

# Evidence-based Pharmacy Practice (EBPP): Gastroenteritis in children

Angelene van der Westhuizen BPharm, MSc (Pharmacology)  
Department of Pharmacology, University of Pretoria

## Abstract

Diarrhoea is one of the most common causes of morbidity and mortality in children worldwide.<sup>1</sup> It causes the death of about two million children under the age of five years each year.<sup>2</sup> Acute gastroenteritis results from infection of the gastrointestinal tract most commonly with a virus, the most common being rotavirus.<sup>3</sup> *Campylobacter* and *Salmonella* are the most common bacterial pathogens; *Cryptosporidium* and *Giardia* are the most common parasites that can cause diarrhoea. Chronic diarrhoea suggests a non-infective cause such as inflammatory bowel disease or coeliac disease.

Loss of intestinal fluid caused by gastroenteritis may lead to severe dehydration, shock and death especially in children less than five years of age.<sup>4</sup> First-line treatment is with oral rehydration solution (ORS) which is often underutilised in the management of diarrhoea in children. Intravenous (IV) rehydration should be limited to patients unable to tolerate or take ORS. Pharmacological agents such as antibiotics, antimotility and antisecretory agents or absorbents should not be routinely used unless clinically indicated. Food restriction and exclusion diets are now considered outdated and feeding should continue after rehydration has been initiated. Food should not be withdrawn for longer than four to six hours after rehydration. Prevention is always better than cure and rotavirus vaccines, hand washing and water purification are all advocated in the prophylaxis of gastroenteritis and other infectious diarrhoea. Pharmacists are well positioned in the community to give the correct advice on the management of diarrhoeal diseases in children and its prevention. They can advocate the importance of using ORS and the correct usage of such and give the recommendation that a supply of ORS must be kept in the home at all times. This is so it can be initiated early in the course of diarrhoea to prevent dehydration which can be fatal especially in very young, malnourished or immunocompromised children. Referral for medical treatment or hospitalisation can also be recommended by the pharmacist upon recognising certain clinical signs and symptoms.

## Definitions

The word *diarrhoea* is derived from the Greek "diarrhoia" which means to flow through.<sup>1</sup> Clinically the term diarrhoea is used to describe the passing of loose or watery stools which is usually accompanied by an increase in stool volume and frequency.<sup>5</sup> *Acute diarrhoea* is generally defined as lasting less than two weeks.<sup>1</sup> *Chronic diarrhoea* is generally defined as lasting longer than fourteen days.<sup>5</sup> *Acute gastroenteritis* is generally defined as a decrease in the consistency of stools (loose or liquid) and/or an increase in the frequency of evacuations ( $\geq 3$  in 24 hours) with or without fever or vomiting. Acute diarrhoea usually lasts less than seven days and not longer than 14 days.<sup>6</sup>

*Dehydration* is the decrease in total body water through a reduction in both the intracellular and extracellular fluid volumes.<sup>7</sup> The clinical manifestations of dehydration are related to the depletion of the intravascular volume which may lead to irreversible shock, intractable seizures and renal failure.<sup>7</sup>

ESPGHAN stands for the *European Society for Paediatric Gastroenterology, Hepatology and Nutrition*.<sup>6</sup>

## Epidemiology

Diarrhoeal diseases are a leading cause of childhood morbidity and mortality in developing countries and an important cause of malnutrition.<sup>8</sup> In developing countries children below six months of age have a significantly higher risk for severe or persistent diarrhoea or death from diarrhoea when compared to older children.<sup>6</sup> On average, children below three years of age in developing countries have three episodes of diarrhoea each year.<sup>8</sup>

Children attending day care centres have a greater risk for developing mild and severe diarrhoea compared with children cared for at home.<sup>6</sup>

In Africa there is a close association between chronic diarrhoea and HIV.<sup>6</sup> The treatment of diarrhoea for HIV positive children is generally the same as for children without HIV.<sup>8</sup> Children who are HIV positive, are more likely to have intolerances to lactose or monosaccharides.<sup>8</sup>

## Aetiology/pathophysiology

In developed countries acute gastroenteritis is mainly caused by viruses (87%) with rotavirus being the most common.<sup>3</sup> Infection with adenovirus or norovirus can also be the cause.<sup>5</sup> In European countries there is a low prevalence of bacterial pathogens.<sup>6</sup> The most common bacterial agents in Europe are *Campylobacter* or *Salmonella*.<sup>6</sup> In developing countries, rotavirus is still a major cause of acute gastroenteritis (82% of worldwide deaths caused by rotavirus occur in these coun-

tries). Rotavirus, norovirus, astrovirus, enteroaggregative *Escherichia coli* and atypical *E. coli* are the main pathogens found in children with persistent diarrhoea.<sup>6</sup>

The parasites that most often cause diarrhoea are *Cryptosporidium* and *Giardia*.<sup>6</sup> *Entamoeba histolytica* can also cause diarrhoea.<sup>6</sup>

Chronic diarrhoea suggests a non-infective cause such as ulcerative colitis or Crohn's disease, coeliac disease or toddler's diarrhoea.<sup>5</sup>

During acute diarrhoea, children become ill and volume depleted more rapidly than adults.<sup>1</sup> Dehydration is the cause of many diarrhoeal deaths.<sup>8</sup> Children who are malnourished are also more likely to die from diarrhoea even if their dehydration is managed well.<sup>8</sup>

## Diagnosis

### Clinical signs

High fever (> 40°C), overt faecal blood, abdominal pain and central nervous system (CNS) involvement each suggests a bacterial pathogen.<sup>6</sup> Vomiting and respiratory symptoms are associated with a viral aetiology.<sup>6</sup> Symptoms of viral gastroenteritis tend to pass more quickly than bacterial gastroenteritis.<sup>5</sup> Loss of appetite, fever, vomiting and mucous in stools are frequently associated with persistent diarrhoea.<sup>6</sup>

In children with gastroenteritis, diarrhoea usually lasts five to seven days and usually stops within two weeks, and vomiting usually lasts for one to two days and usually stops within three days.<sup>9</sup>

A careful history must be taken from the patient so as to determine whether the diarrhoea could be traveller's diarrhoea, or due to swimming in contaminated water or drinking from suspicious fresh water sources.

