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Diarrhoea in children with HIV: a clinical review

By Theo Smart

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Diarrhoea a major cause of death in children with HIV

Thandi is 10 months old when her grandmother brings her into the clinic because she has diarrhoea. Her grandmother says that her mother died a few months ago of tuberculosis (TB). A short while after her mother's death Thandi developed diarrhoea, which has lasted for a couple of months, and she is quite small and frail for her age. She also has a severe diaper rash that looks painful, a low-grade fever, oral thrush, and generalized lymphadenopathy.

The nurse recognises that she will need to treat Thandi for persistent diarrhoea and address the child's malnutrition, but she is also fairly certain she will have to test and treat HIV as well (and broach the subject of HIV to the grandmother). She also wants to relieve the child's discomfort.

Diarrhoea is the second leading killer globally of children of under five (after pneumonia), responsible for nearly one in five childhood deaths (~1.5 million each year).¹ Around 40% of these deaths occur in Africa.²

Outcomes may be even worse for those children who have fallen through the cracks of programmes to prevent vertical transmission of HIV. Many young children with undetected HIV, like Thandi, first present for care with persistent diarrhoea (it is one of the several clinical features that is suggestive of HIV infection).

Studies, mostly conducted before there was more widespread access to ART, reported diarrhoea to be one of the most common complications of HIV disease among young children — even in the US, where sanitation and water safety are good.³ In parts of the world where sanitation and water safety are poorer, diarrhoea is much more common; and studies have suggested that diarrhoea was even more likely in children with HIV, and the leading cause of death among HIV-infected infants.^{4,5,6}

Persistent diarrhoea contributes to mortality causing malnutrition and wasting that weaken the child — and one study found that persistent diarrhoea was eleven times as likely to be associated with death in children with HIV than in those without, although other concurrent complications could also be contributing factors.⁷ Even so, persistent diarrhoea is considered to be a marker for rapid progression of HIV disease.⁸

But over the last several years, much has changed that should improve the outlook for children at risk of diarrhoea — including those with HIV.

First, many programmes have adopted the very clear guidelines and algorithms for the management of acute diarrhoea produced by WHO's Integrated Management of Childhood Illness (IMCI) project.

Secondly there is wider promotion of simple interventions (such as vitamin A and zinc supplementation) that should improve survival — especially oral rehydration therapy (ORT) for the management of dehydration related to diarrhoea.

In addition, there has been a recent push from global health activists who are advocating for wider access to effective treatment

and preventive interventions — as well as improved access to safe drinking water, sanitation and hygiene.

These developments should benefit children with HIV as well — in fact, UNICEF and the IMCI guidelines assert that case management should be the same whether the child is HIV-infected or not. This is especially true of initial case management, although children with HIV and persistent diarrhoea who do not respond to IMCI's case management protocols may require further diagnostic investigations (see below).

Also, early infant HIV diagnosis could lead to the earlier detection of children with HIV and the provision of an effective antiretroviral therapy (ART) regimen and other HIV care for both infant and mother. These should reduce the risk of diarrhoea and of poor outcomes related to the condition. In fact, ART is the only treatment shown to be effective against some of the causes of diarrhoea in HIV.

Nevertheless, many children still present with diarrhoea — and sometimes too late. The palliative care needs of these children (how to recognise pain and alleviate the suffering that diarrhoea and conditions triggering diarrhoea can cause) has, however, received less attention, though some materials have been printed on this subject.

This HATIP seeks to review the guidelines for management of diarrhoea. It discusses how and when these guidelines may differ for children with or exposed to HIV, as well as discussing a palliative care approach: how to reduce the suffering of the child and family while the child is undergoing the diagnostic process and after being placed on treatment, and how to cope if that treatment comes too late. A palliative care approach aims to alleviate the physical, emotional, spiritual and psychological suffering of the child and family.

A backgrounder on diarrhoea

Diarrhoea is defined as having abnormally frequent stools or unformed watery stools. Although many cases are mild and may resolve on their own without treatment, fluid replacement should begin at the onset of diarrhoea since it can very rapidly become severe and cause life-threatening dehydration.⁹

Any number of things can cause diarrhoea, though most cases are due to infections:

- Viral: rotavirus is the single most common cause of severe diarrhoea but other viruses, such as adenovirus, and even measles can cause diarrhoea too. CMV can be associated with colitis in HIV disease — and HIV infection itself may directly cause or contribute to malabsorption and diarrhoea;
- Bacterial: *enterobacter*, disease-causing *Escherichia coli*, *Shigella* species, *Salmonella* species, *Camphylobacter*, *mycobacterium avium intracellulare*(MAI), or disseminated TB, *yersinia*; and
- Protozoal infections: cryptosporidiosis, isosporiasis, microsporidiosis, cyclospora, giardia, *strongyloides stercoralis* and *Entamoeba histolytica*.

