

GASTROINTESTINAL MANIFESTATIONS OF HIV INFECTION

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OBJECTIVES

1. Review specific subjective and objective information important in the assessment of nausea, vomiting, and diarrhea in patients with human immunodeficiency virus (HIV)/AIDS.
2. Discuss the possible causes of, types of, and management approaches to diarrhea in patients with HIV/AIDS.
3. Classify the signs of dehydration in relation to their level of severity.
4. Identify the appropriate rehydration plan for use with patients experiencing dehydration.
5. Describe the specific symptoms associated with wasting syndrome in patients with HIV/AIDS.
6. Describe the symptoms and causes of hepatitis in HIV-infected children.

KEY POINTS

1. Patients with HIV/AIDS are at high risk of having gastrointestinal complications.
2. Careful assessment using subjective and objective information is important when evaluating patients with HIV/AIDS who are experiencing nausea, vomiting, or diarrhea.
3. Patients with diarrhea and/or vomiting should be monitored for signs and symptoms of dehydration.
4. Oral rehydration fluids should be used to prevent and treat dehydration.
5. Wasting syndrome is a severe form of weight loss associated with HIV/AIDS.
6. Hepatitis B and C are common coinfections in HIV-infected patients.

OVERVIEW

People infected with human immunodeficiency virus (HIV) have a high likelihood of developing gastrointestinal (GI) complications at some point during their illness. Diarrhea is the most common GI manifestation in

HIV-infected patients. Others include vomiting, wasting, hepatitis, esophagitis, malabsorption, jaundice, and failure to thrive. Most of these GI problems are related to infections and may be caused by HIV itself or other viruses such as cytomegalovirus (CMV) and hepatitis B and C; by bacteria such as *Mycobacterium avium* complex (MAC), *Salmonella*, and *Shigella*; by parasites such as *Cryptosporidium* and *Giardia*; and by fungi such as *Candida*. This module will discuss the causes of the most common GI manifestations in HIV-infected patients and approaches to the assessment and treatment of these conditions.

NAUSEA AND VOMITING

Nausea and vomiting are common physical complaints with many causes. Causes include infection and/or inflammation of the GI tract, gastroesophageal reflux, an overfilled stomach, protein intolerance, urinary tract infection, pregnancy, increased intracranial pressure, meningitis, hepatitis, biliary tract disease, pancreatitis, malignancies, mechanical obstruction, sepsis, food poisoning/toxins, and altered metabolism. Many medications can also cause nausea and vomiting, including antiretroviral agents, drugs used to treat or prevent opportunistic infections, and antineoplastic (anticancer) drugs. (Please refer to the chapter on antiretroviral treatment for a list of specific medications that may cause nausea and vomiting, hepatitis, or pancreatitis as side effects.) Determining the exact cause of an individual patient's nausea and vomiting will often be difficult.

Assessment

The assessment of a patient with nausea and vomiting should include both subjective and objective data. Most episodes of nausea and vomiting are self-limited and not dangerous. The assessment should focus on determining the hydration status of the patient and evaluating for the presence of danger signs that might indicate a

serious cause of the patient's symptoms. Some danger signs include bilious (dark green) emesis, hematemesis (vomit with blood), jaundice, severe headache, altered mental status, focal neurologic signs, and severe flank or abdominal tenderness on exam.

Subjective data include the following:

- Onset of vomiting, quantity of emesis, presence of blood or bile
- Relationship of vomiting to meals, time of day, activities, or medications
- History of trauma or ill contacts
- Presence of associated signs and symptoms, such as diarrhea, fever, pain, dysuria, flank or abdominal pain, vision changes, headache, seizures, high-pitched cry (especially in an infant), jaundice, irritability, behavior changes, polydipsia, polyuria, polyphagia, or anorexia
- Changes in patterns or quantity of urination and amount of oral intake

Objective data include the following:

- Patient's current weight and last known weight.
- Volume of intake and output, as well as vital signs (temperature, heart rate, blood pressure, respiration rate).
- Assessment of skin turgor (skin pinch), mucous membranes, and the presence or absence of tears.
- Nuchal rigidity; level of consciousness; and any behavioral changes, such as irritability or lethargy.
- When laboratory studies can be obtained, a complete blood count, serum pH, electrolytes, blood urea nitrogen, creatinine, AST (aspartate aminotransferase), ALT (alanine aminotransferase), bilirubin, amylase, lipase, urine analysis, and urine culture may be helpful in determining the cause of nausea/vomiting and degree of dehydration.

Clinical Considerations

Considerations for patients with nausea and vomiting include restoring and/or maintaining adequate hydration and identifying the cause of nausea and vomiting. The patient and family should be educated about the signs of dehydration and the importance of maintaining adequate fluid intake. The patient's weight, intake, and output should be assessed daily. Intake should include all oral and intravenous fluids; output should include urine, stool, and emesis. Hydration fluids should be administered as available. This module's rehydration

section discusses the types of fluids. Patients should be instructed to drink fluids frequently, small volumes at a time; eat five to six small meals a day; avoid greasy, high-fat foods; and eat food at room temperature.

In addition to restoring and maintaining adequate hydration, treatment should be directed at the underlying cause of nausea and vomiting if appropriate. Antiemetic medications can be sedating and may be harmful in the pediatric setting and are not recommended for children.

DIARRHEA

Overview

Diarrhea remains one of the most common causes of death worldwide among children younger than 5 years. It is also one of the most common manifestations of advanced HIV disease in both adults and children, and in Africa it is estimated that 60%-97% of children with AIDS suffer from diarrhea at some point. Diarrhea is an excessive loss of fluid and electrolytes in the stool resulting in three or more loose stools in a 24-h period. The consistency of the stools is the most important factor, and frequent passage of soft or well-formed stools should not be considered diarrhea.

Infections, toxins, medications, anatomic abnormalities such as tumors, and dietary intolerance can cause diarrhea. Infectious causes of diarrhea are the most common. These may be of bacterial, viral, fungal, or parasitic origin. Infections can be classified as causing predominantly watery, large-volume diarrhea due to a small-bowel infection or bloody, small-volume dysentery due to a predominant colonic infection. Pathogens that infect the GI tract are similar worldwide, but the likelihood of infection depends on the patient's age, immune status, geographic location, and exposure history. Agents such as rotavirus, Norwalk virus, adenoviruses, enteroviruses, *Vibrio cholerae*, enterotoxigenic *Escherichia coli*, *Giardia*, and *Cryptosporidium* commonly cause watery diarrhea. See this module's section on dysentery for common causes of bloody diarrhea. *Campylobacter* spp., *Salmonella*, *Shigella*, and MAC are particularly common bacterial causes of diarrhea in the setting of AIDS. Diarrhea caused by enteric viruses is no more common among children with AIDS than in the general population, although CMV and herpes simplex virus may cause opportunistic infection. *Candida albicans* can infect the GI tract of people with

AIDS, and parasites such as *Cryptosporidium* and *Isospora* are more likely to cause chronic diarrhea in an immunosuppressed host.

