Causes and management of diarrhoea in children in a clinical setting

Diarrhoeal disease and its complications remain a major cause of morbidity and mortality in children, especially in developing countries. It is the second most common cause of death in children under five years of age worldwide and is responsible for 2.4 million deaths each year.1 The Medical Research Council Burden of Disease report indicates that in South Africa, it is the third biggest killer of children under five, responsible for over 10 000 deaths annually (10.2% of total deaths).2 There are approximately 1.5 billion episodes of diarrhoea per year so knowledge of aetiology and appropriate management is essential for all health care practitioners. The most recent advances in the area of acute diarrhoeal disease include zinc supplementation, reduced osmolarity oral rehydration solution (ORS) and rotavirus vaccination.

Definitions
Diarrhoea is characterised by an increased frequency and volume, and decreased consistency of stool from the norm. It must be remembered that frequency of passing stool varies with age and is higher in infants.4 Dysentery is defined as the passage of blood and mucous in diarrhoeal stools. Persistent diarrhoea occurs when the duration of symptoms exceeds seven days and chronic diarrhoea when it lasts more than 14 days.4,5

Causes of diarrhoea
The commonest causes of infectious diarrhoea are shown in Table I. The incidence of these pathogens varies between developed and developing world settings. In developed countries about 70% of
diarrhoea cases are of viral (40% rotavirus), 10–20% of bacterial and < 10% of protozoal origin.3,5,6,7 In developing countries 50–60% of cases are of bacterial (Enteropathogenic E. Coli 25%, Campylobacter jejuni 10–18%, Shigella spp and Salmonella spp 5% each), 35% of viral (15–25% rotavirus) origin, and in many the cause is unidentified or mixed.3,5,6,7,8 In developing countries the prevalence of diarrhoea also varies widely by country. For instance, there are many more

Table I: Common pathogens causing childhood diarrhoea

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Bacteria</th>
<th>Protozoa</th>
<th>Unidentified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus</td>
<td>Campylobacter jejuni</td>
<td>Cryptosporidium parvum</td>
<td>Mixed infections</td>
</tr>
<tr>
<td>Norovirus</td>
<td>Non-typhoid Salmonella spp</td>
<td>Giardia lamblia</td>
<td></td>
</tr>
<tr>
<td>Enteric adenovirus</td>
<td>Enteropathogenic E. Coli</td>
<td>Entamoeba histolytica</td>
<td></td>
</tr>
<tr>
<td>Other: caliciviruses, astroviruses, enteroviruses</td>
<td>Shigella spp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella typhi</td>
<td>Salmonella spp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shiga-toxin producing E. Coli (ETEC)</td>
<td>Vibrio cholera</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S Afr J Clin Nutr 2010;23(1) Supplement:S42-S46
cases of cholera in India and South East Asia, whilst in Africa rotavirus has been shown to be the causative agent in 28-49% of cases in Ethiopia but only 14 % of cases in Tanzania. The incidence of rotavirus diarrhoea varies widely even within each country with studies from South Africa indicating a range of 14–34% of cases in Johannesberg, 20–55% in Durban and 18% in Cape Town. There is also a marked seasonality that is associated with the incidence of infectious childhood diarrhoea. This is best reflected in rotavirus infection, classically described in dry winter months in temperate climates. This is documented in studies from Durban and Johannesberg, but not in the summer peak of diarrhoea in Cape Town and other developing countries. This pattern is most likely due to the Mediterranean climate in Cape Town with wet winters and hot dry summers.

Bacterial pathogens like Campylobacter jejuni and Salmonella spp invade the lining of the small and large intestine and trigger inflammation so children tend to have higher fevers and a dysentery-like picture. These organisms can spread systemically especially in young children. Shigella dysenteriae and ETEC infections can also be complicated by the haemolytic uraemic syndrome.

Certain organisms are more closely associated with chronic diarrhoea, and these include Giardia lamblia and Cryptosporidium parvum.