### Degree of dehydration

The best measure of dehydration is the percentage loss of body weight.<sup>6</sup> According to the World Health Organisation (WHO) and the Centers for Disease Control (CDC), patients are classified into one of three subgroups<sup>6</sup>:

- Minimal or no dehydration (< 3% loss of body weight)
- Mild to moderate dehydration (3%–9% loss of body weight)
- Severe dehydration (> 9% loss of body weight)

It can be difficult to determine the exact degree of dehydration due to the signs being imprecise and inaccurate.<sup>6</sup> The most useful signs for predicting 5% dehydration or more are<sup>6</sup>:

- Prolonged capillary refill time
- Abnormal skin turgor
- Abnormal respiratory pattern

Inaccurate assessment of dehydration can result in a delay in administering urgent treatment or unnecessary intervention.<sup>6</sup> Refer to Table I for a guide to clinical signs of dehydration.

**Notes: In hypernatraemia the above signs underestimate the degree of dehydration. Signs of cerebral irritation occur early.**

**Shock may precede other evidence of dehydration when losses are rapid and severe.**

**Table I: Clinical signs of dehydration<sup>10</sup>**

Body weight loss %	Clinical state	Signs
< 5	Not unwell	Thirst Dry mucous membranes
5–10	Apathetic, unwell	Sunken eyes or fontanelle Reduced tissue turgor Tachypnoea Oliguria Lack of tears
> 10	Usually shocked	Peripheral circulatory failure Small pulse volume Tachycardia Diminished consciousness Hypotension

Children and infants are at an increased risk of dehydration if they are<sup>5</sup>:

- Passing six or more diarrhoeal stools in 24 hours
- Vomiting three or more times in 24 hours
- Unable to keep fluids down
- Below 12 months of age (especially < 6 months)

Infants of low birth weight who are not being breast-fed as a result of illness are at increased risk of dehydration.<sup>5,9</sup>

### Stool sample

Stool cultures are expensive and the least useful microbiological tests; so should not be routinely performed on children with acute gastroenteritis.<sup>6</sup> They should be considered in children with persistent diarrhoea when treatment with an antibiotic is being considered or when there is an outbreak or when intestinal infection must be excluded to confirm diagnosis of another aetiology such as inflammatory bowel disease.<sup>6</sup> They should be performed if septicaemia is suspected or if there is blood and or mucous in the stool or if the child is immunocompromised.<sup>8</sup>

### Bowel endoscopy

There is no indication for endoscopy in the management of acute gastroenteritis except for in a few clinical circumstances such as in inflammatory bowel disease.<sup>6</sup>

### Electrolytes

Electrolytes should be measured in children with moderate diarrhoea whose symptoms and physical examination are inconsistent with diarrhoeal disease, in severely dehydrated children and in all children starting IV (intravenous) therapy as well as during therapy.<sup>6</sup>

### Differential diagnosis

Toddler's diarrhoea, which is also known as chronic non-specific diarrhoea, is by far the most frequent cause of diarrhoea in

children between the ages of one and five in developed countries.<sup>5,11</sup> There may be frequent foul smelling stools with undigested vegetable matter present, with or without cramping. The gut transit time is short. It has been found in children on very low fat diets (to prevent coronary heart disease) and those with a very high fluid intake with fluids that have a high osmolarity (such as fruit juices).<sup>11</sup> Food intolerances need to be excluded.<sup>5</sup> Adjusting the diet by decreasing the intake of full strength juices and increasing fat intake may help. (Fat should make up 35-40% of the diet).<sup>5</sup> Full cream milk and dairy products should be given and increased fibre by way of fruit, wholemeal bread and vegetables should be encouraged to increase stool bulk.<sup>5</sup>

Vomiting with little or no diarrhoea can indicate a urinary tract infection, pneumonia, otitis media or meningitis and patients should be referred for further investigation.<sup>5</sup>

Conditions such as appendicitis, gallbladder disease, pancreatitis or diverticulitis may cause similar symptoms to gastroenteritis but should be revealed as a specific tenderness in the abdomen under physical examination.

Chronic diarrhoea is usually due to irritable bowel syndrome, malabsorptive states, such as lactose intolerance and coeliac disease, or inflammatory conditions such as ulcerative colitis and Crohn's disease.<sup>12</sup> The possibility of a colonic tumour or faecal impaction should also be investigated.<sup>12</sup>

### Clinical approaches to the child with gastroenteritis for the pharmacist

Pharmacists should advise parents and caregivers to have a supply of oral rehydration solution (ORS) in the home at all times. Rehydration should be commenced as soon as diarrhoea begins regardless of the cause.<sup>6</sup> The proper reconstitution of ORS should be advised to parents and care-givers making sure that previously boiled and cooled water is used and the correct measured volume of water is used to reconstitute powdered preparations. This can vary between brands so the instructions should always be followed. (Refer to Table II)

Pharmacists can also advise patients on common misconceptions regarding the treatment of gastroenteritis such as:

- It is necessary to restrict the child's diet, and

- That ORS will make the diarrhoea go away

They should advise parents and caregivers that the child should continue on their usual diet (avoiding carbonated soft drinks, fruit juice and liquids with a high sugar content) and to give ORS where there is an episode of diarrhoea. If the child is also vomiting then small amounts of ORS should be administered via a teaspoon or oral syringe.<sup>4</sup> Children less than two years of age should be offered a teaspoonful every one to two minutes and older children may take frequent sips directly from the cup.<sup>8</sup>

Pharmacists can give general advice about the treatment of gastroenteritis (including the use of ORS, anti-diarrhoeal, antiemetic and antimotility agents) but should refer a child for medical attention if any of the following are present:<sup>6</sup>

