (Huckabee, 1961a, b). Hence, giving lactate results in increasing the blood lactate level further; moreover, for lactate to work it has to be oxidized to bicarbonate.

A formula for correction of metabolic acidosis has been developed by Astrup (Astrup *et al.*, 1960) (kilograms weight $\times 0.3 \times$ base deficit = mEq

sodium bicarbonate) (an 8.4% solution is available and 1 ml of this solution contains 1 mEq of sodium bicarbonate). Heese *et al.* (1966) showed that addition of bicarbonate to a standard regime of intravenous half-strength Darrow-2.5% dextrose solution led to the more rapid return to normal of acid-base status than the standard regime without bicarbonate. This requires the use of the Astrup apparatus for estimating pH, P_{CO_2} and standard bicarbonate, and should be regarded as a bed-side rather than a laboratory procedure. The correction of metabolic acidosis in such a way is efficient, rapid and safe (Kuzemko, Fielding & Hudson, 1969).

Hypernatraemia

This is a serious and still an unsolved problem. Macaulay & Watson (1967) estimated that there were about 1000 children of school age in England and Wales whose educational and social difficulties could be attributed to hypernatraemia in infancy. He has also pointed out that approximately 100 deaths a year may be due to this condition. If Macaulay's estimates are correct hypernatraemia presents a large medical problem which should receive more attention than it does at present.

'Hypernatraemia' is defined as a serum sodium greater than 150 mEq/l (Finberg & Harrison, 1955) or more accurately as a plasma osmolality over 310 m-Osmol/l since this takes into account not only the electrolytes but other molecules such as glucose and urea which are often significantly raised (Maxwell, Burnell & Hill, 1967).

Clinically children with hypernatraemia show various central nervous system disorders ranging from irritability to convulsions and coma. There appears to be a close correlation between the recurrence of fits and the serum sodium levels. Many have shown that if the serum sodium is less than 160 mEq/l about 10% of children will convulse, but if it is above 160 mEq/l about 70% will have fits (Morris-Jones, Houston & Evans, 1967; Maxwell *et al.*, 1967).

The mortality associated with hypernatraemic dehydration and gastro-enteritis is well over 10% (Finberg & Harrison, 1955; Macaulay & Blackhall, 1961; Macaulay & Watson, 1967; Morris-Jones *et al.*, 1967; Maxwell *et al.*, 1967) (Table 3).

Normally the concentrations of potassium and sodium in ECF are 4.5 mEq/l and 140 mEq/l, respectively, in ICF they are 164 mEq/l and 10 mEq/l. To maintain osmotic equilibrium water moves freely across cell membranes and rapidly diffuses in all the compartments. Hence, if the sodium concentration in ECF rises, water will move out of brain cells in order to achieve osmotic equilibrium. The result is that brain cells shrink, oedema occurs and stretching of vessels leading to tearing and haemorrhage. Also

TABLE 3. Mortality and residual brain damage from gastro-enteritis associated with hypernatraemia

	No. of cases	Mortality (%)	Residual damage (%)
Finberg & Harrison (1955)	69	12	Not stated
Macaulay & Blackhall (1961)	30	10	11
Macaulay & Watson (1967)	47	8	
Morris-Jones <i>et al.</i> (1967)	33	15	10
Maxwell <i>et al.</i> (1967)	47	15	Not stated

the water will increase in the vascular and perivascular spaces causing oedema, rupture of small vessels and bleeding, which result in further brain damage. Direct damage may occur from the increased capillary permeability as it has been shown that a fall in CSF pressure and volume and rise in protein content occur (Finberg, 1959).

Many factors relate to hypernatraemia and these include the previous intake of fluids, the ability of kidneys to concentrate effectively, loss of water through the skin and lungs, and the temperature of the child and of the environment.

Treatment

The treatment of hypernatraemic dehydration remains unsatisfactory. There is no uniform agreement as to which solution is the best or how much sodium these solutions should contain. The majority of people agree that whatever solution is used it should be given slowly, i.e. over a 24-hr period, and a solution containing not more than 40 mEq/l of sodium is generally preferred (Sotos *et al.*, 1960; Finberg, 1967). Some have suggested that hypernatraemia may result from deficient or faulty rehydration of a child who cannot effectively control his thirst mechanism (*Lancet*, 1962; *Brit. med. J.*, 1963).

Peritoneal dialysis, which is useful in salt poisoning, has no advantage over intravenous treatment (Finberg, Kiley & Littrell, 1963), but is worth trying in desperately ill infants (Gellis & Kagan, 1968).

More attention should be paid to the blood viscosity in hypernatraemia. It is known that in peripheral circulatory insufficiency blood-flow is slow and that with slow rates viscosity rises to at least ten times the normal; as a result aggregates occur between red cells and various proteins, especially fibrinogen, leading to clotting in small vessels. Should this become extensive, bleeding occurs as clotting factors have been used up. For this reason a low molecular weight Dextran may be useful in treatment and ideally an osmometer should be available to determine osmolality periodically.

Finally, it is believed by some that damage to the brain occurs with the initial rise of serum osmolality (Macaulay & Blackhall, 1961) and that no

amount of rehydration will reverse the process, so prevention is the only successful method of treatment.

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