Many of these infections are spread when food, water or something else contaminated with faecal matter (animal or human) gets into the child's mouth. Good sanitation is much more difficult in under-resourced, over-crowded communities. Notably, diarrhoea can become much more common and severe when civil conflict or natural disasters force displaced populations to live in temporary, overcrowded shelters where the water supply and food can become contaminated and where it is difficult to achieve adequate sanitation and practice good hygiene.¹⁰ In addition, children who

are malnourished or in poor health are more susceptible to severe diarrhoea and dehydration than healthy children.¹¹

But there are many other causes as well. For instance, medications themselves can cause diarrhoea. In rare cases, overuse of antibiotics can lead to overgrowth of the normally harmless intestinal bacteria *Clostridium difficile* – which releases a toxin that causes diarrhoea that is quite difficult to treat. Some of the antiretroviral medications, particularly the protease inhibitors, commonly cause diarrhoea as a side-effect. Children who become constipated may appear to have ‘diarrhoea’ when watery stool overflows around a hard impaction.^{12,13} Irritable bowel syndrome or lactose intolerance can also cause chronic diarrhoea; while ano-rectal irritation caused by infections or candida overgrowth can also lead to incontinence in a child.¹⁴

Types of diarrhoea

The IMCI classifies childhood diarrhoea broadly into one of three kinds on the basis of its duration and type:

- **Acute diarrhoea**
(if an episode of diarrhoea has lasted for less than 14 days): acute watery diarrhoea causes dehydration and contributes to malnutrition but most deaths are due to dehydration.
- **Persistent diarrhoea** (if the diarrhoea lasts 14 days or more): often leading to malnutrition and weight loss.
- **Dysentery**: Diarrhoea with blood in the stool, with or without mucous – in young children, this is generally caused by *Shigella*.

While these classifications streamline the clinical management for children, it should be pointed out that in HIV disease, a number of other infections can also lead to blood or mucous in the stool – and some of this diarrhoea may become persistent and will not respond to treatments for shigellosis.

In adults with HIV-related diarrhoea, diagnostic algorithms make a point of distinguishing between small bowel disease, which causes voluminous watery diarrhoea generally without mucous or blood, and large bowel disease (both colitis and dysentery), where bowel movements are frequent but the diarrhoea may be small in volume and may contain blood or mucus. From a palliative care perspective, this can be an important distinction to make because large bowel disease is more often associated with severe abdominal pain and cramping that healthcare providers may miss and fail to manage in a child.

Assessing and classifying diarrhoea

The IMCI case management approach is highly recommended because it relies on simple clinical assessments and should get most children onto appropriate treatment as quickly as possible (much faster than if treatment were based on laboratory findings).

The IMCI recommends following a sequence of steps and actions to assess, classify and manage the most common causes of serious illness and mortality in young children, starting with looking for general danger signs to take care of emergencies first, and then asking about the most common syndromes in sequence, identifying and dealing with most life-threatening aspects of each clinical syndrome. Except where otherwise cited, the following section is drawn primarily from the IMCI Handbook, and WHO's *Pocket Book of Hospital Care for Children*.^{15,16}

At the primary care level the health provider is advised to ask the caregiver two key questions in order to classify the diarrhoea: How long has the child had diarrhoea? Has there ever been blood in the stool?

Then regardless of the level of care, it is critical to assess for dehydration, since diarrhoea rapidly depletes the child's body of water and electrolytes (sodium, potassium and bicarbonate). If these fluids and salts aren't quickly replenished, dehydration can be life threatening.

The assessment for dehydration is quite straightforward. The health provider should:

- Check whether the child is lethargic/or has reduced consciousness (*this is a general danger sign*);
- Check if the child is restless or irritable all the time or when not breastfeeding. If the child can be calmed down, he or she is not restless and irritable;
- Assess whether the child has sunken eyes? The caregiver should be asked to confirm. A child should be classified as dehydrated even if some of the sunkenness appears due to malnutrition;
- Ask the caregiver to offer the child a drink. Does the child **drink eagerly and act thirsty**, does he or she **drink poorly** or is the child **unable to drink**?
- Pinch the skin of the abdomen to see whether the skin goes back slowly or very slowly. The slower the skin returns to normal, the worse the dehydration.