- Greater than eight episodes of diarrhoea per day (with high stool volumes)
- Severe underlying disease e.g. diabetes, renal impairment
- If aged less than two months of age
- Vomiting and diarrhoea lasting three days or more<sup>5</sup>
- Diarrhoea lasts more than 14 days, in the absence of vomiting<sup>5</sup>
- Vomiting lasts longer than 24 hours, in the absence of diarrhoea<sup>5</sup>
- Abdominal pain is worsening<sup>5</sup>

Hospital admission should be recommended if the child has any of the following<sup>6</sup>:

- Shock
- Severe dehydration (> 9% loss of body weight)
- Lethargy, seizures
- Intractable or bilious vomiting

Table II: Oral rehydration solutions available in South Africa<sup>13</sup>

Brand name	Formulation	Ingredients	Preparation
Elektropak	Powder for solution	NaCl 0.4 g Na-bicarb 0.5 g KCl 0.3 g Dextr Monohyd 4 g/5.48 g	Use previously boiled and cooled water Sachets: add 200 ml Bulk pack: 2 medicine measures (5.48 g) in 200 ml
Hydrol	Milk flavour powder	NaCl 2g Na citrate 2.9 g KCl 1.5 g Dextr Anhydr = (glucose 20 g) 18.185 g	Dissolve 1 sachet in 1 litre previously boiled and cooled water
Rehidrat	Powder	NaCl 0.44 g KCl 0.38 g Na bicarb 0.42 g Glucose 4.1 g Sucrose 8.1 g/14 g sachet	Dissolve contents in 250 ml previously boiled and cooled water
Scripto-lyte	Solution	KCl 335.8 mg Na citrate 469.8 mg NaCl 473.68 mg Dextr Monohydr 3.96 g/30 ml	Dilute 30 ml in 150 ml water
Sorol citrate	Powder	NaCl 1.75 g KCl 0.75 g Na citrate 1.45 g Dextr Monohyd 10 g Flavourant 0.05 g	Dissolve one 14 g sachet in 500 ml previously boiled and cooled water

- ORS treatment failure
- Inability of carers to provide adequate care at home due to logistical or social circumstances
- Suspected surgical conditions (e.g. appendicitis)

In addition to advice on how to give appropriate treatment, the pharmacist can also give the following advice on prevention of gastroenteritis:

- Hand washing is the most important method of preventing spread of the pathogens that cause gastroenteritis. Hands should be washed well with soap (liquid if possible) and warm water and carefully dried **after** going to the toilet, assisting a child with going to the toilet and washing their hands after toileting, changing nappies, handling soiled linen and clothing, and cleaning up diarrhoea and vomit and **before** preparing or serving food or drinks or smoking.<sup>5,9</sup>
- Toilets should be cleaned with a disposable cloth and disinfectant. Flush handles, door handles, taps and wash basins need to also be cleaned with disinfectant. Toilet bowls and potties should be cleaned after each use.<sup>5</sup>
- Towels should not be shared.<sup>5,9</sup>
- Linen, towels and clothing that have been soiled by diarrhoea or vomit should be washed in as hot water as possible. The washing machine should not be overfilled.<sup>5,14</sup> Make sure that the outer surfaces of the washing machine are also kept clean.
- Children should be kept out of school, preschool or day care while they have gastroenteritis and for 48 hours after the last bout of vomiting or diarrhoea.<sup>5,9,14</sup>
- Children should not use paddling or swimming pools for 14 days after the last episode of diarrhoea.<sup>5,9,14</sup>

### Available treatment options

**Rehydration** is first line therapy in the management of diarrhoea of any cause.

**Pharmacological treatment** when clinically indicated.

**Complementary and alternative medicine.**

**Nutrition and feeding** are extremely important especially if the child is malnourished.

**Prevention** is always better than cure!

### Therapeutic objectives

Acute gastroenteritis is usually self-limiting, but if it is left untreated then it may result in morbidity and mortality due to dehydration and electrolyte and acid-base disturbance.<sup>3</sup>

The aims of treating acute gastroenteritis include<sup>3</sup>:

- to prevent and treat dehydration
- to reduce the duration of diarrhoea and quantity of stool output
- to prevent vomiting
- to promote weight gain after rehydration
- to prevent persistent diarrhoea associated with lactose intolerance

The essential components of management of a child with diarrhoea due to any cause are<sup>8</sup>:

- the provision of ORT and continued feeding

- the use of antimicrobials only for those with bloody diarrhoea, severe cholera cases, or serious non-intestinal infections
- parents and caregivers should be educated about appropriate hygiene and feeding practices to prevent dehydration and reduce diarrhoeal morbidity.

### Rehydration

Oral rehydration therapy (ORT) should be given first line for the management of children with acute gastroenteritis<sup>6</sup> with mild to moderate dehydration.<sup>4</sup> ORT is used to treat dehydration due to diarrhoea independent of age, causative agent, or initial sodium values.<sup>6</sup> Advantages of using ORT over intravenous (IV) therapy include: lower cost, elimination of the need for an IV line and treatment can be continued at home.<sup>6</sup>

If it is not possible to give ORT, then enteral hydration by way of a naso-gastric tube is as effective and may be better than IV rehydration.<sup>6</sup> Enteral hydration is associated with fewer adverse effects and a shorter stay in hospital when compared with IV therapy.<sup>6</sup> Children who are able to receive ORT should not be given IV fluids.<sup>6</sup> Initiation of intravenous hydration should be undertaken if the patient is unable to adequately take enough ORT, if there is persistent vomiting, or if dehydration with ORT is failing.<sup>4</sup> In children with acute gastroenteritis and vomiting, a single dose of ondansetron will reduce vomiting and allow administration of ORT decreasing the need for intravenous hydration and hospitalisation.<sup>4</sup> Ondansetron is available as an IV injection, an oral tablet and a tablet that dissolves on the tongue before being swallowed.<sup>13</sup>