Rotavirus diarrhoea is the most important aetiological agent worldwide implicated in severe dehydrating diarrhoea requiring hospitalisation. The annual burden of disease is estimated as more than 110 million diarrhoeal episodes, 25 million clinic visits, 2 million hospitalisations and 600 000 childhood deaths per year. More than 90% of rotavirus deaths occur in developing countries. Improvements in water supply and sanitation have been shown to reduce the transmission of enteric bacteria and parasites, but do not appear to have a major impact on rotavirus diarrhoea, so the introduction of a vaccine shows the greatest promise in reducing the burden of disease. The peak age of infection is quoted as six months to two years. In developing countries, however, children often present younger, with the median age of hospitalisation of all-cause diarrhoea being nine months when compared with that of six months in rotavirus diarrhoea, with 97% of cases occurring in children younger than 18 months. More than 8%, of patients with rotavirus diarrhoea were < 6 months of age. A small infectious dose is required (< 100 virus particles) for the virus to enter the small intestinal epithelium where it elaborates a potent enterotoxin which damages epithelial cells causing blunted villi and massive viral shedding. This results in a profuse watery non-inflammatory diarrhoea, rapid dehydration and electrolyte disturbances. It is often associated with initial fever and vomiting for two to three days, and the course of the infection lasts two to seven days.

The recent outbreak of cholera in Zimbabwe with rice-water stools and rapid dehydration, has highlighted the risks of the spread and severity of illness. A travel history is important when considering the aetiology of diarrhoea as management may differ, including the need for isolation and notification. When a child presents with diarrhoea, especially in chronic non-dehydrating diarrhoea, noninfectious causes must also always be considered in the differential diagnosis (Table II).

### Table II: Differential diagnosis in children presenting with diarrhoea

- Infections outside the GIT, like meningitis and urinary tract infection
- Surgical conditions like intussusception and malrotation, especially if prominent/bile-stained vomiting is present
- Immunodeficiency e.g. HIV disease
- Spurious diarrhoea – faecal impaction with overflow
- Side-effects of medications e.g. antibiotics
- Primary gastrointestinal tract pathology e.g. cystic fibrosis, inflammatory bowel disease, coeliac disease

**GIT** = Gastrointestinal tract

The aetiological approach in nosocomial diarrhoea will also differ as one needs to consider Clostridium difficile infection. This is a spore forming anaerobe, and patients colonised with a toxin producing strain can develop disease especially when treated with antibiotics. Rotavirus and astrovirus are other important causes of nosocomial diarrhoea outbreaks through the faecal-oral transmission and contamination of environmental surfaces.

Although it is important to recognise the specific microbiological causation of diarrhoea in order to target appropriate treatment, the broader preventive aspects put forward by the WHO indicate the fundamental contributors to the massive burden of disease in developing countries. In a global setting where up to a quarter of children are malnourished, over a billion people do not have access to safe water and over two billion have inadequate sanitation, together with a low breastfeeding prevalence, social disruption from war and natural disasters as well as poor maternal education, the vicious cycle of infection, diarrhoea and malnutrition is perpetuated.

### Management

Management of a child presenting with acute diarrhoea must include a thorough history and examination with evaluation of hydration status, nutritional status and comprehensive clinical evaluation for any complications or associated illnesses. A decision then needs to be made on method of rehydration, feeding, and if there are indications for any specialised investigations. Pharmacologic therapy is usually limited to micronutrient support.

### Clinical evaluation

After obtaining a history of diarrhoea with or without vomiting, the first priority in initial evaluation is to identify and treat shock. The clinical features and initial management of shock are shown in Table III. These children require rapid venous access, and after the initial fluid bolus, a 10 ml/kg bolus should be repeated if signs of shock persist. Such children may also need additional general supportive care including oxygen and must be continuously and very intensively monitored.
Invited communication: Causes and management of diarrhoea in children in a clinical setting

Table IV: Indications for hospitalisation

<table>
<thead>
<tr>
<th>No visible dehydration</th>
<th>Some dehydration</th>
<th>Severe dehydration</th>
<th>Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Features:</td>
<td>2 or more signs:</td>
<td>2 or more signs:</td>
<td>Signs of:</td>
</tr>
<tr>
<td>• alert with normal eyes</td>
<td>• restless and irritable</td>
<td>• lethargic or sleepy</td>
<td>• depressed level of consciousness or weakness</td>
</tr>
<tr>
<td>• not thirsty</td>
<td>• thirsty and drinks eagerly</td>
<td>• deeply sunken eyes and fontanelle</td>
<td>• weak or absent peripheral pulses</td>
</tr>
<tr>
<td>• normal skin pinch</td>
<td>• skin pinch returns slowly</td>
<td>• very slow skin pinch</td>
<td>• a prolonged capillary refill time of &gt; 3 seconds</td>
</tr>
</tbody>
</table>