This should be done with the assistance of the caregiver to frighten the child as little as possible. The caregiver should be asked to place the child flat on his or her back, arms by their sides and legs straight, either on the examining table or lying flat in her lap.

The nurse/clinician should use their thumb and first finger to pinch the skin on the child between the umbilicus and the side of the abdomen, and avoid using fingertips as this could cause pain. The pinch should be in a line up and down the body (not across) and pick up all the layers of skin and tissue underneath.

When the skin is released, does it go back immediately, **slowly** (stays up a brief moment) or **very slowly** (does it take more than 2 seconds to return)? Although skin may go back slowly in a child with severe malnutrition, it should still be used to classify dehydration.

When a child with diarrhoea presents to a first level referral hospital, a few other diagnoses may be possible, so WHO guidelines recommend that a careful feeding history be taken. The caregiver should also ask about the number of stools the child is having each day; and whether there have been local reports of a cholera outbreak. Has the child recently been taking antibiotics or other treatments? Has the child had fits of crying with pallor?

The clinician should also look for blood in a stool specimen and check for signs of severe malnutrition (for instance, the presence of oedema in both feet or severe wasting (<70% weight-for-height/length), a very thin appearance, without fat, severe wasting of the shoulders, arms, buttocks and thighs, with visible rib outlines?) Does the child have an abdominal mass or an abdominal distension? Stool cultures are not routinely required but may be called for in certain circumstances.

These investigations should help to differentiate a number of different diagnoses:

- If there is no blood in the stools, and more than three stools a day, and a duration of less than 14 days, the child has acute watery diarrhoea.
- If the child has diarrhoea with severe dehydration during a cholera outbreak and there is a positive stool culture for *V. cholerae* O1 or O139 it is likely to be cholera (although cholera is more common in older children).
- If the child has been on a recent course of broad-spectrum antibiotics, that may have caused the diarrhoea.

- Blood in the stool generally indicates dysentery, but if there is an abdominal mass and attacks of crying with pain and pallor in the infant, the child may have an intussusception (a form of bowel obstruction in which one segment of the intestine telescopes into the next) and may need to be referred to a surgeon.

As noted earlier, persistent diarrhoea is diarrhoea that has lasted for more than 14 days – however, if it is also associated with severe malnutrition, it requires a somewhat different approach to care.

Other investigations in children suspected of having HIV

While the abovementioned interventions should help manage most diarrhoea in children regardless of HIV status, those with persistent diarrhoea, and other signs suggestive of HIV should be screened for HIV. In a case like Thandi's where the mother is no longer living, a rapid HIV test can be used to demonstrate whether a child has been exposed to HIV, but cannot confirm HIV infection until 18 months after birth or last breastfeeding. Dried blood spots should be sent in for early infant diagnosis by HIV DNA PCR or RNA assays where available. However, it may be necessary to make a clinical diagnosis of HIV, based on the presence of three or four symptoms strongly associated with HIV such as oral thrush, lymphadenopathy, recurrent pneumonia, very low weight, parotid enlargement, past or present ear discharge, and the persistent diarrhoea.¹⁷

If the child is believed to be HIV-infected, clinical staging or a low CD4 cell percentage may indicate an increased risk for less common infectious causes of diarrhoea such as *mycobacterium avium intracellulare*, CMV, microsporidiosis and cryptosporidiosis. Many guidelines for people with HIV experiencing diarrhoea recommend a workup that should include microscopy (modified ZN and parasites) and culture.

The Handbook on Paediatric AIDS in Africa recommends that "because of the occurrence of unusual pathogens, healthcare workers should conduct standard stool microscopy and stool culture on all HIV-infected children with diarrhoea."¹⁸ However, many of these unusual pathogens are difficult to diagnose and treat in resource-limited settings, and in any case, appear to respond best to ART.

Management: dehydration

The first priority is to manage dehydration.