The ideal composition of ORT is still being debated. The original full-strength ORS recommended by the WHO contains Na<sup>+</sup> 90mmol/L. The current WHO recommended ORS also known as the 'reduced osmolarity solution' contains Na<sup>+</sup> 75mmol/L.<sup>6</sup> (Refer to Table III) This new ORS has been shown to reduce the need for supplemental IV fluid therapy after rehydration by 33%.<sup>8</sup> It also reduces the incidence of vomiting by 30% and stool volume by 20%.<sup>8</sup> The ORS recommended by the South African Paediatric Association (SAPA) differs from the WHO formulation in that the sodium content is lower i.e. 64 mmol/L.<sup>12</sup> The 'hypotonic osmolarity solution'

**Table III: Composition by weight and molar concentrations of reduced (low) osmolarity ORS solution<sup>8</sup>**

Reduced osmolarity ORS	grams/litre	Reduced osmolarity ORS	mmol/litre
Sodium citrate	2.6	Sodium	75
Glucose anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Glucose anhydrous	75
Trisodium citrate, dihydrate	2.9	Potassium	20
		Citrate	10
		Total osmolarity	245

Potassium prevents serious hyperkalaemia  
Citrate prevents or corrects base deficit acidosis  
Glucose promotes absorption of sodium and water in small intestine



containing Na<sup>+</sup> 60 mmol/L is recommended by ESPGHAN and is used in Europe.<sup>6</sup>

Oedematous eyelids are a sign of overhydration.<sup>8</sup> If this occurs then ORS should be stopped and breast milk and plain water should be given.<sup>8</sup> A diuretic should not be given.<sup>8</sup> When the oedema has resolved, ORT can be resumed.<sup>8</sup>

### Rice-based oral hydration solutions (ORS)

These ORS may decrease diarrhoea by adding more substrate to the gut lumen with increased osmolarity-providing additional glucose molecules for glucose mediated absorption.<sup>6</sup> It is not recommended for children with non-cholera diarrhoea and it does not result in any additional benefit compared with standard ORS.<sup>6</sup> It may reduce the 24-hour stool output in children and adults with cholera.<sup>6</sup>

### Super ORS

Substances other than rice have been added to ORS to enhance clinical efficacy.<sup>6</sup> These substances include:

- amylase-resistant starch
- guar gum
- a mixture of nondigestible carbohydrates
- probiotics
- zinc
- glutamine

There is insufficient evidence to recommend the use of any of these 'Super ORS' above the use of standard ORS in the management of diarrhoea in children.<sup>6</sup>

### Contraindications to the use of ORS

ORT should not be given in children with the following conditions:

- abdominal distension with paralytic ileus, which may be caused by opiate drugs (e.g. codeine, loperamide) and hypokalaemia<sup>8</sup>
- glucose malabsorption, indicated by a marked increase in stool output when ORS is given, failure of the signs of dehydration to improve and a large amount of glucose in the stool when ORS is given<sup>8</sup>

### Time taken for rehydration

Rehydration with ORT is usually carried out over a period of four hours.<sup>9</sup> Rehydration with IV fluid therapy has traditionally been undertaken over 24 hours.<sup>9</sup> The WHO recommends that IV rehydration should be completed in three to six hours. This would allow oral treatment to be started earlier and would also shorten the length of hospital stay.<sup>9</sup>

### How much ORS is required?

The amount of fluid required for oral rehydration depends on the severity of dehydration. Children below five years of age should receive small sips of ORS at a rate of 50 ml/kg body weight over the first four hours.<sup>5,9</sup> ORS should be used instead of the child's usual drinks or feeds for this period but where the child is breastfed this should be continued.<sup>5,9</sup> Stopping breastfeeding may be detrimental to both mother and baby by caus-

ing discomfort (and possible mastitis) and permanent cessation of breastfeeding.<sup>5</sup> Children over the age of five years should receive 200 ml ORS after each loose stool as well as encouraging them to maintain their usual fluid intake.<sup>5,9</sup>

### Non-physiological fluids

Drinks commonly found in the household such as tea, fruit juice, sports drinks, and soft drinks (even those allowed to go 'flat' i.e. degassed) have too little sodium and nearly all (except unsweetened tea) have a much higher carbohydrate and osmolality content than recommended.<sup>4</sup> These drinks should not be used in children with diarrhoea as they may increase the incidence of hyponatraemia and actually increase diarrhoeal output.<sup>4</sup> Severe hyponatraemia can be associated with lethargy and less often seizures.<sup>8</sup>

Coffee and some medicinal teas or infusions should also be avoided due to their stimulant, diuretic or purgative effects.<sup>8</sup>

### Chicken soup

Chicken soup or broth has an excess sodium concentration compared with glucose and will also increase diarrhoeal losses. Water will be drawn from the child's tissues and blood into the bowel, causing the concentration of sodium in extra-cellular fluid to rise. The water then remains in the bowel causing osmotic diarrhoea.<sup>4,8</sup> Hypernatraemia may also result from the use of fluids with a high sodium concentration.<sup>4</sup>

### Homemade sugar and salt solutions

Major errors can occur if a homemade solution using sugar and salt is administered.<sup>6</sup> The recipe is often forgotten, the ingredients may not be available or too little may be given.<sup>8</sup> Standard commercial ORS (including pre-packaged solutions) are recommended for use at home.<sup>6</sup> The South African Essential Drugs List states that a home made sugar and salt solution may be used if an oral rehydration solution is not available.<sup>15</sup> (Refer to Table IV)

### Pharmacological treatment

Paracetamol is the drug of choice for pain or fever since ibuprofen may cause gastrointestinal side effects.<sup>5</sup> Suppositories may also be an option for children who cannot tolerate oral therapy.<sup>5</sup>