Food- or waterborne pathogens may cause diarrheal infections in immunocompromised hosts at a smaller inoculum than that needed to infect healthy hosts; they may also cause opportunistic infections. Opportunistic AIDS-defining diarrheal illnesses include chronic *Cryptosporidium* (lasting >14 days in children or >1 month in adolescents and adults), CMV disease, histoplasmosis, isosporiasis, MAC, and septicemia from *Salmonella*. (The module on opportunistic infections gives more details regarding these infections and their treatment.)

Bacterial toxins present in food may also cause acute diarrhea, usually in association with vomiting. *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium perfringens* can cause food poisoning. Management of toxin ingestion is supportive care. Other causes of diarrhea include medications, such as antiretrovirals, which may cause diarrhea as a side effect (refer to the chapter on antiretroviral treatment for a listing of specific medications associated with diarrhea). Many antibiotics also cause loose stools because of their effect on normal flora, and *Clostridium difficile* infection may occur in the setting of recent broad-spectrum antibiotic therapy. Inflammatory processes such as celiac sprue (malabsorption syndrome characterized by marked atrophy and loss of function of the small intestinal lining), surgical procedures, and tumors can change the anatomy and function of the intestines and result in diarrhea. (Please refer to the chapter on HIV-associated malignancies for more information about Kaposi sarcoma and smooth-muscle tumors such as leiomyosarcomas and leiomyomas, which may present with diarrheal symptoms in patients with HIV/AIDS.) Osmotic diarrhea can occur with lactose deficiency and overfeeding, whereas bloody stools may occur with allergy to cow's milk or soy protein.

Though diagnosis of the exact cause of diarrhea may be difficult, for treatment purposes one can usually divide diarrhea into four clinical types and then manage accordingly:

1. Acute diarrhea—diarrhea that has lasted less than 14 days
2. Dysentery—diarrhea with visible blood
3. Persistent diarrhea—diarrhea that has lasted more than 14 days
4. Diarrhea and severe acute malnutrition

Assessment

Assessment of a patient with diarrhea should include both subjective and objective information. The focus of the assessment should be twofold: to determine the degree of dehydration and to determine the type of diarrhea (acute, dysentery, persistent, or with severe acute malnutrition).

Subjective data include the following:

- Onset, duration, amount, frequency, odor, and appearance of stool—presence of mucus or blood
- Presence of any associated symptoms, such as fever, pain, vomiting, cramping, flatus, abdominal distension, tenesmus
- Dietary changes that might correlate with the increase in the amount of stool
- Family members with similar illness or other GI diseases and any unusual exposure history (travel, animals, antibiotics)

Objective data include the following:

- Assess for signs of dehydration, such as sunken fontanel in the infant, poor skin turgor, dry mucous membranes, lack of tears, decreased urine output, and changes in level of consciousness.
- Compare patient's current weight and previous weight.
- Assess for alterations in tissue perfusion (e.g., tachycardia, delayed capillary refill, hypotension).
- Examine stool for color, consistency, blood, mucus, pus, odor, and volume.
- If possible, evaluate stool for ova and parasites, bacterial culture, and white blood cells.
- Assess for the presence of acute malnutrition—visible wasting, edema, mid-upper-arm circumference, weight for height (see chapter on nutrition).

Clinical considerations. Diagnosis of the cause of diarrhea is often difficult because of the many pathogens that produce infection. Whenever possible, appropriate enzyme immunoassays and bacterial, parasite, and special stool stains and cultures should be sent for definitive diagnosis. Bacterial, mycobacterial, and CMV blood cultures may facilitate diagnosis in febrile patients with HIV/AIDS and diarrhea.

Dehydration occurs when water output exceeds water intake. Patients with vomiting and diarrhea are at high

risk of dehydration. The patient's weight and intake and output should be assessed daily or even more often if he or she is very sick. Intake should include all oral and intravenous fluids; output should include urine, stool, and emesis. For management purposes dehydration can be classified as none, some (mild or moderate), or severe (**Table 1**). As dehydration develops, signs include a sunken fontanel in infants, poor skin turgor, dry mucous membranes, lack of tears, decreased urine output, changes in the level of consciousness, increased heart rate, and decreased weight. Fluid and electrolyte replacement and maintenance are the mainstays of diarrhea management, and the next section lists recommended protocols for giving hydration fluids on the basis of the assessed level of dehydration. Dietary changes may alleviate diarrhea, and high-protein, high-calorie foods that are low in fat and free of lactose and caffeine may be helpful. Patients should increase soluble fiber and avoid hot, spicy foods.

Some general principles apply to managing all types of diarrhea. Support of appropriate nutrition, prevention and treatment of dehydration, and follow-up are the key components of management in all cases of diarrhea.

Antimicrobial agents may be indicated for the treatment of diarrhea in some situations but should not be used routinely on an empiric basis. When prescribing antimicrobial agents, one should instruct patients on the

importance of finishing all medications prescribed. With patients and caregivers, emphasize good perineal hygiene to prevent skin breakdown and frequent hand washing to prevent transmission of infection. Antidiarrheal medications, such as loperamide, have no practical benefit for children with diarrhea, do not prevent dehydration or improve nutritional status, may have dangerous and even fatal side effects, and should not be given to children younger than 5 years. Avoid bismuth subsalicylate compounds in the setting of vomiting or flu because of their possible association with Reye syndrome.

Zinc deficiency is common in children in many resource-limited areas and may contribute to diarrhea in this setting. Many studies have now shown that giving zinc to children with diarrhea can reduce the severity, duration, and frequency of recurrence of diarrhea. The World Health Organization (WHO) recommends that all children with diarrhea be given zinc (10-20 mg/day) for 10-14 days.

Acute Diarrhea

Acute diarrhea is diarrhea that has lasted less than 14 days. The preceding section discussed the causes of acute diarrhea. The most important aspect of managing acute diarrhea is assessing the level of hydration (**Table 1**) and preventing and treating dehydration according to the following treatment plans. See **Figures 1-3** for condensed versions of WHO Treatment Plans A, B, and C.

Table 1. Assessment of level of dehydration in children with diarrhea

Action	A	B	C
Look at: Condition* Eyes† Thirst	Well, alert Normal Drinks normally, not thirsty	Restless, irritable Sunken Thirsty, drinks eagerly	Lethargic, unconscious Sunken Drinks poorly, or not able to drink
Feel: Skin pinch‡	Goes back quickly	Goes back slowly (<2 s)	Goes back very slowly (>2 s)
Decide	The patient has no signs of dehydration	If the patient has two or more signs in B, there is some dehydration	If the patient has two or more signs in C, there is severe dehydration
Treat	Use Treatment Plan A	Weigh the patient, if possible, and use Treatment Plan B	Weigh the patient and use Treatment Plan C urgently
*Being lethargic and sleepy are not the same. A lethargic child is not simply asleep—the child's mental state is dull and the child cannot be fully awakened. †In some infants and children the eyes normally appear somewhat sunken. It may help to ask the mother if the child's eyes are normal or more sunken than usual. ‡The skin pinch is less useful in infants and children with marasmus or kwashiorkor. Signs of dehydration in severely malnourished children may be different from those in other children—see nutrition chapter for more information.			