Even before bringing a child into care, HIV and Maternal Child Health (MCH) programmes should educate mothers and caregivers about the risks of dehydration associated with diarrhoea, and that they should begin administering available home fluids immediately upon onset of diarrhoea in a child. Continued feeding or increased feeding during and after the diarrhoeal episode should also be emphasised.¹⁹

Recipes for homemade oral rehydration fluids for children

(from *A Clinical Guide to Supportive and Palliative Care for HIV/AIDS in Sub-Saharan Africa*)²¹

Oral rehydration solution	Rice-based oral rehydration solution	Maize-based oral rehydration solution
1 8 tsp sugar	1 Fistful of dry rice grain (25 g)	1 Add 50 g maize to 1 litre water
2 ½ level tsp salt		

3 1 litre boiled water	2 Wash and soak until soft	2 Cook for 5-8 minutes
4 Mix well and store covered in a cool place. Make a fresh solution every day.	3 Grind to paste	3 Add 1 tsp salt once cooled
	4 Put 2 cups of water in pan and mix with paste	
	5 Heat and stir until bubbling	
	6 Cool and use within 6-8 hrs	

If possible, mothers and caregivers should be provided in advance with oral rehydration salts (ORS) for suspension in clean water. Over the past few years WHO and UNICEF have been encouraging countries to make and use a new ORS formula (low-osmolarity ORS) on the basis of data showing it to be more effective than the original formula.²⁰ But it is more likely that the caregiver will only be able to use homemade fluids based on boiling water with whatever grain or root crop is readily available – in which case, parents should be given instructions for making them.

But if such solutions cannot be given, mothers or caregivers should be told that almost any fluid can help prevent dehydration (with the exception of caffeinated drinks). Infants should also continue to be breastfed if possible.

Once a child has been brought in for assessment, IMAI recommends the following classifications for dehydration (note the following section is adapted from [WHO's Pocket Handbook of Hospital Care for Children](#)).

Classifying the severity of dehydration in children with diarrhoea

Classification	Signs or Symptoms	Treatment
Severe dehydration	Two or more of the following signs: <ul style="list-style-type: none"> ● lethargy/unconsciousness ● sunken eyes ● unable to drink or drinks poorly ● skin pinch goes back very slowly (≥2 seconds) 	Start intravenous (IV) fluids for severe dehydration immediately (or refer urgently to a nearby site that can) (See treatment plan C)
Some dehydration	Two or more of the following signs: <ul style="list-style-type: none"> ● restlessness, irritability ● sunken eyes ● drinks eagerly, thirsty ● skin pinch goes back slowly 	Give fluid and food for some dehydration (Treatment Plan B) After rehydration, advise caregiver on home treatment and when to return immediately Follow-up in 5 days if not improving
No dehydration	Not enough signs to classify as some dehydration	Give fluid and food to treat at home (see Diarrhoea Treatment Plan A.) Advise caregiver on when to return immediately Follow up in 5 days if not improving

Intravenous rehydration in case of severe dehydration

Treatment Plan C provides a decision tree to guide the best choices for intravenous rehydration based upon the health facility's resources and capacity:²³

If the facility can give IV fluids, these should be started immediately

(if the child can drink, give ORS by mouth while the drip is set up). 100 ml/kg Ringer's lactate solution is recommended (or, if not available, normal saline), divided as follows:

- For infants under 12 months, first give 30 ml/kg in 1 hour and repeat once if radial pulse remains very weak or undetectable. Then give 70 ml/kg in 5 hours.
- For children 12 months to 5 years, give 30 ml/kg in 30 minutes (again repeating once based on radial pulse response), then 70 ml/kg in 2 ½ hours.

The child should be reassessed every 15-30 minutes. The drip should be given more rapidly if the hydration status is not improving. As soon as the child can drink give ORS (about 5 ml/kg/hour): usually after 3-4 hours (infants) or 1-2 hours (children).

Reassess an infant after 6 hours and a child after 3 hours. Classify dehydration again, and choose the appropriate plan (A, B, or C) to continue treatment.

If the facility can't give IV fluids, but there is a facility nearby that can (within 30 minutes):

Refer *urgently* to hospital for IV treatment. If the child can drink, provide the caregiver with ORS solution and show her how to give the child frequent sips during the trip.

If there isn't a hospital nearby that can give IV fluids, but the healthcare provider is

trained to use a nasogastric (NG) tube for rehydration: Start rehydration by NG tube (or, if the healthcare provider can't use an NG tube but the child can drink, by mouth) with ORS solution: 20 ml/kg/hour for 6 hours (total of 120 ml/kg). Reassess the child every 1-2 hours: Give fluid more slowly if there is repeated vomiting or increasing abdominal distension; and if hydration status is not improving after 3 hours, send the child for IV therapy. After 6 hours, reassess the child. Classify dehydration again and choose the appropriate plan (A, B, or C) to continue treatment. Note: If possible, observe the child for at least 6 hours after rehydration to be sure the caregiver can maintain hydration giving the child ORS solution by mouth.