Table IV: Homemade sugar and salt solution<sup>15</sup>

#### HOMEMADE SUGAR AND SALT SOLUTION (SSS)

**children:** ½ level medicine measure of table salt

**adults:** 1 level medicine measure of table salt

**and**

8 level medicine measures of sugar (no more)

dissolved in 1 litre of boiled (if possible) then cooled water

1 level medicine measure = approximately 1 level teaspoon

### Antiemetics

Gastroenteritis triggers vomiting by the release of neurotransmitters either by direct stimulation from abdominal distension or by viral or bacterial toxins.<sup>16</sup> The treatment of vomiting in children with acute gastroenteritis with antiemetics is controversial.<sup>6</sup> Antiemetics are not recommended to be routinely used in the treatment of children with acute gastroenteritis.<sup>6</sup> They may have a place in persistent or severe vomiting.<sup>6,9</sup> There is some evidence that suggests that antiemetics such as ondansetron (a 5HT<sub>3</sub> antagonist) and metoclopramide (a dopamine antagonist) when compared to placebo reduce the number of vomiting episodes in children with acute gastroenteritis.<sup>6</sup> The increase in diarrhoea which has been reported when using these antiemetics could be a result of the retention of fluids and toxins that would have otherwise been removed from the body by vomiting.<sup>6</sup> The cost of using ondansetron and the troublesome side effects associated with the use of metoclopramide such as sedation and extrapyramidal reactions are inhibitory factors to their use.<sup>6</sup> Ondansetron has been used extensively in the management of chemotherapy-induced vomiting in children.<sup>17</sup>

### Antimotility agents

These include loperamide, diphenoxylate with atropine, codeine and morphine.<sup>8</sup> These opiate or opiate-like drugs may reduce the frequency of stools in adults but they do not reduce the volume of stool in children to any great extent.<sup>8</sup> They may cause severe paralytic ileus which can be fatal and they may also prolong infection by delaying elimination of the organisms causing the diarrhoea.<sup>8</sup> Sedation may also occur at therapeutic doses and fatal CNS toxicity has been reported with some substances.<sup>8</sup> These agents are not recommended for the management of diarrhoea in infants and children.<sup>8</sup>

Loperamide is an opioid receptor agonist that decreases intestinal lumen motility.<sup>6</sup> In children who are less than three years of age, or who are malnourished, moderately or severely hydrated, systemically ill or with bloody diarrhoea should not be given loperamide as the risk of adverse effects outweigh the benefits.<sup>6</sup> In children older than three years of age with no or minimal dehydration, loperamide may be useful along with ORT.<sup>6</sup> (Refer to Table V)

### Adsorbents

These include kaolin, attapulgite, activated charcoal and cholestyramine.<sup>8</sup> These drugs are included in 'antidiarrhoeal' preparations on the basis that they have the ability to bind and inactivate bacterial toxins or other substances that cause diarrhoea and the 'claim' that they protect the intestinal mucosa.<sup>8</sup> There is insufficient evidence to recommend any of these products in the treatment of acute gastroenteritis.<sup>6</sup> (Refer to Table V)

### Antisecretory agents

**Bismuth subsalicylate** is not routinely used in the treatment of acute gastroenteritis in children.<sup>6</sup> Its mechanism of action is thought to be due to antisecretory and antimicrobial properties.<sup>6</sup> Side effects include temporary darkening of the stool and

Table V: Antidiarrhoeal preparations marketed in South Africa

Brand name	Formulation	Ingredients
Adco-Biskapect	Suspension	Kaolin light 8 g Apple pectin 250 mg Bismuth carbonate 200 mg/30 ml
Adco-Loperamide	Tabts	Loperamide 2 mg
	Syrup	Loperamide 1 mg/5 ml
Betapect	Suspension	Light kaolin 6 g Apple pectin 450 mg/30 ml
Betaperamide	Tabts	Loperamide 2 mg
Chloropect	Suspension	Kaolin 3 g Bismuth carb 600 mg Pectin 45 mg Chlorodyne 0.5 mg/15 ml
Cipla-loperamide	Tabts	Loperamide 2 mg
Enterodyne	Suspension	Bi-carbon 200 mg Ca-carb 113.33 mg Chlorof Et morphine tinct. 0.2 ml Nutmeg oil 0.002 ml Clove oil 0.0027 ml Extr Pro Cardemon tinct.0.02 ml Catechu tinct 0.2 ml Cinnamon conc Water 0.1 ml Cinnamon oil 0.00067 ml Aromat Ammon Liq. 0.2 ml/5 ml
Electrolyte	Suspension	Kaolin 600 mg Pectin 120 mg K chlor 41.4 mg Na chlor 78.9 mg Na lact 86.4 mg/30 ml
Gastron	Tabts	Loperamide 2 mg
	Syrup	Loperamide 1 mg/5 ml
Gastropect	Suspension	Kaolin 1 g Pectin 0.05 g/5 ml
Imodium	Caps	Loperamide 2 mg
	Tabts	Loperamide 2 mg
	Melt tabs	Loperamide 2 mg
	Syrup	Loperamide 0.2 mg/ml
Imodium Plus	Chew tabs	Loperamide 2 mg Simethicone 125 mg
Kantrexil	Suspension	Kanamyc. Sulph 100 mg Aminopentamide 0.033 mg Pectin 25 mg Bism. Subcarbon 250 mg Act Attapulgitte 500 mg/5 ml
	Tabts	Kanamyc. Sulph 100 mg Aminopentamide 0.033 mg Pectin 25 mg Bism Subcarbon 250 mg Act Attapulgitte 500 mg
Kaostatex	Susp	Kaolin 6 g Pectin 0.12 g Na-lactate 0.0864 g KCl 0.0414 g NaCl 0.0789 g/30 ml
Lomotil	Tabts	Diphenoxylate 2.5 mg Atropine 0.025 mg
Loperastat	Syrup	Loperamide 1 mg/5 ml
Norimode	Tabts	Loperamide 2 mg
Pectin-K	Suspension	Kaolin 3 g Apple pectin 0.220 g/15 ml
Pectrolyte	Suspension	Chlorodyne 2 ml Kaolin 20 g Pectin 0.4 g Na-lact 0.29 g KCl 0.14 g NaCl 0.26 g/100 ml
Prodium	Tabts	Loperamide 2 mg

tongue and it has also been reported to cause salicylate toxicity in children.<sup>6</sup> It is not suitable for the use in children under 16 due to a risk of Reye's syndrome.<sup>5</sup>