Table adapted from World Health Organization: Department of Child and Adolescent Health and Development (CAH). *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*. Geneva, Switzerland: WHO, 2005, p. 8.

Counsel the Caregiver on the 4 Rules of Home Treatment

Rule 1: Give the child more fluids than usual to prevent dehydration

- Instruct the caregiver to do the following:
 - Breast-feed frequently and for longer at each feed.
 - If the child is exclusively breast-fed, give ORS or clean water in addition to breast-feeding.
 - If the child is not exclusively breast-feeding, give ORS or clean water (if ORS is not available, soup, rice water, or yogurt drinks may be used).
 - Avoid inappropriate fluids: commercial carbonated beverages, commercial fruit juices, sweetened tea, coffee, medicinal teas.
- Teach the caregiver how to mix the ORS and make sure that he or she has at least 2 sachets.
- Tell the caregiver to give as much water as the child wants, but as a guide he or she should give the following in addition to the usual intake:
 - Younger than 2 years—give 50–100 mL with each watery stool.
 - Older than 2 years—give 100–200 mL with each watery stool.
- Teach the mother how to give the ORS.
 - Give frequent small sips from a cup or spoon.
 - If the child vomits, wait 10 min and then continue, but more slowly.
 - Continue giving the fluids as above until diarrhea resolves.

Rule 2: Give zinc supplements

- Tell the caregiver how much zinc to give.
 - Younger than 6 months—1/2 tab (10 mg) once daily for 10–14 days
 - 6 months and older—1 tab (20 mg) once daily for 10–14 days
- Instruct caregiver how to give the zinc—if child cannot chew tablet, crush or dissolve in small amount of clean water, ORS, or expressed breast milk and give with a cup or spoon.
- Remind the caregiver to give the zinc for the full 10–14 days, regardless of whether the diarrhea resolves.

Rule 3: Continue feeding

- Instruct the caregiver what food to give.
 - Infants who are breast-fed should continue to breast-feed as often and as much as they want. During diarrheal illness infants may want to breast-feed more than usual; this should be encouraged.
 - Infants who are not breast-fed should continue to be given their usual milk feeds at least every 3 h. Special commercial formulas are unnecessary and should not be routinely given.
 - If the child is taking soft foods he or she should continue taking these in addition to milk.
- Instruct the caregiver how much food to give and how often.
 - Offer the child foods every 3–4 h (at least 6 times per day)
 - Frequent, small feeds may be better tolerated than large feeds.
 - The child may need extra food for at least 2 weeks after an episode.

Rule 4: When to return

- Instruct the caregiver to return to a health worker if the child
 - Begins passing frequent, watery stools
 - Has repeated vomiting
 - Becomes very thirsty
 - Is eating or drinking poorly
 - Develops a fever
 - Has blood in the stool
 - Does not get better in 3 days

Adapted from World Health Organization. *Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Illnesses with Limited Resources* (Geneva, Switzerland: World Health Organization, 2005), and *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*—4th rev. (Geneva, Switzerland: World Health Organization, 2005).

Figure 1. WHO Diarrhea Treatment Plan A: Treat Diarrhea at Home.

Give recommended amount of ORS in the clinic over 4 h

Give ORS

- Determine the amount of ORS to give over 4 h—see table below
 - Use the age only when the weight can't be determined. The approximate amount of ORS can be calculated by multiplying the weight by 75 (75 mL of ORS per kg).
 - If the child wants more ORS than shown, give it.

Age	<4 mo	4-11 mo	12 mo-2 yrs	2-4 yrs	5-14 yrs	≥15 yrs
Weight (kg)	<6	6-7.9	8-10.9	11-15.9	16-29.9	≥30
ORS (mL)	200-400	400-600	600-800	800-1200	1200-2200	2200-4000

- Instruct caregiver on how to give ORS.
 - Give frequent, small sips with a cup, spoon, or syringe.
 - Vomiting is not unusual in the first 1–2 h, especially if the child drinks too fast, but rarely prevents successful rehydration and usually stops. If the child vomits, wait 10 min and then continue but more slowly.
 - Continue breast-feeding whenever the child wants.
 - Children can also be offered as much clean water they want in addition to the ORS as above.
- Monitor during the 4 h to ensure that the child is taking the ORS appropriately.
- If the child develops signs of dehydration at any time switch to Treatment Plan C.

Reassess after 4 h

- Assess and classify the level of dehydration after 4 h of rehydration and select the appropriate treatment plan based on the new hydration assessment.
 - If now has no dehydration, switch to Treatment Plan A for home treatment.
 - If the child still has some dehydration, repeat Treatment Plan B.
 - If the child has severe dehydration, start Treatment Plan C immediately.
- Begin feeding the child in clinic if able—see below.

Give zinc

- After first 4 h of rehydration, begin supplemental zinc.
 - Younger than 6 months—1/2 tab (10 mg) once daily for 10–14 days
 - 6 months and older—1 tab (20 mg) once daily for 10–14 days

Begin giving food

- Except for breast milk, food should not be given during the first 3–4 h of rehydration
- After the first 4 h of rehydration, children should begin receiving food as described in Treatment Plan A and should be fed every 3–4 h.

If caregiver must leave before completing treatment

- Show the caregiver how to mix ORS.
- Instruct her on how much ORS to give to complete the 4 h of rehydration.
- Give her enough ORS to complete the rehydration and at least 2 packets for home treatment.
- Explain the 4 rules of home treatment—see Treatment Plan A.

Adapted from World Health Organization. *Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Illnesses with Limited Resources* (Geneva, Switzerland: World Health Organization, 2005), and *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*—4th rev. (Geneva, Switzerland: World Health Organization, 2005).

Figure 2. WHO Diarrhea Treatment Plan B: Treat Some Dehydration with ORS.