If none of the above are possible, or effective:

Refer urgently to nearest facility that can provide IV or NG treatment.

Treatment of mild dehydration (treatment Plan B):

Give recommended amount of ORS in clinic over 4-hour period based upon weight or age if weight is not available:

Age	Up to 4 months	4 months up to 12 months	12 months up to 2 years	2 years up to 5 years
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Weight In ml	< 6 kg 200-400	6-<10 kg 400-700	10-<12 kg 700-900	12-19 kg 900-1400
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The precise amount of ORS can also be calculated by multiplying the child's weight (in kg) by 75 ml. If the child wants more ORS than shown, give more.

Show the mother/caregiver how to give ORS solution.

- Give frequent small sips from a cup.
- If the child vomits, wait 10 minutes. Then continue, but more slowly.
- Continue breastfeeding whenever the child wants.

After 4 hours:

- Reassess the child and classify the child for dehydration.
- Select the appropriate plan to continue treatment.
- Begin feeding the child in clinic.

If the mother/caregiver must leave before completing treatment:

- Show her how to prepare ORS solution at home.
- Show her how much ORS to give to finish 4-hour treatment at home.
- Give her enough ORS packets to complete rehydration. Also give her 2 packets as recommended in Plan A.
- Explain the four rules of home treatment (see treatment plan A below).

ORS solution is not effective in a minority of children with severe persistent diarrhoea whose glucose absorption is impaired. If their stool volume increases markedly, thirst increases, signs of dehydration develop or worsen, and the stool contains a large amount of unabsorbed glucose when they are given ORS, these children will require IV rehydration until the child can tolerate ORS.

Treating diarrhoea at home (treatment plan A)

Counsel the mother on the 4 rules of home treatment: Give extra fluid, zinc supplements, continue feeding, and explain when to return

1. Give extra fluid (as much as the child will take).

Tell the mother to:

- Breastfeed frequently and for longer at each feed.
- If the child is exclusively breastfed, give ORS or clean water in addition to breastmilk.
- If the child is not exclusively breastfed, give one or more of the following: ORS solution, food-based fluids (such as soup, rice water, and yoghurt drinks), or clean water.

It is especially important to give ORS at home when:

- the child has been treated with Plan B or Plan C during this visit.
- the child cannot return to a clinic if the diarrhoea gets worse.

Teach the mother how to mix and give ORS. Give the mother two packets of ORS to use at home.

Show the mother how much fluid to give in addition to the usual fluid intake:

- Up to 2 years: 50 to 100 ml after each loose stool
- 2 years or more: 100 to 200 ml after each loose stool

Tell the mother to:

- Give frequent small sips from a cup.
- If the child vomits, wait 10 minutes. Then continue, but more slowly.
- Continue giving extra fluid until the diarrhoea stops.

2. Give zinc supplements.

Tell the mother how much zinc to give:

- Up to 6 months 1/2 tablet (10 mg) per day for 10–14 days
- 6 months and more 1 tablet (20 mg) per day for 10–14 days

Show the mother how to give the zinc supplements:

- Infants, dissolve the tablet in a small amount of clean water, expressed milk or ORS in a small cup or spoon.
- Older children, tablet can be chewed or dissolved in a small amount of clean water in a cup or spoon.

Remind the mother to give the zinc supplements for the full 10–14 days.

3. Continue feeding:

and provide mother with nutritional counselling.

4. Explain when to return:

Advise the mother to return immediately to the clinic if the child becomes more sick, or is unable to drink or breastfeed, or drinks poorly, or develops a fever, or shows blood in the stool. If the child shows none of these signs but is still not improving, advise the mother to return for follow-up at 5 days. Also explain that this same treatment should be given in the future as soon as diarrhoea develops.

About zinc supplementation

Zinc supplements are recommended for all children with diarrhoea (unless they are vomiting). Zinc deficiency is common in most resource-limited settings – and diarrhoea further depletes the body of zinc.²⁴ Furthermore, in clinical trials, a 10- to 14-day treatment course with zinc reduced the duration and severity of both persistent and acute diarrhoea. In another study, zinc was associated with a 25% reduction in the duration of acute diarrhoea, and a 40% reduction in treatment failure and death in persistent diarrhoea.²⁵

Zinc has also been shown to be safe and beneficial in children with HIV. For instance, investigators at Grey's Hospital in KwaZulu Natal, South Africa randomised 96 children with HIV (who were already taking cotrimoxazole) to receive 10mg of zinc or a placebo daily for six months.²⁶ The children receiving zinc had roughly half as much watery diarrhoea (diagnosed at 7.4% of clinic visits in the zinc group, compared to 14.5% of the placebo group, $p=0.001$), as well as a statistically significant weight gain.