**Racecadotril (acetorphan)** is an antisecretory drug that exerts its antidiarrhoeal effects by inhibiting intestinal enkephalinase which prevents the breakdown of endogenous opioids (enkephalins) in the gastrointestinal tract and decreases secretion of water and electrolytes into the gut.<sup>6</sup> It has been shown, when taken as an adjunct to ORT, to reduce stool output, duration of diarrhoea and intake of ORS when taken by children with severe watery diarrhoea.<sup>6</sup> It may be considered in the management of acute gastroenteritis in children but more trials are needed to determine safety.<sup>6</sup>

**Probiotics** are living organisms; either bacteria or yeasts that are taken orally to help restore the microbial balance in the intestinal tract.<sup>18</sup> They are thought to be effective in the treatment and prevention of diarrhoea by modifying the composition of the colonic microflora and act against enteric pathogens.<sup>6</sup> They have been found to have a significant statistical effect and moderate clinical benefit in the treatment of acute watery diarrhoea (primarily due to rotavirus) mainly in infants and young children.<sup>6</sup> Only those probiotics with proven efficacy namely *Lactobacillus GG* and *Saccharomyces boulardii* in appropriate doses for children can be recommended as an adjunct in the management of diarrhoea in children.<sup>6</sup>

**Prebiotics** are defined as non-digestible food that beneficially affect the host by selectively stimulating the growth or activity of one or a limited number of bacteria in the colon thereby improving the health of the host.<sup>6</sup> They are not recommended in the management of acute gastroenteritis due to the limited data available.<sup>6</sup>

### 'Bowel cocktail'

In a small percentage of children (the very young or malnourished), severe dehydrating diarrhoea may persist for more than seven days.<sup>10</sup> There is a risk of complications from dehydration and continued nutrient loss.<sup>10</sup> The treatment recommended is (otherwise known as the 'Bowel cocktail'):

- Oral kanamycin, 100 mg/kg/24 hours, 4 hourly for three days (use 1 g/3 ml IMI ampoule and add it to 37 ml water – 1 ml of this mix = 25 mg) and oral cholestyramine 1 g 6 hourly for five days. (A mild metabolic acidosis often occurs while on cholestyramine)<sup>10</sup>

### Combination preparations

There are products available which combine adsorbents, antimicrobials, antimotility drugs and other agents. (Refer to Table V). There is little published information supporting the use of these agents.<sup>8</sup> They are not recommended for the management of acute diarrhoea in children as ORT is considered first-line therapy.<sup>8</sup>

### Micronutrients

**Zinc** deficiency is common in young children in developing countries. It is associated with impaired water and electrolyte absorption, decreased brush border enzymes and impaired cellular and

humoral immunity.<sup>6</sup> In developing countries, clinical trials have shown that zinc supplementation reduces the duration and severity of acute diarrhoea when given with ORS.<sup>6</sup> UNICEF and WHO recommend zinc supplementation; 10mg for infants less than six months of age and 20 mg in those older than six months for 10 to 14 days as a universal treatment for children with diarrhoea.<sup>6,8</sup>

**Folic acid** is not recommended in the treatment of diarrhoea.<sup>6</sup>

**Glutamine** is an important fuel for rapidly dividing cells such as enterocytes and lymphocytes.<sup>6</sup> Supplementation of glutamine in catabolic states preserves intestinal mucosal structure and function, decreases bacterial translocation and supports normal immunological response.<sup>6</sup> It has been proposed to decrease the duration of diarrhoea but it is not recommended in guidelines for use in the management of acute gastroenteritis in children.<sup>6</sup>

### Antimicrobial therapy

Antibiotics should not be used routinely. It is not possible to distinguish between episodes of diarrhoea that will respond (e.g. enterotoxigenic *E. coli*) from those that will be unresponsive to antibiotics (e.g. rotavirus).<sup>8</sup> The use of antibiotics also increases the risk of adverse drug reactions and enhances the development of resistant bacteria.<sup>8</sup> They may also be a further cause of diarrhoea.<sup>5</sup> Acute gastroenteritis is usually self-limiting and even if it is caused by bacteria, clinical recovery frequently occurs within a few days (even without antibiotics) and the causative organism is usually excreted in a few days or weeks.<sup>6</sup>

Antibiotics for acute bacterial gastroenteritis are only indicated for specific pathogens in defined clinical settings.<sup>8</sup>

Antibiotics should be given to all children<sup>9</sup>:

- with suspected or confirmed septicaemia
- with extra-intestinal spread of bacterial infection
- younger than six months with salmonella gastroenteritis
- who are malnourished or immunocompromised with salmonella gastroenteritis
- with *Clostridium difficile*-associated pseudomembranous enterocolitis, giardiasis, dysenteric shigellosis, dysenteric amoebiasis or cholera

### Complementary and alternative medicines

#### Homoeopathy

The role of homoeopathic remedies in the treatment of acute childhood diarrhoea is still controversial. It is widely used but there is insufficient evidence to recommend its use for the treatment of diarrhoea in children.<sup>6</sup>

#### Herbal medicines

There is insufficient evidence to recommend use of herbal medicines in the treatment of diarrhoea in children.<sup>6</sup>

#### Nutrition and feeding

It has been shown in randomised controlled trials (RCTs) that

early feeding improves weight gain without increasing the duration of vomiting or diarrhoea or the duration of hospital stay.<sup>6</sup> It was previously thought that food restriction (including exclusion diets and the exclusive intake of clear fluids) and bowel rest would decrease stool output, but this concept of 'gut-rest' is now outdated.<sup>6</sup> Early nutritional intervention is crucial to avoid poor outcomes such as malnutrition, persistent diarrhoea and death.<sup>6</sup> Children who are not dehydrated should continue to eat. Food should not be withdrawn for longer than four to six hours after the onset of rehydration.<sup>6</sup> Food should be offered to the child every three to four hours (six times a day).<sup>8</sup> Frequent small feedings are tolerated better than less frequent, large ones.<sup>8</sup>