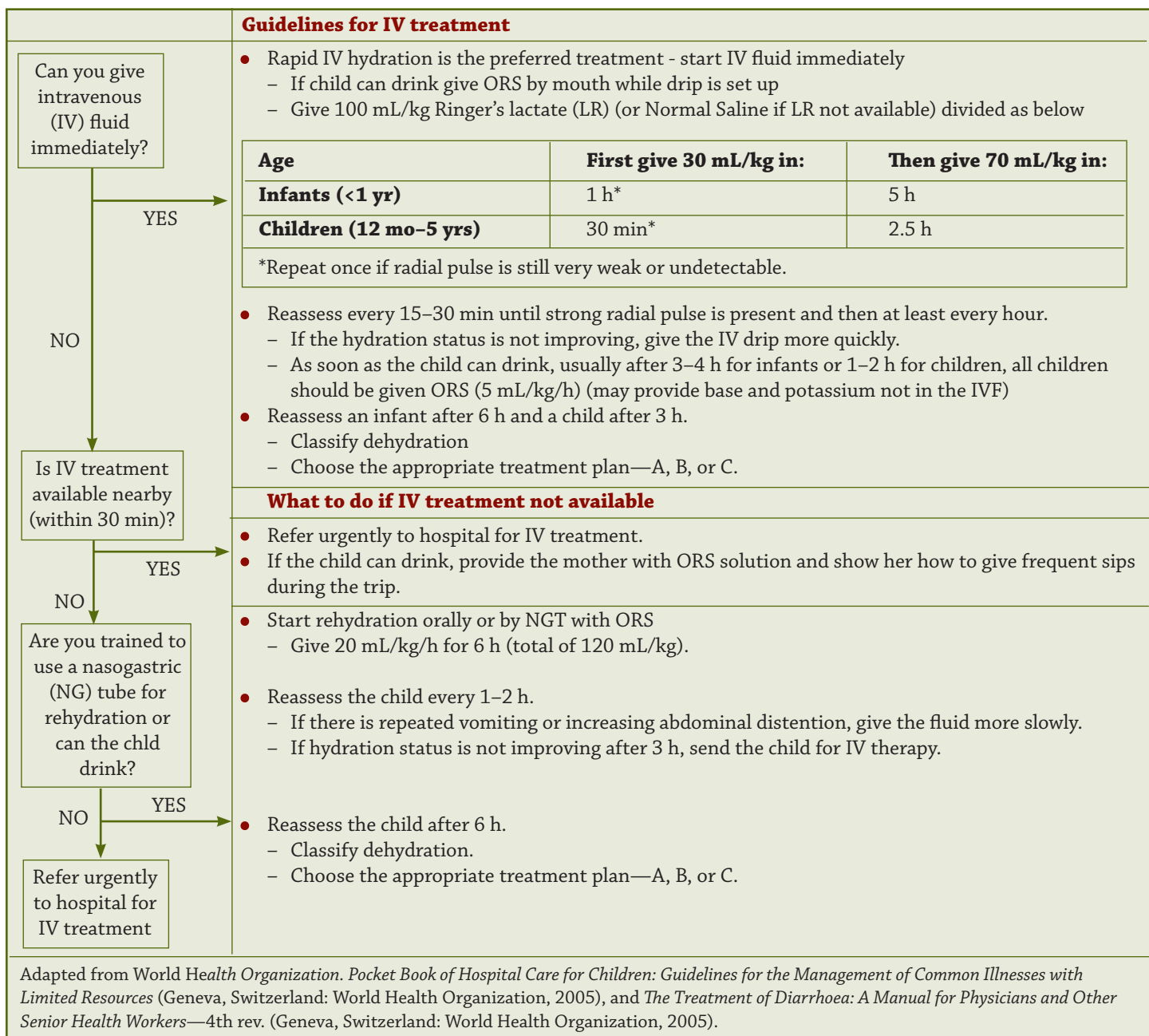


Figure 3. WHO Diarrhea Treatment Plan C: For Patients with Severe Dehydration.

WHO Treatment Plan A. The WHO has outlined the treatment of diarrhea at home as Treatment Plan A. Early intervention at home may prevent dehydration and nutritional deficits. Plan A should be used to treat patients who have

- been seen at a health facility and found to have no signs of dehydration,
- been treated at a health facility with Treatment Plan B or C until dehydration was corrected, or
- recently developed diarrhea but have not visited a health facility.

The four basic rules of home therapy using Plan A are as follows.

1. Give the patient more fluids than usual to prevent dehydration.

Which fluids to give: Fluids that should be used at home to prevent dehydration include “recommended home fluids,” which include oral rehydration salt (ORS) solutions or any fluid recommended by the national WHO program for Control of Diarrhoeal Diseases, and other drinks usually available in the home. Many countries have recommended specific home fluids for use in oral replacement treatment.

These include food-based drinks, such as undiluted cereal gruel, and sugar-salt solution. These fluids are suitable for home treatment of most children with diarrhea. Some fluids, such as carbonated beverages, commercial fruit juices, and coffee, could be dangerous and should not be given to children with diarrhea.

For patients who have been treated for dehydration at a health facility using Treatment Plan B or C, ORS solution should also be used. Recipes for oral rehydration solutions are shown in **Table 2**. Please remember to measure all quantities precisely; even minor deviations from these recipes could be dangerous.

How much fluid and how often: In general, children having diarrhea should be given as much fluid as they want. The following is a general guide for the amount of fluid to be given at home after each loose stool; continue using until diarrhea resolves.

- Children aged 2 years or younger: 50-100 mL
- Children aged 2-10 years: 100-200 mL
- Children aged 10 years or older and adults: as much as they want

2. Give supplemental zinc (10-20 mg/day for 10-14 days) to the child.

3. Give the patient plenty of food to prevent undernutrition. The child's usual diet should be continued, with the goal to give as much nutrient-rich food as the child can take. The appropriate food to give a child with diarrhea depends on the child's age and his or her preillness feeding regimen. In general, foods suitable for a healthy child are what should continue to be given to a child with diarrhea. Breast-

feeding should be continued without interruption in those children who are breast-feeding. Infants younger than 6 months who normally take formula or cow's milk and are not yet taking soft foods should continue to receive their usual feeds. Special formulas are not routinely necessary, and formula or cow's milk should not be diluted. For other infants and children, the usual cow's milk should be given throughout the illness.

Children who are aged 6 months or older, younger infants who have already begun to take soft foods, and adults should also be given soft or semisolid weaning foods. During diarrhea, give the patient as much food as he or she wants. Offer food every 3-4 h (six times a day). Small, frequent feedings are tolerated better than large feedings given less often.

4. Take the patient to a health facility if the diarrhea does not get better or if signs of dehydration or another serious illness develop.

WHO Treatment Plan B. Treatment Plan B should be used for children with some (i.e., mild to moderate) dehydration. Treatment Plan B is often initiated in the clinic or outpatient setting.

1. Giving oral rehydration therapy

- Estimate the amount of ORS solution to be given during the first 4 h with the following formula: $75 \text{ mL} \times \text{weight (in kilograms)} = \text{amount of ORS solution}$. If the patient wants more ORS than shown, give more.
- Show family members how to give the solution. Give 1 teaspoonful (5 mL) of fluid every 1-2 min to children younger than 2 years; offer frequent sips from a cup to older children and adults. Give the determined amount of fluid in 4 h.
 - If the patient vomits, wait 10 min and then continue giving ORS solution, but more slowly: 1 teaspoonful (5 mL) every 2-3 min.
 - Meet normal fluid needs. Breast-feeding should continue. For infants younger than 6 months who are not breast-fed, also give 100-200 mL of clean water during this period. Older children during this time should be offered as much plain water as they would like in addition to the ORS.