Treatments for diarrhoea

After addressing dehydration, each of the three major classes of diarrhoea need to be treated differently, but WHO guidelines stress that antibiotics and antidiarrhoeal medications should not be routinely administered to children with diarrhoea. Indeed, antibiotics have no effect on the most common cause of diarrhoea (rotavirus), and antidiarrhoeal medications “do not prevent dehydration or improve nutritional status and some have dangerous, sometimes fatal, side-effects,” according to the *Pocket Book of Hospital Care for Children* (unless otherwise noted, the following section on treatment is condensed from the *Pocket Book*).²⁷

Acute diarrhoea:

for the most part, the clinical management for acute diarrhoea is contained in Treatment Plan A. Some children, however, do have non-intestinal or intestinal infections that require specific antibiotic therapy. For instance, if cholera is the suspected cause of acute diarrhoea, an oral antibiotic should be given that is effective against strains of *Vibrio cholerae* in the area (possibly tetracycline, doxycycline, cotrimoxazole, or erythromycin).

Dysentery:

Children with blood in their diarrhoea are classified as having dysentery, which can also cause abdominal pain, fever, convulsions, lethargy, dehydration and rectal prolapse. Any infant under 2 months of age with dysentery or with severe malnutrition should be hospitalised. Likewise, if the child is lethargic, has abdominal distension and tenderness or convulsions, he or she may be at high risk of sepsis and should be hospitalised.

In young infants (under 2 months) dysentery should be treated with IM/IV ceftriaxone (100 mg/kg) once daily for 5 days. In older children, dysentery should first be treated with an oral antibiotic (for 5 days), to which most local strains of *Shigella* are sensitive, usually ciprofloxacin, pivmecillinam, and other fluoroquinolones.

If there is no improvement after a couple of days (no fever, fewer stool, less blood), clinicians should look for other conditions, stop the first antibiotic and try a second one. If there is still no response, the recommendations are to continue looking for other conditions, and treat for possible amoebiasis with metronidazole (10 mg/kg, 3 times a day) for 5 days. (Again, it is important to point out that children with HIV can have other causes of infections that can cause bloody diarrhoea or even lesions such as KS – so failure to respond should increase the index of suspicion for an HIV-related condition).

Complications of dysentery:

Rectal prolapse should be pushed gently back in using a surgical glove or a wet cloth. Another option is to apply a compress with a warm solution of saturated magnesium sulphate to reduce the prolapse by decreasing the oedema. High fevers should be managed with paracetamol; repeated or prolonged convulsions with IM paraldehyde, and potassium depletion with ORS (when indicated) or foods rich in potassium like bananas (for children eating solid foods). The child should also be encouraged to breastfeed or eat more. Since this may be difficult when he or she lacks an appetite, the child should be encouraged to frequently eat small amounts of his or her preferred foods.

Persistent diarrhoea:

According to IMAI guidelines, children with persistent diarrhoea and signs of dehydration should be classified as severe persistent

diarrhoea and require hospitalisation — partly to address dehydration, but partly to make certain that the child receives adequate feeding and avoids developing severe malnutrition. (Severely malnourished children with persistent diarrhoea also require hospitalisation, but need specialised care including a cautious approach to feeding (such as low osmolality/lactose feeds) since the child's physiological state is fragile).

Children with severe persistent diarrhoea should be examined for non-intestinal infections as well (especially if they are suspected of having HIV) and treated accordingly. Blood in the diarrhoea should be treated with antibiotics as dysentery.

Consider giving treatment for amoebiasis (oral metronidazole: 7.5 mg/kg, 3 times a day, for 5 days) only if laboratory tests reveals trophozoites of *Entamoeba histolytica* within red blood cells of a fresh stool sample, or if two different antibiotics, which are usually effective for local *Shigella* strains have been tried without clinical improvement.