Initial fluid management

<table>
<thead>
<tr>
<th>No visible dehydration</th>
<th>Some dehydration</th>
<th>Severe dehydration</th>
<th>Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial fluid management</td>
<td>• ORS orally or nasogastrically</td>
<td>• Intravenous rehydration with ½ Darrow Dextrose</td>
<td>• Rapid venous access, either an intravenous or intraosseous line</td>
</tr>
<tr>
<td>• treated at home with additional fluids</td>
<td>• Continue breastfeeding or formula milk within 4 hours</td>
<td>• Continue breastfeeding or formula milk within 4 hours</td>
<td>• Bolus of 20 ml/kg of Ringers lactate or Normal Saline.</td>
</tr>
<tr>
<td>• Other supportive measures</td>
<td>• Replace ongoing losses with ORS</td>
<td>• Replace ongoing losses with ORS</td>
<td></td>
</tr>
</tbody>
</table>

Further history should include information on the duration and frequency of diarrhoea, presence of blood or mucous in the stool, vomiting and whether it is bile stained, use and mixing of home rehydration fluids, as well as other usual aspects of the paediatric history including past illnesses, immunisation status, feeding, medications and related side effects. The Integrated Management of Childhood Illness (IMCI) has simplified the classification dehydration into i) no signs of dehydration, ii) some dehydration (correlating with the old classification of 5% dehydration), and iii) severe dehydration (correlating with the old classification of 10% dehydration)\(^2\) (Table III). The indications for hospitalising a child with diarrhoea are shown in table IV.

Table V: Indications for intravenous fluids

<table>
<thead>
<tr>
<th>No visible dehydration</th>
<th>Some dehydration</th>
<th>Severe dehydration</th>
<th>Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Shock</td>
<td>• Severe dehydration, especially if depressed level of consciousness</td>
<td>• Intravenous rehydration</td>
<td>• Rapid venous access, either an intravenous or intraosseous line</td>
</tr>
<tr>
<td>• Paralytic ileus</td>
<td>• Moderate dehydration with vomiting all fluid</td>
<td>• Continue breastfeeding or formula milk within 4 hours</td>
<td>• Bolus of 20 ml/kg of Ringers lactate or Normal Saline.</td>
</tr>
<tr>
<td>• Children with profuse watery stools unable to keep up with fluid losses</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Intravenous fluids should be avoided in children who are malnourished or with underlying cardiac or respiratory disease including associated pneumonia.

The WHO, European Society of Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) and American Academy of Paediatrics(AAP) all recommend rapid rehydration over four hours in mild to moderate(IMCI “some”) dehydration. Rehydration should be slower over 6–24 hours in children under three months of age, those with respiratory or cardiac disease, those with suspected or proven hypernatraemia and in malnourished children.\(^5\),\(^13\)

There has been ongoing controversy regarding the ideal composition of ORS. Initial WHO preparations had higher sodium concentration due to its development in areas with high incidence of cholera (which is complicated by hypotatraemia). After multiple modifications the current WHO Guidelines recommend a reduced osmolality ORS with lower concentrations of sodium (75 mmol/l vs 90 mmol/l) and glucose (75 mmol/l vs 111 mmol/l). A meta-analysis has shown its safety and efficacy in both cholera and non-cholera diarrhoea, with lower use...
of intravenous fluid rescue, reduced vomiting and similar rates of hyponatraemia when reduced osmolarity is compared with standard ORS.3,4 ESPGHAN in fact recommends an even lower concentration of sodium of 60 mmol/l for use in children with diarrhoea in Europe due to the different aetiology of diarrhoea in European settings.4

Multiple other modified formulations of ORS have also been extensively studied. Rice-based ORS can be used as an alternative therapy to standard ORS in cholera, as it adds additional substrate to the gut lumen without increasing osmolality, thereby providing additional glucose molecules for glucose-mediated absorption. However, there is no additional benefit in children with non-cholera diarrhoea. Other modifications include ORS-containing amylase-resistant starch, as it is postulated that the non-absorbed carbohydrates increase short-chain fatty acids availability which enhance colonic absorption of sodium and water, but further trials are needed to demonstrate superiority. ORS has also been combined with guar gum, a mixture of non-digestible carbohydrates, as well as with probiotics, zinc and glutamine but there is currently insufficient evidence for any of their use bearing in mind the additional considerations of increased cost, instability and availability of additional compounds.4

Prevention of further dehydration by supplementing maintenance fluid with ORS with each loose stool to replace ongoing losses is an essential part of further management (50–100ml per loose stool). The child’s hydration status must be re-assessed regularly at least every four to six hours including a weight check, and fluids modified according to whether there is improvement or not.5