Table 2. Recipes for rehydration solutions

Homemade ORS
1/2 teaspoon of salt (2.5 g) 6 level teaspoons of sugar (30 g) 1 L of safe drinking water
ReSoMal (for severely malnourished children with diarrhea)
1 packet of standard WHO-recommended ORS Dilute in 2 L of safe drinking water 50 g of sugar (25g/L) 40 mL of mineral-vitamin mix (20 mL/L) or 1 scoop of Therapeutic CMV

ORS, oral rehydration solution; CMV, combined mineral-vitamin mix.

- Monitor treatment and reassess the patient periodically until rehydration is completed.
- Identify patients who cannot be treated satisfactorily with ORS solution by mouth and adopt a more appropriate method of treatment.

2. Monitoring treatment

- Ensure that the caregiver is giving ORS solution correctly and that the patient is taking it satisfactorily.
- Record the amount of solution taken and the number of diarrhea stools.
- Observe for signs of worsening dehydration (e.g., further loss of skin elasticity, increasing lethargy) or increasing stools, and move to Treatment Plan C accordingly.
- Observe for puffy eyelids; swollen digits; or wet, coarse breath sounds, which can indicate overhydration; if these are seen, ORS solution should be stopped, although breast-feeding and the provision of plain water should continue. When the puffiness disappears, return to Treatment Plan A guidelines if stable.
- Reclassify patient to Treatment Plan A, B, or C after 4 h. If no signs of dehydration are present, give instructions for continuing treatment at home per Treatment Plan A. If signs of severe dehydration are present, proceed to Treatment Plan C.

3. Start supplemental zinc (10-20 mg/day) after the initial 4-h period of rehydration.

4. Giving food.

- Food should not be given during the first 4-h period with the exception of breast milk.
- After the first 4-h period, all children should resume taking foods as described in Treatment Plan A.

WHO Treatment Plan C. Treatment Plan C is for patients with severe dehydration. Patients with signs of severe dehydration can die quickly from hypovolemic shock. They should be treated immediately, per Treatment Plan C:

- Decide how the fluid will be given—by intravenous (IV) drip, by nasogastric (NG) infusion, or orally.
- Decide how much IV fluid to give, and then give the fluid and reassess the patient frequently.
- Shift to Treatment Plan B or A when the patient is no longer severely dehydrated.

1. Administration guidelines, Plan C

IV Replacement

The treatment of choice for severe dehydration is IV rehydration because it is the fastest way to restore the depleted blood volume. Ringer's Lactate Solution (also called Hartmann's Solution for Injection) and normal saline (0.9% NaCl) are the preferred commercially available solutions. If these are not available, half-strength Darrow's solution with 2.5% or 5% dextrose or half-normal saline in 5% dextrose may be used. IV solutions containing only dextrose (glucose) should not be used.

Infants should be given IV fluid at a rate of 30 mL/kg of body weight in the first hour, followed by 70 mL/kg over the next 5 h, providing a total of 100 mL/kg in 6 h.

Older children and adults should be given IV fluid at a rate of 30 mL/kg within 30 min, followed by 70 mL/kg in the next 2.5 h, providing a total of 100 mL/kg in 3 h. After the first 30 mL/kg has been given, a strong radial pulse should be easily felt. If it is still weak and rapid, a second infusion of 30 mL/kg should be given at the same rate; however, doing so is rarely necessary. Small amounts of ORS solution should also be given by mouth (about 5 mL/kg/h) as soon as the patient can drink to provide additional potassium and base. Doing so is usually possible after 3-4 h in infants and after 1-2 h in older children and adults.

NG Replacement

If IV therapy is not possible, an NG tube can be used to give ORS solution, provided that there is a person trained in the tube's placement and maintenance. This approach is not as satisfactory as IV infusion because the fluid cannot be given as rapidly, and additional time is required for it to be absorbed from the intestine. The maximum rate of fluid infusion is about 20 mL/kg/h. When higher volumes are administered, abdominal distension and repeated vomiting are frequent problems.

Oral Replacement

If IV and NG therapy are not possible or will be delayed, and if the patient can drink, ORS solution should be given by mouth at a rate of 20 mL/kg/h. This approach has the same disadvantages as those of NG therapy, and it cannot be used for patients who are lethargic or unconscious. Children younger than 2 years should be given ORS solution by spoon, about 1 teaspoonful (5 mL)/min. Older

children and adults may drink the solution from a cup. Patients with abdominal distension caused by paralytic ileus should not be given ORS solution either orally or by NG tube.

2. Reassessing the patient

Signs of a satisfactory response to rehydration are return of a strong radial pulse, improved level of consciousness, ability to retain oral fluids, improved skin turgor, and urinary output nearly equal to fluid intake. When these signs are observed, the interval between assessments can be lengthened. If the signs of dehydration remain unchanged or worsen, and especially if the patient continues to pass watery stools, the rate of fluid administration and the total amount of fluid given for rehydration should be increased.

In addition to rehydration therapy, the patient's normal need for water must be met. Breast-feeding should be resumed as soon as an infant can suck. Infants younger than 6 months who are not breast-fed should be given 100-200 mL of plain water during the first 6 h if they can drink. Older children and adults should be given water to drink as soon as they desire it, provided that vomiting has subsided. This water is in addition to any ORS solution being given.

3. Transition to Treatment Plans B and A

At the end of the planned rehydration period outlined in Treatment Plan C (usually 3-6 h), the patient's hydration status should be carefully reassessed. If signs of severe dehydration are still present, rehydration therapy must be continued per Treatment Plan C. Otherwise, further treatment should follow Plan B if some signs of dehydration remain or Plan A if there are no signs of dehydration. In either case, ORS solution should be used. Before removing the IV line, however, it is wise to give ORS solution for at least 1 h to ensure that oral replacement therapy is feasible. If possible, patients presenting with severe dehydration should be hospitalized until the diarrhea subsides. Otherwise, they should be observed for at least 6 h after rehydration before returning home to make sure that the caregiver can maintain their hydration by using the ORS solution.

Dysentery

Dysentery is diarrhea with visible blood in the stool. Abdominal cramps, tenesmus (unproductive, painful straining), fever, and poor appetite are common

associated symptoms. Infection with *Shigella* is the most common cause of dysentery, but other potential causes include infections with *Salmonella*, enterohemorrhagic and enteroinvasive *E. coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Schistosoma*, and *Entamoeba histolytica*. The diagnosis of dysentery can be made by history of blood in the stool or by visual inspection of stool for blood. A stool sample should be sent to a lab, if available, for microscopy for fecal leukocytes and ova and parasites, and for culture and sensitivities, though in many settings doing so may not be possible. Populations at risk for severe disease and poor outcomes related to dysentery include the following: infants younger than 1 year, especially those not breast-feeding; malnourished children; children recovering from measles infection in the last 6 weeks; and those who develop severe dehydration, altered consciousness, or have an associated convulsion. Malnourished children with dysentery should be admitted to a hospital for inpatient care, and strong consideration should be given to admitting these other high-risk populations. In the absence of these risk factors, most children can be treated as outpatients.