Give treatment for giardiasis (metronidazole: 5 mg/kg, 3 times a day, for 5 days) if cysts or trophozoites of *Giardia lamblia* are seen in the faeces. Note, metronidazole may also be effective for some of the less common infections seen in HIV — however, treatment of *C. difficile* related diarrhoea typically requires a longer course.²⁸

Again, feeding is very important, and food should only be withheld in children while they are being rehydrated (using plans B and C) for at most four to six hours. Children who are in the hospital need special diets with a daily intake of at least 110 calories per kg to make certain that they gain weight.

For young infants under 6 months, exclusive breastfeeding should be encouraged. If the child is not breastfeeding, a low lactose breast milk substitute such as yoghurt should be used. Children who have moved onto solid foods should be encouraged to start eating again as soon as possible, although, initially, naso-gastric feeding may be necessary.

The *Pocket Book* recommends the following two diets for children over 6 months of age with severe persistent diarrhoea. The goal should be to achieve weight gain, which needs to occur for at least three consecutive days. Children who are responding well should be given fresh fruit and vegetables if available.

After seven days on an effective diet, the child's regular diet may resume as long as they are getting at least 110 calories per kg. Children who are sent home should continue to receive regular follow-up however, to make certain that they are continuing to gain weight.

Diet for persistent diarrhoea, first diet: A starch-based, reduced milk concentration (low lactose) diet

Diet should provide at least 70 calories/100 g, use milk or yoghurt as a source of animal protein, but no more than 3.7 g lactose/kg body weight/day, and should provide at least 10% of calories as protein. The following example provides 83 calories/100 g, 3.7 g lactose/kg body weight/day and 11% of calories as protein:

- full-fat dried milk (or whole liquid milk: 85 ml): 11g
- rice: 15 g
- vegetable oil: 3.5 g
- cane sugar: 3 g
- enough water to make 200 ml

If the first diet is not successful (there is an increase in diarrhoea) or failure establish a solid weight gain after 7 days, the second diet should be given:

Diet for persistent diarrhoea, second diet: A no-milk (lactose-free) diet with reduced cereal (starch)

The second diet should contain at least 70 calories/100 g, and provide at least 10% of calories as protein (egg or chicken). The following example provides 75 calories/100 g:

- whole egg: 64 g
- rice: 3 g
- vegetable oil: 4 g
- glucose: 3 g
- water to make 200 ml

Finely ground, cooked chicken (12 g) can be used in place of the egg to give a diet providing 70 calories/100 g.

All children with persistent diarrhoea should be given daily supplementary multivitamins and minerals for two weeks, including at least two recommended daily allowances of folate, vitamin A, zinc, magnesium and copper.

Healthcare providers should continue daily monitoring of hospitalized children for weight, diet adherence, temperature and number of diarrhoea stools. As for children who have been sent home, caregivers should bring them in again in five days or sooner if diarrhoea worsens or other problems develop.

Children with persistent diarrhoea that is not as severe should also receive an adequate caloric intake (and supplements), and eat frequent small meals. Caregivers should be advised that the child may have difficulty digesting milk (animal milk) other than breast milk.

Other pragmatic palliative and supportive measures

Palliative care guides make a number of other useful suggestions that could improve outcomes in a child, and help the child's family manage. In *Children's Palliative Care in Africa*, Amery et al recommend using a waterproof plastic undersheet covered with cotton sheet or absorbent material.²⁹ The child's caregiver should be given counselling about the risks of cross-infection, while the family should be advised regarding nutrition and household hygiene (especially handling the baby's water and food).

In *A Clinical Guide to Supportive and Palliative Care for HIV/AIDS in Sub-Saharan Africa*, Barigye et al recommend obtaining "serum electrolytes and a full blood count because anaemia and thrombocytopaenia are relatively frequent complicating factors." In addition, they recommend giving skin care when diarrhoea or incontinence threaten skin integrity.³⁰ Amery et al suggest using a barrier cream; treating for candidiasis (nappy rash); administering metronidazole rectally if there is an offensive discharge and considering steroid suppositories or retention enema.

For children with HIV who appear to be having diarrhoea due to a side-effect of antiretroviral therapy, consider switching drug regimens if possible, if diarrhoea is caused by an antiretroviral agent.³¹ Likewise, after excluding serious treatable causes, they recommend trying loperamide, codeine, or low-dose morphine to help with intractable diarrhoea (which may be caused by HIV enteropathy for instance).

This should be done cautiously though. In fact, the *Pocket Book* advises: "Never give drugs for symptomatic relief of abdominal pain and rectal pain, or to reduce the frequency of stools, as they can increase the severity of the illness."