### **BRAT diet**

The BRAT diet which consists of bread, rice (or rice cereal), apple (or apple sauce) and toast (or tea) has not been studied and is not recommended in any guidelines for the treatment of gastroenteritis in children.<sup>6</sup> It is commonly used and recommended in many childcare texts for the treatment of acute diarrhoea. The BRAT diet is low in energy density, protein and fat.<sup>6</sup> Some data does exist in the evaluation of the role of bananas and rice in the treatment of diarrhoea.<sup>19</sup> Banana is rich in amylase-resistant starch, which has been postulated to protect the gastrointestinal mucosa in animals and improve symptoms of non-ulcer dyspepsia and peptic ulcer in humans.<sup>19</sup> There is some in vitro data to suggest that rice may possess anti-secretory properties.<sup>19</sup> Rice-based oral rehydration solutions (ORS) have also been shown to reduce the volume of stools and duration of diarrhoea in patients with cholera.<sup>19</sup>

### **Breastfeeding**

Breastfeeding should be continued during acute gastroenteritis. It has been shown to decrease the duration of diarrhoea in rotavirus gastroenteritis.<sup>6</sup>

### **Dilution of formula**

Formula dilution and gradual reintroduction of feeding is not needed and can actually result in weight loss.<sup>6</sup>

### **Lactose-free formula**

Most children with acute gastroenteritis can safely continue to receive lactose-containing milk formula as it has not been shown to have any effect on treatment.<sup>6</sup> No advantage has been shown by switching to a soy-based formula.<sup>6</sup>

### **Prevention of gastroenteritis**

Asymptomatic infections probably play an important role in the spread of infection.<sup>17</sup> Virus excretion can begin before symptoms occur and persist after symptoms resolve which makes it difficult to identify the source of exposure.<sup>17</sup>

### **Vaccines**

The WHO recommends that the rotavirus vaccine should be administered in all national immunisation programmes.<sup>20</sup> In South Africa Rotarix<sup>®</sup> which is a live oral monovalent human rotavirus (RV1) vaccine is available. The vaccination is for oral administration only. The course consists of two doses the first one being between the ages of six and 14 weeks and the second dose must be given between the ages of 14 and 24 weeks.<sup>13</sup> The interval between doses must not be less than four weeks.<sup>13</sup> A repeat dose is not indicated if the infant spits out, regurgitates or vomits after administration.<sup>13</sup> The virus is shed in the stools so good hygiene measures are required when changing nappies.<sup>13</sup>

Measles vaccination has also been shown to substantially reduce the incidence and severity of diarrhoeal diseases.<sup>8</sup>

### **Avoiding contact with infected individuals**

There is an increased risk of children contracting rotavirus in day care centres and whilst staying in hospital but often these places are unavoidable.<sup>21</sup> Avoiding crowded spaces such as markets, theatres or shopping centres may help in preventing infection in those that have a weak resistance.

### **Passive prevention or therapy**

Some trials have demonstrated that passive immunisation with orally administered antibodies were effective in preventing rotavirus gastroenteritis but only during the treatment phase.<sup>21</sup> They did not offer long-term protection.<sup>21</sup> This may be of benefit in certain groups such as premature babies in hospital but the use of these antibodies is limited because there is no commercially available product for oral administration.<sup>21</sup>

### **Probiotics**

Trials have not given enough evidence to recommend probiotics for long term use for the prevention of gastroenteritis in infants and young children.<sup>21</sup> There is evidence that they have an effect for short-term use in hospital but this is only during the supplementation phase and no evidence is seen for continued protection after this.<sup>21</sup> Cost is also an implication in advocating their long term use without sufficient evidence.

### **Breastfeeding**

Early breastfeeding has been shown to give some protection against diarrhoea caused by all pathogenic agents.<sup>21</sup> However, breastfeeding has not been shown conclusively in trials to prevent rotavirus infections but has been seen to postpone infection rather than prevent it.<sup>21</sup>

### **Chemoprophylaxis**

Antibiotic therapy in the prevention of gastroenteritis in children is not recommended especially since the main causes are viral



in origin. Antibiotics may have a limited role in the prevention of traveller's diarrhoea in adults.<sup>22</sup>

### Hand washing

Rotavirus can survive on human hands for at least four hours, and for up to 10 days on dry nonporous surfaces in a low-humidity environment.<sup>21</sup> Certain disinfectants can minimise the spread of rotavirus such as hypochlorite or sodium dichloroisocyanurate.<sup>21</sup> Rotavirus is also inactivated by 70% ethanol solution.<sup>21</sup> Alcohol-based hand-hygiene products eliminate rotavirus from the skin and are more effective than medicated and non-medicated soaps in reducing the titres of rotavirus found on the fingertips.<sup>21</sup>

### Water purification

In developing countries disinfection of water from unsafe water sources is an important means of preventing diarrhoea.<sup>17</sup> Methods of disinfection include<sup>17</sup>:

- boiling for 10 minutes
- addition of chlorine containing tablets and solutions
- **Solar disinfection:** using clear one litre polyethylene terephthalate bottles that have the bottom one half painted black. The bottles are filled with water and placed in a location that receives maximum sunlight for at least 24 hours.