Antibiotic treatment is recommended for children with dysentery, though resistance to routinely given antibiotics is a growing problem. The following antibiotics are ineffective against *Shigella*, and none of these should be given for the treatment of dysentery: metronidazole, tetracyclines, chloramphenicol, amoxicillin, aminoglycosides (gentamicin, kanamycin), nitrofurans (nitrofurantoin, furazolidone), and first- or second-generation cephalosporins. Cotrimoxazole and ampicillin were effective for *Shigella*, but there is now widespread resistance and these antibiotics should not be used empirically. Nalidixic acid is an antibiotic that was commonly used to treat dysentery but is currently not recommended for this indication.

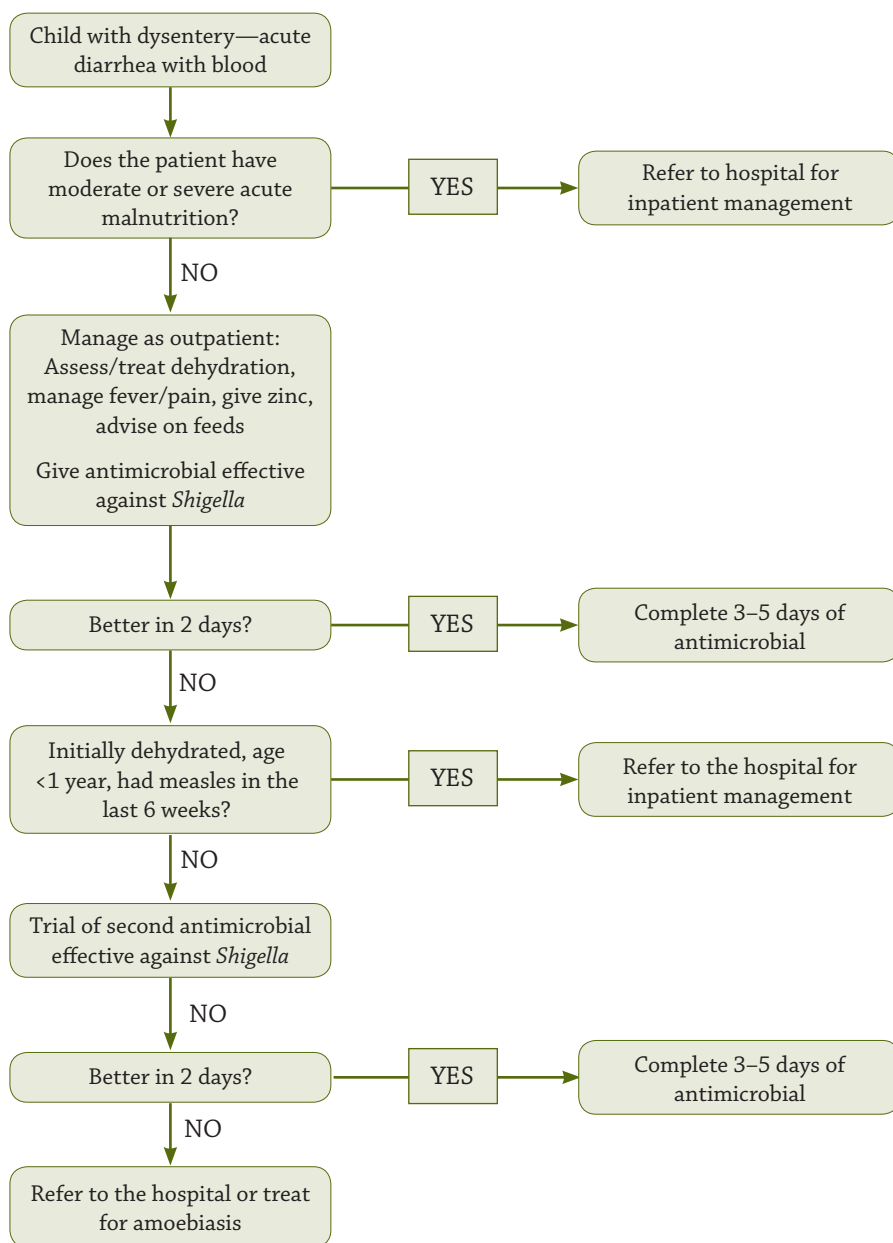
Treatment of dysentery should be guided by the local sensitivity pattern of *Shigella* isolates. In the absence of known local resistance patterns, the WHO recommends ciprofloxacin as the first-line treatment for dysentery. The use of fluoroquinolones such as ciprofloxacin in children has been restricted because of the concern for joint damage that was seen as a side effect of these medications in animals. Sometimes, though, the benefits outweigh the small risks, and a short course of ciprofloxacin is both safe and effective for use in the treatment of dysentery in children. Other antibiotic options include extended-

spectrum cephalosporins (ceftriaxone, cefotaxime) and pivmecillinam. See **Figure 4** for dosing information on these medications for adults and children. Empiric treatment for *E. histolytica* should not be given routinely because it is a rare cause of dysentery in children. Treatment for *E. histolytica* in children is recommended only when the results of stool microscopy from a reliable lab show evidence of infection or when a child has failed to respond to two antibiotics to which *Shigella* is susceptible.

See **Figure 4** for an algorithm for the management of dysentery. Supportive care, including management of dehydration, appropriate feeding, provision of zinc, and control of fever and pain, should be given to all children just as in acute diarrhea according to the protocols referred to in the previous section. Malnourished children with dysentery should be admitted to a hospital for inpatient care. Most other children may be managed safely as outpatients. An antibiotic to which *Shigella* is sensitive should be given and its effect reassessed in 2 days. If the child is improved, as manifested by resolution of fever, fewer stools, less blood in the stools, and improved appetite and activity, the child should complete a 3- to 5-day course of the antibiotic. If the child is not improved after 2 days, the child should be given a second antibiotic to which *Shigella* is sensitive and reassessed 2 days later. If the child is improved at this point, a 5-day course of this antibiotic should be completed. If the child is still not improved, both admission to a hospital and a course of treatment for amoebiasis should be considered.

Persistent diarrhea

Persistent diarrhea is diarrhea, with or without blood, that lasts for more than 14 days. Persistent diarrhea may be



Ciprofloxacin Dosing	Children			Adults 500 mg twice a day for 3 days
	15 mg/kg twice a day for 3 days			
	<1 yr	1–4 yrs	5–14 yrs	
Tablets, 500 mg	1/4 tab 2 times a day for 3 days	1/2 tab 2 times a day for 3 days	1 tab 2 times a day for 3 days	1 tab 2 times a day for 3 days
Tablets, 250 mg	1/2 tab 2 times a day for 3 days	1 tab 2 times a day for 3 days	2 tab 2 times a day for 3 days	2 tab 2 times a day for 3 days

Algorithm adapted from World Health Organization: Department of Child and Adolescent Health and Development. *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*. Geneva, Switzerland: WHO, 2005. Table adapted from World Health Organization. Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* 1. Geneva, Switzerland: WHO, 2005.

