Approach to the child with acute diarrhea in resource-limited countries

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INTRODUCTION — Diarrhea is the passage of loose or watery stools at least three times in a 24 hour period. Illness is the second leading cause of child mortality; among children younger than five years, it causes 1.5 to 2 million deaths annually [1,2]. In resource-limited countries, infants experience a median of six episodes annually; children experience a median of three episodes annually [3].

Diarrheal illness may consist of acute watery diarrhea, invasive (bloody) diarrhea, or chronic diarrhea (persistent ≥14 days). This classification facilitates the approach to management of childhood diarrhea. Issues related to the etiology, clinical assessment, treatment, and prevention of acute watery diarrhea and invasive diarrhea in children in resource-limited countries are reviewed here. Issues related to chronic diarrhea in children are discussed separately. (See "Persistent diarrhea in children in resource-limited countries").

ETIOLOGY — Most cases of acute diarrhea in resource-limited countries are caused by infectious gastroenteritis. Less commonly, acute diarrhea can be a symptom of a systemic infection or an intra-abdominal surgical emergency.

Infectious gastroenteritis — The most common microbiological causes of infectious gastroenteritis differ by age group, geographical region, and type of diarrhea. In a large study of children five years or younger at seven sites in Asia and Africa, stool samples from 9439 children with moderate to severe diarrhea and from 13129 controls were tested for a panel of microorganisms [4]. Rotavirus, Cryptosporidium, Shigella, and enterotoxigenic Escherichia coli (ETEC) were important pathogens at all study sites, and most attributable cases of diarrhea were due to these organisms. Rotavirus was the most common pathogen among children under two years old, whereas Shigella was the most frequently isolated pathogen in children aged two to five. Cryptosporidium was the second most common pathogen among infants under one year old, but was infrequently detected in children older than two years. Aeromonas was a frequent pathogen in Pakistan and Bangladesh, and Campylobacter jejuni in Pakistan, Bangladesh, and India. Vibrio cholerae was an important cause of diarrhea at those three Asian sites as well as Mozambique.

Acute diarrhea can also be classified as watery versus invasive, bloody diarrhea, and the microbiological etiologies differ by type, as discussed below (table 1) [5].

Acute watery diarrhea — In infants and young children, acute watery diarrhea is most often due to rotavirus; in older children, it is most often due to E. coli (ETEC) [5]. Cryptosporidium also appears to be an important cause among infants, even in the absence of HIV infection [4]. Many etiologic agents of acute watery diarrhea cause symptoms that are clinically indistinguishable. It is usually not necessary to identify a specific microbiologic diagnosis in order to provide supportive care, and antibiotics are not usually indicated. (See "Clinical manifestations and diagnosis of rotavirus infection" and "Pathogenic Escherichia coli").

V. cholerae is an important bacterial cause of childhood diarrhea in endemic areas, and often occurs in large epidemics.

Invasive (bloody) diarrhea — Shigellosis is the most common etiology of invasive, or bloody, diarrhea among children in resource-limited countries. It is a major cause of mortality and is associated with a high incidence of bacteremia, seizures, and several other life-threatening complications. The four species are Shigella dysenteriae, Shigella flexneri, Shigella boydii, and Shigella sonnei. S. flexneri is the predominant species in children in resource-limited settings [6]. Children with shigellosis benefit from treatment with antibiotic therapy (table 2). (See "Shigella..."
Associated conditions — Systemic infections associated with diarrhea include influenza, measles, dengue fever, human immunodeficiency virus infection, and malaria. Serious bacterial infections associated with diarrhea include pneumonia, urinary tract infection, meningitis, and sepsis. Surgical emergencies such as intussusception or appendicitis also may present with diarrhea. These concomitant illnesses are major causes of mortality among children brought to medical attention for acute diarrhea [7-9].

Recurrent episodes of acute diarrhea may be a presenting feature in children with HIV infection, although HIV disease is more commonly associated with persistent diarrhea (which constitutes an AIDS defining illness). The diagnosis of HIV infection should be considered in children presenting with diarrhea, failure-to-thrive, adenopathy, and/or hepatosplenomegaly. (See "Diagnostic testing for HIV infection in infants and children younger than 18 months of age".)