Maintain nutrition

Consensus from WHO, ESPGHAN and the AAP based on level 1 evidence is to continue breastfeeding at all times, and to continue normal feeds in uncomplicated gastroenteritis within four hours. There is no role for dilution or gradual re-introduction of formula or for special formulae like soya-based or lactose free. Beverages with high sugar content should not be used. An extra meal a day for at special formulae like soya-based or lactose free. Beverages with high sugar content should not be used. An extra meal a day for at

Management of diarrhoea is otherwise usually supportive and non-pharmacologic. Antimotility agents like loperamide have been associated with prolonged disease in Shigellosis, toxic megacolon in C. difficile infection, and haemolytic-uraemic syndrome in children with Shiga-toxin producing E. Coli and are not recommended.3,4,5 The older anti-emtics are also not recommended due to risk of extra-pyramidal side-effects but some newer agents like ondansetron are effective without side-effects.1,5 There is no evidence to support the use of prebiotics, glutamine, folic acid, kaolin-pectin, attapulgite, activated charcoal or bismuth. There may however be potential benefit in the use of smectite, an alumimagnesium silicate that binds digestive mucus.4 Vitamin A does not influence the course of acute diarrhoea but should be given according to national guidelines for its effect on reducing overall mortality.4 Antibiotics are not routinely recommended in viral or uncomplicated bacterial gastroenteritis (Table VI).
Table VI: Indications for systemic antibiotics.

<table>
<thead>
<tr>
<th>Indications</th>
<th>Antibiotic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial gastroenteritis complicated by sepsis</td>
<td>Usually ampicillin and gentamicin OR ceftriaxone</td>
</tr>
<tr>
<td>Neonates</td>
<td></td>
</tr>
<tr>
<td>III immunocompromised children</td>
<td></td>
</tr>
<tr>
<td>Associated infection e.g. urinary tract infection or pneumonia</td>
<td></td>
</tr>
</tbody>
</table>

**Dysentery**
- Shigella
- Salmonella spp (non-typhoid)
- Campylobacter

First try to exclude ETEC due to the associated with HUS

**Specific infections:**
- Amoebiasis
- Giardiasis
- Enteroptysis if complicated by severe dehydration
- E. Coli

- Usually ampicillin and gentamicin OR ceftriaxone
- Metronidazole
- Metronidazole or oral vancomycin
- Usually ampicillin and gentamicin OR ceftriaxone
- Nalidixic acid, fluoroquinolone or ceftriaxone
- Erythromycin or one of above

ETEC = Enterotoxigenic E. Coli; HUS = Haemolytic Uraemic Syndrome

Management of children with chronic diarrhoea

As for the child presenting with acute diarrhoea, there should be a thorough history, including family history, and comprehensive clinical evaluation including effect on nutritional status for those with chronic diarrhoea. It is important to differentiate whether this is a persistent diarrhoea following an acute dehydrating diarrhoeal episode, as causes may include small bowel bacterial overgrowth, acquired disaccharidase deficiency, deconjugation and dehydroxylation of bile salts which induces diarrhoea, protein sensitisation i.e clinical disaccharidase deficiency, and worsening as the day progresses. The need for any specialised investigation and treatment will depend on the clinical picture of the child and would usually include stool MC&S to exclude parasites, stool reducing substances and elastase, and possibly sweat test or coeliac serology.

Prevention

On discharge of a child with an episode of diarrhoea, advice must be given on measures to try to prevent another episode and appropriate home management to prevent dehydration.

The WHO Enhanced Diarrhoeal Disease Control (EDDC) focuses on a combination of public health issues like handwashing, preparation and storage of food as well as drinking water and sanitation; promotion of breastfeeding (which affords a six-fold protection); zinc supplementation and rotavirus vaccines. The enormous burden of rotavirus disease has been mentioned and vaccine introduction in developing countries is thought to have the potential to save 600 000 children's lives per year and help towards the achievement of the Millenium Development Goal of reducing childhood mortality by 2/3 by 2015. Rotarix has been licensed in South Africa since 2006 and was introduced in the Extended Programme of Immunisation in 2009. It is a live attenuated human rotavirus strain, with two doses given orally four weeks apart, not after six months. In studies in middle-income countries the vaccine has a very good safety profile and efficacy of 85% protection. There are some concerns though about its use in the developing world. Such concerns include interference by high titres of maternal antibodies, interference by gut microorganisms as well as safety and immunogenicity in HIV-infected children. Nevertheless, the vaccine holds promise as an extremely important and much needed public health intervention to reduce the significant morbidity and mortality from diarrhoeal disease.

References