Figure 4. Algorithm for the management of dysentery.

related to poor absorption of nutrients by the intestines because of damage done by previous infections. Changes in the diet may help to restore adequate nutrition and hydration while allowing the intestine to heal so that a normal diet can be resumed. In children with HIV it is more likely that persistent diarrhea is related to an infection. Organisms that almost never cause infection in immunocompetent children, such as CMV and MAC, may cause persistent diarrhea in HIV-infected children. Other organisms that usually cause a self-limited infection in immunocompetent children, such as *Cryptosporidium* spp.; *Isospora* spp.; *Microspora* spp.; and even common viral and bacterial infections such as rotavirus, adenovirus, *Salmonella* spp., *Shigella* spp., and *Campylobacter* spp., may result in persistent diarrhea in HIV-infected children. *Giardia* spp. is another infection that may cause persistent diarrhea with variable frequency. Most infectious causes of persistent diarrhea in HIV-infected children are more likely in the presence of advanced or severe immunodeficiency. Other causes of persistent diarrhea include HIV enteropathy (malabsorption without any other identifiable cause), postinfectious enteritis, inflammatory bowel disease, thyrotoxicosis, encopresis, and pancreatic or liver disease causing fat malabsorption—though these causes will be much less common than infections. When possible, stool specimens should be sent to the laboratory for an evaluation to include microscopy for leukocytes, ova, and parasites; culture and sensitivities; and any available tests for specific organisms.

Most children with persistent diarrhea can be managed as outpatients. Children with acute malnutrition and persistent diarrhea should be referred to a hospital for inpatient care. Inpatient referral should also be strongly considered for children with persistent diarrhea who are younger than 4 months, have signs of significant dehydration, or have other serious infections such as pneumonia or sepsis.

Treatment of persistent diarrhea includes four major components:

- Appropriate fluids to prevent and treat dehydration
- A nutritious diet that does not cause diarrhea to worsen
- Supplementary vitamins and minerals including zinc
- Antimicrobial treatment when appropriate

Patients should be assessed for dehydration and given appropriate fluids as described in previous sections. Children with persistent diarrhea require nutritious diets that are low in lactose. Infants younger than 6 months should be given exclusive breast-feeding if possible or, for those who cannot breast-feed, yogurt or lactose-free formula, if available. Children older than 6 months should be given one of the recommended diets as listed in **Table 3**. The first diet is low in lactose and will result in improved diarrhea for 65% of children. If the child fails the first diet, as indicated by an increase in stool frequency (usually >10 per day) and worsening dehydration, or a failure to gain weight after 7 days of the first diet, then the second diet, which is low in lactose and in starch, should be given. All children with persistent diarrhea should receive supplementary vitamins and minerals once a day for at least 14 days.

For most children, routine treatment of persistent diarrhea with antimicrobials is not effective and should not be given but may be appropriate in certain circumstances. Any nonintestinal infections, such as pneumonia, sepsis, or urinary tract infection, should be identified and treated according to national guidelines.

Table 3. Recommended example diets for children older than 6 months with persistent diarrhea

First Diet	
Ingredient	Amt (g)
Full-fat dried milk	11 (or whole liquid milk 85 mL)
Rice	15 (uncooked rice)
Vegetable oil	3.5
Cane sugar	3.0
Water to make total vol of 200 mL	
With this diet, 130 mL/kg gives 110 kcal/kg. This diet provides 83 kcal/100 g, 3.7 g of lactose/kg of body weight/day, and 11% of calories as protein.	
Second Diet	
Ingredient	Amt (g)
Whole egg	64
Rice	3
Vegetable oil	4
Glucose	3
Water to make total vol of 200 mL	
With this diet, 145 mL/kg gives 110 kcal/kg. This diet provides 75 kcal/100 g. If finely ground, cooked chicken can replace the whole egg, giving 70 kcal/100g.	

Table adapted from World Health Organization: Department of Child and Adolescent Health and Development (CAH). *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*. Geneva, Switzerland: WHO, 2005, p. 21.

Persistent diarrhea may not resolve until these non-intestinal infections have been adequately treated. Children with persistent diarrhea with blood should be treated as described in the section on dysentery. Patients should not be treated for amoebiasis or giardiasis unless laboratory examination confirms infection with these organisms. HIV-infected children with advanced or severe immunodeficiency are at higher risk for an infectious cause of their persistent diarrhea. When appropriate lab facilities are available, antibiotic treatment should not be given empirically and should be based on results of laboratory examination. In areas where lab facilities are not available, consideration may be given to empiric treatment of ill HIV-infected children with persistent diarrhea and advanced or severe immunosuppression with ciprofloxacin (to cover most bacterial causes), cotrimoxazole (to cover treatable parasitic infections), and metronidazole (to cover giardiasis). Persistent diarrhea lasting longer than 14 days and not responding to appropriate treatment is a WHO Clinical Stage 3 condition. Reconstitution of the HIV-infected child's immune system with antiretroviral treatment will sometimes be the only effective way to treat persistent diarrhea in these children.

Diarrhea in severe acute malnutrition

Severely malnourished children who develop diarrhea have a higher risk of developing serious complications from their diarrhea and have much worse outcomes than those of well-nourished children. Children with severe malnutrition are also sensitive to fluids and can develop life-threatening heart failure from overhydration. For this reason, all children with diarrhea should have an assessment for severe acute malnutrition, and those who are noted to be malnourished should be assessed and managed according to the following protocol.

The assessment for the presence and severity of dehydration in malnourished children is difficult: many of the signs and symptoms described in the preceding section on dehydration are unreliable. Some signs and symptoms that are more reliable indicators of dehydration in malnourished children include a history of diarrhea, recently sunken eyes, cool hands and feet, weak or absent pulses, and diminished urine flow. A child's mental state, skin elasticity/skin pinch, dry mouth, and lack of tears may be less reliable signs of hydration status in these children.

With the exception of the child with shock, rehydration in severely malnourished children should be done orally. The standard ORS solution has too much salt for these children, so ReSoMal should be used instead for rehydration. ReSoMal is commercially available but also can be prepared using ORS packets (see **Table 2** for a ReSoMal recipe). Usually 70-100 mL/kg of fluid is enough to restore adequate hydration, but this volume should be given over 12 h. ReSoMal should be given at a dosage of 5 mL/kg every 30 min for 2 h. The total amount of fluid given should depend on resolution of the signs of dehydration, the child's thirst, and passage of urine. If there is ongoing watery diarrhea, these fluid losses should be replaced with ReSoMal, with children younger than 2 years getting 50-100 mL with each watery stool and older children receiving 100-200 mL with each stool. These children should be monitored for any signs of overhydration, such as engorged neck veins, edema including puffy eyelids, and increased respiratory and heart rates. If any of these signs appear, rehydration should be stopped immediately. If the child refuses to or cannot take fluids orally, an NG tube should be placed and fluids administered through the tube.