Prevention

Almost a year ago, global health activists put out a 'call to action' demanding the implementation of many of the simple interventions that could dramatically reduce the burden of diarrhoea-related death and illness (). In addition to treatment including ORS and zinc supplementation, the activists focus on many preventive interventions such as safe drinking water and improved sanitation.

The preventive package is described in more detail in Unicef and WHO's report *Diarrhoea: Why children are still dying and what can be done?* and includes five main elements:

- 1 rotavirus and measles vaccinations (WHO recommends that the rotavirus vaccine be included in all national immunisation programmes);
- 2 promotion of early and exclusive breastfeeding and vitamin A supplementation;
- 3 promotion of handwashing with soap;
- 4 improved water supply quantity and quality, including treatment and safe storage of household water;
- 5 community-wide sanitation promotion.

The interventions make good common sense, and there are data specific to the effectiveness of some of these interventions in people with HIV. Furthermore, vitamin A supplementation reduces diarrhoeal morbidity in HIV-positive children under 5 years old and all-cause mortality by 30%.³²

Use of home-based safe water interventions have been demonstrated to significantly reduce diarrhoea frequency and severity among adults with HIV living in Africa, and are now recommended by WHO as one of the Essential Prevention and Care Interventions for Adults and Adolescents Living with HIV in Resource-Limited Settings.³³

However a longitudinal study in children with HIV conducted in Kenya found that the benefit for infants was less clear-cut.³⁴ The study assessed the incidence of diarrhoea in children in the Kisumu breastfeeding study, which evaluated the impact of antiretroviral therapy on vertical HIV transmission during the breastfeeding period. The study did not analyse results according to the HIV status of the infants.

In this study mothers weaned when the infant was five-and-a-half months old, with a two-week weaning period. The safe-water intervention was introduced midway through the study, allowing a comparison of rates of diarrhoea before and after the introduction.

Although rates of diarrhoea were lower before and after weaning, there was no significant difference during the weaning period itself. Indeed infants in the Kisumu Breastfeeding study experienced significantly higher rates of diarrhoea (relative risk 1.60) if weaned at six months, when compared with infants of 6-7 months of age in a previous Kisumu vertical transmission study who were weaned later.

What caused higher rates of diarrhoea at the time of weaning in this study is unclear. The authors note that although weaning foods may contain pathogens such as *E.coli* and *Shigella*, two studies of bacterial causes of diarrhoea in infants and young children in western Kenya failed to identify any bacterial cause in two-thirds of cases. Although protozoal and viral causes cannot be ruled out, the authors suggest that dietary change itself is enough to provoke infant diarrhoea. They also note that if pathogens in foods were the cause, one would not expect to see the dramatic decline in diarrhoea after the weaning period observed in this study – unless a rapidly maturing immune system soon provides much greater protection against foodborne pathogens.

In an accompanying editorial Louise Kuhn and Grace Aldrovandi note that the finding "further supports the idea that breastfeeding protects less by keeping the germs out and more by putting the good stuff in".³⁵

Breastfeeding has now been shown to be protective against diarrhoea in infants with HIV in a number of studies, which is one of the reasons *recent WHO guidance* has recommended that wherever possible, mothers with HIV should breastfeed HIV-negative infants or those with unknown HIV status exclusively for the first six months of life and receive antiretroviral therapy while doing so. After this point complementary foods should be introduced, and weaning considered once the child reaches twelve months of age. Breastfeeding should only stop once a nutritionally adequate and safe diet without breast milk can be provided. If the mother cannot receive antiretroviral therapy, the infant should receive daily nevirapine until weaning is over.

In the case of infants with HIV, the mother should breastfeed for the first two years of life

in order to maximise the protection offered by breast milk.

Thus, safe water interventions should be considered as an adjunct to breastfeeding, not a replacement, argue Louise Kuhn and Grace Aldrovandi.

Studies also suggest that rotavirus vaccination should be evaluated in children with HIV.³⁶

But as already mentioned several times in this article, however, **another essential measure** to prevent poor diarrhoeal outcomes in young children with HIV is **to identify them as early as possible and put them (and their mothers) on ART** and other HIV care (including cotrimoxazole – which also improves survival, though the data is a little unclear on its effect on diarrhoea in children). Putting infants with HIV onto ART cuts their risk of death in half.

Nevertheless, even if ART puts children with HIV on par with children not exposed to HIV, all children are at risk of severe diarrhoea and diarrhoea-related mortality.

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