### Evidence-based recommendations

The following evidence-based recommendations are based on the clinical guidelines according to:

- *ESPGHAN-ESPID European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases Evidence-based Guidelines for the Management of Acute Gastroenteritis in Children in Europe*<sup>6</sup>
- *NICE clinical guideline 84: Diarrhoea and vomiting in children*<sup>9</sup>
- *World Health Organisation*<sup>8</sup>

1. Rehydration is the key treatment with ORT being first line in the management of diarrhoea in infants and children. Reduced or low osmolarity ORS should be used and it should be offered as much as it is desired by the child. Breastfeeding should be continued and fruit juices and carbonated drinks should be avoided.<sup>6,8,9</sup>
2. Hospitalisation of children with diarrhoea should be reserved for those who require procedures that can only be carried out in hospital such as IV rehydration.<sup>6</sup>
3. Regular feeding should not be interrupted and should be carried on after initial rehydration. Regular milk formulas which contain lactose are appropriate in the majority of cases and do not need to be substituted with lactose-free or soy-based formulas.<sup>6,9</sup>
4. Drugs such as antimotility agents, antisecretory agents, adsorbents are generally not necessary. Antiemetics such as ondansetron may be beneficial in severe or persistent vomiting to allow ORT to be given.<sup>4</sup> Specific probiotics may reduce the duration and intensity of symptoms.<sup>6</sup> Drugs such as racecadotril may have a role in the management of diarrhoea in children but further investigations regarding safety are required.<sup>6</sup>
5. Antibiotic therapy is not needed in most cases of acute

gastroenteritis. They may induce a carrier state in the case of *Salmonella* infection. It is effective mainly in *Shigellosis* and in the early stages of *Campylobacter*.<sup>6</sup> It is indicated in suspected or confirmed septicaemia as well as extra-intestinal spread of bacterial infection.<sup>9</sup>

6. Prevention with antirotavirus vaccination is recommended for all children<sup>6</sup> and is strongly recommended in countries where diarrhoeal diseases account for more than 10% of deaths in children less than 5 years of age.<sup>8,20</sup>

### Conclusion

ORT is the first choice treatment in a child with acute gastroenteritis. Non-physiological fluids such as soft drinks should be avoided for rehydration. If the child is vomiting, a single dose of ondansetron may be beneficial in reducing vomiting and allowing ORT to be administered. The use of restrictive or exclusion diets is outdated and the feeding of an age-appropriate diet once rehydration has been instituted is recommended. Breastfeeding and full-strength formula feeding should be continued. Antimotility and anti-diarrhoeal agents should be avoided in children with acute diarrhoea. Antibiotics should only be used when clinically indicated and should definitely not be prescribed routinely. □

### References:

1. UpToDate. Version 17.3 Pathogenesis of acute diarrhea in children. Author Mark A Gilger, Section Editor William J Klish, Deputy Editor Alston G Hopkin. Last updated June 5 2007.
2. World Health Organization. Children's environmental health. <http://www.who.int/ceh/en/> (last accessed 26 May 2010)
3. Dalby-Payne J, Elliott E. Gastroenteritis in children. *BMJ Clinical Evidence* 2009; 09: 314. Available at <http://clinicalevidence.bmj.com>
4. UpToDate. Version 17.3 Oral rehydration therapy. Authors Bonita Stanton, Joshua B Evans, Bobby Batra. Section Editor Tej K Mattoo, Anne M Stack, Deputy Editor Melanie S Kim. Last updated 8 July 2009.
5. Marshall S. Diarrhoea and vomiting in a child. *PJ Online* March 2010
6. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases Evidence-based Guidelines for the management of acute gastroenteritis in children in Europe. *J Pediatr Gastroenterol Nutr* 2008; 46 Suppl 2:S81.
7. Alhashimi D, Al-Hashimi H, Fedorowicz Z. Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents. *Cochrane Database of Systematic Reviews* 2009, Issue 2.
8. World Health Organisation. The Treatment of diarrhoea: a manual for physicians and other senior health workers. 4<sup>th</sup> rev © World Health Organisation 2005.
9. National Collaborating Centre for Women's and Children's Health. 2009. Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years (full NICE guideline). Royal College of Obstetricians and Gynaecologists. Available at [www.nice.org.uk](http://www.nice.org.uk).
10. Harrison V ed. *The Oxford handbook of Paediatrics*. Oxford University press, 6<sup>th</sup> edition 2004 (latest impression 2007)
11. Hoekstra SH. Toddler diarrhoea: more a nutritional disorder than a disease. *Arch Dis Child* 1998; 79:2-5.
12. South African Medicines Formulary (SAMF). 8<sup>th</sup> Edition. Edited by CJ Gibbon. Claremont: Health and Medical Publishing Group of the South African Medical Association
13. MIMS Volume 50 Number 2 February 2010.
14. Health protection Agency. Rotavirus. Available at [www.hpa.org.uk](http://www.hpa.org.uk) (accessed on 12 March 2010)
15. South African Standard Treatment Guidelines and Essential Drugs List for Primary Health Care 2003 Edition.
16. Levine DA. Antiemetics for acute gastroenteritis in children. *Current Opinion in Pediatrics* 2009, 21: 294-298.
17. UpToDate Prevention and Treatment of viral gastroenteritis in children. Author David O Matson, Section Editor Morren S Edwards, Deputy Editor Mary M Torchis. Last updated 9 July 2009.
18. McFarland LV. Diarrhoea associated with antibiotic use. *BMJ* 2007; 335: 54-5.
19. Duro DS, Duggan C. The BRAT Diet for Acute Diarrhea in Children: Should it be used? *Practical Gastroenterology* June 2007 60, 65-68.
20. World Health Organisation Weekly epidemiological record 18 December 2009, 84<sup>th</sup> year No 51-52, 2009, 84, 533-540 Rotavirus vaccines: an update [http://www.who.int/wer/2009/wer\\_84\\_51\\_52.pdf](http://www.who.int/wer/2009/wer_84_51_52.pdf)
21. Mrukowicz J, Szajewska H, Vesikari T. Options for the Prevention of Rotavirus Disease Other Than Vaccination. *Journal of Pediatric Gastroenterology and Nutrition*. 46: S32-S37, 2008.
22. Nathan A. Treating acute diarrhoea in adults. *The Pharmaceutical Journal* August 2008 p217.