IV fluids should be reserved for cases of shock, in which either half-strength Darrow's solution with 5% glucose, Ringer's Lactate with 5% glucose, or half-normal saline with 5% glucose should be given at 15 mL/kg over 1 h. When signs of shock have resolved, further rehydration can be continued orally as described earlier.

Feeding should begin promptly in severely malnourished children. Breast-feeding should not be interrupted, even during rehydration. F-75 should be given as soon as possible, usually within 2-3 h after starting rehydration. See the chapter on nutrition for further information on caring for severely malnourished children.

WASTING SYNDROME

Wasting syndrome is an AIDS-defining condition and is a WHO Clinical Stage 4 diagnosis for both adults and children. For adults, the WHO defines wasting syndrome as

- unexplained involuntary weight loss (>10% of baseline body weight), with obvious wasting or body mass index less than 18.5 plus
 - unexplained chronic diarrhea (loose or watery stools more than three times daily) reported for more than 1 month, or

- reports of fever or night sweats for more than 1 month without other cause and lack of response to antibiotics or antimalarial agents.

For children, WHO defines wasting as follows:

- persistent weight loss not explained by poor or inadequate feeding or other infections; and/or
- visible wasting of muscles, with or without edema of both feet; and/or
- weight for height of -3 standard deviations from the mean, as defined by the WHO Integrated Management of Childhood Illness guidelines; and
- not adequately responding in 2 weeks to standard therapy.

Wasting causes loss of lean body mass. In developing countries in Africa, failure to gain weight and weight loss are the most common presenting signs of HIV disease, explaining why HIV was known as “slim disease” in many places. Wasting syndrome can be attributed to inadequate caloric intake, malabsorption of nutrients from the GI tract, increased metabolic rates, and other direct effects of HIV infection. See the chapter on nutrition for a more in-depth discussion of causes of weight loss in HIV-infected patients.

Evaluation of a patient with wasting syndrome should include performing a nutritional assessment. The nutritional assessment should include growth measurements and dietary history (see chapter on nutrition). The patient should be assessed for any clinical signs or symptoms that suggest malabsorption, such as chronic diarrhea. Wasting can sometimes be alleviated with the use of antiretroviral agents and/or nutritional supplements. Oral supplementation should be offered to increase caloric intake. If oral supplementation fails, enteral supplementation should be used. See the nutrition chapter for more information on nutritional assessments and interventions.

HEPATITIS

Hepatitis is inflammation of the liver. Signs and symptoms of hepatitis can include jaundice, fever, liver enlargement, abdominal tenderness, pruritus (itching), nausea/vomiting, and diarrhea. Often patients with hepatitis will have no symptoms, and the only indication of liver inflammation will be elevated liver enzymes in the blood (AST/ALT). The most common causes of hepatitis in HIV-infected patients are infections. Many different viral infections cause hepatitis, including hepatitis viruses A-E and G, Epstein-Barr virus, CMV, and HIV

itself. Many of the medications taken commonly by HIV-infected adults and children can cause liver damage, which may present with signs, symptoms, and laboratory abnormalities identical to those of infectious hepatitis. Some medications well known to cause liver damage include nevirapine, stavudine, ritonavir, trimethoprim-sulfamethoxazole, rifampicin, isoniazid, pyrazinamide, fluconazole, and ketoconazole.

Infection with two or more organisms is known as coinfection. Coinfection with HIV and the hepatitis viruses is common, and detailed discussions of hepatitis B and C infections follow.

Hepatitis A

Hepatitis A is a virus spread by fecal-oral route, often through contaminated food, and hand washing and good hygiene can help prevent transmission of the virus. Immunization to prevent hepatitis A is recommended in HIV-infected patients with chronic hepatitis B and C infection but may not be available in many settings. Hepatitis A infection is treated symptomatically, is usually self-limited, and rarely progresses to liver failure.

Hepatitis B

Hepatitis B is transmitted by contact with blood, through sexual contact, or from mother to child, but many cases have no known risk factor. Condoms can reduce the risk of sexual transmission. Hepatitis B may or may not cause a symptomatic hepatitis at the time of acute infection and sometimes may progress to chronic hepatitis. The likelihood of developing chronic hepatitis B depends strongly on age at the time of infection, with 90% of perinatally infected infants but only 2%-6% of people infected as older children or adults developing chronic infection. Adults and children with chronic hepatitis B are at high risk for developing other serious liver diseases, including cirrhosis and primary hepatocellular carcinoma, a cancer of the liver. Vaccination against hepatitis B is recommended for HIV-infected patients, and routine childhood vaccination is becoming more widespread. Indications for treatment of chronic hepatitis B infection include evidence of ongoing viral replication (detectable hepatitis B virus [HBV] DNA in the blood) for 6 months, persistent elevation of transaminases, and/or evidence of chronic hepatitis on liver biopsy. Medications approved for the treatment of chronic hepatitis B infection in adults include interferon α , lamivudine (3TC), adefovir, and entecavir, though only lamivudine and interferon α

have been approved for use in children. New treatments for hepatitis B are currently being studied, including the antiretroviral medication tenofovir disoproxil fumarate (TDF). In HIV-HBV-coinfected adults and children, lamivudine and tenofovir should never be given alone as treatment for HBV because HIV will rapidly develop resistance. In many settings, these complex tests and treatments are not available, and the best intervention to offer HIV-HBV-coinfected patients with chronic hepatitis will be highly active antiretroviral therapy.

Hepatitis C

Hepatitis C coinfection with HIV is becoming more common worldwide, especially among IV drug users. Hepatitis C virus is spread primarily by contact with infected blood, and perinatal transmission of hepatitis C is increasing among children born to women who are coinfecting with HIV and hepatitis C. As with hepatitis B, many cases have no known risk factor. Acute infection with hepatitis C is usually asymptomatic, but 50%-60% of children and 60%-70% of adults will go on to develop chronic hepatitis, of which many will progress to cirrhosis and primary hepatocellular carcinoma. All infants born to women coinfecting with HIV and hepatitis C should be screened for hepatitis C if blood testing is available. Treatment for hepatitis C is available and does not appear to interfere with HIV treatment. Treatment should be started in patients with chronic hepatitis C progressing to cirrhosis. The two treatment regimens that are currently used are interferon alfa alone and interferon alfa in combination with ribavirin. A recent study of peginterferon alfa-2a plus ribavirin found that this combination was more effective in treating HIV-hepatitis C-coinfecting patients than the combination of interferon alfa and ribavirin or peginterferon alfa-2a alone. In many settings, these complex tests and treatments may not be available, and the best intervention to offer HIV-hepatitis C-coinfecting patients with chronic hepatitis will be highly active antiretroviral therapy.

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