CLINICAL ASSESSMENT — The assessment of the child with diarrhea can be divided into four components of clinical management:

- Classification of the type of diarrheal illness
- Assessment of hydration status
- Assessment of nutritional status
- Assessment of co-morbid conditions

Classification of diarrhea — The assessment of a child with diarrhea should include a history of the duration, frequency, and character of the diarrhea, as well as an assessment of the stool (picture 1 and picture 2). Patients can be classified as having:

- Acute watery diarrhea — loose or watery stools at least three times in a 24 hour period.
- Invasive diarrhea — (synonymous with dysentery) gross blood (by history or inspection) in the stool of <14 days duration (picture 2), typically accompanied by fever. It is usually the result of exudative inflammation of the distal small bowel and colonic mucosa in response to bacterial invasion.
- Persistent diarrhea — loose, watery, or bloody stools of ≥14 days. (See "Persistent diarrhea in children in resource-limited countries".)

Other characteristics of the diarrhea and associated symptoms may be clues as to the etiology. As an example, the diagnosis of cholera is suggested by a short history (usually less than 24 hours) of vomiting and passage of voluminous watery diarrhea, which may have a characteristic rice-water appearance, associated with severe dehydration (picture 1). It is important to distinguish cholera from other causes of acute watery diarrhea because patients with severe cholera may have more rapid fluid losses and typically benefit from antibiotic therapy. (See "Overview of cholera".)

Hydration status — Death due to dehydration is an important cause of mortality in resource-limited settings. It can occur because the initial dehydration status is underestimated and/or because the extent of ongoing fluid loss is underappreciated.

The degree of dehydration should be assessed at presentation based on physical signs and symptoms. Several studies have demonstrated that using a combination of three to four physical signs reliably predict dehydration of 3 to 5 percent or greater [10-12]. The World Health Organization (WHO) has issued recommendations for assessing dehydration based on four clinical signs that have been associated with dehydration in several studies (table 3) [10-12]. (See "Clinical assessment and diagnosis of hypovolemia (dehydration) in children".)

Following the initial assessment, ongoing fluid losses should be estimated based on the volume of emesis and stool. These assessments are essential for determining the volume, route, and pace of rehydration therapy needed.

Individual clinical signs and symptoms have important limitations if used as independent predictors of the degree of dehydration. The absence of any particular dehydration sign is not sufficient proof that the patient has been adequately hydrated. For example, a sunken anterior fontanelle is a poor predictor of dehydration in infants, a patient who sheds tears may still be dehydrated, and hypotension is a late finding in dehydrated children (and may be absent even in severe dehydration) [13].
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Children presenting with diarrhea in resource-limited countries should be assessed for malnutrition according to WHO standards, which are reviewed separately [17]. (See "Malnutrition in children in resource-limited countries: Clinical assessment".)

Children with acute diarrhea and malnutrition are at increased risk for developing fluid overload and heart failure during rehydration. The risk of serious bacterial infection is also increased. As a result, such children require an individualized approach to rehydration, nutritional care, and antibiotics. (See 'Malnourished children' below.)

**Physical examination** — Assessment of a child with acute diarrhea should include evaluation of the following:

- **Temperature** — Fever is common in the setting of diarrheal illness. The presence of fever or hypothermia in a patient with watery diarrhea should also raise clinical suspicion of a comorbid illness. Fever in areas where malaria is endemic should prompt appropriate diagnostic evaluation. (See "Diagnosis of malaria".)

- **Respiratory tract** — Tachypnea can be a sign of pneumonia in the setting of cough or difficulty breathing; uses the following parameters: infants <2 months: >60 breaths/min; infants 2 to 12 months: >50 breaths/min; children 1 to 5 years: >40 breaths/min; children ≥5 years: >20 breaths/min [18]. Children with dehydration should be reassessed for pneumonia following initial rehydration. In some cases, a chest radiograph may be required for diagnosis of pneumonia, particularly in severely malnourished and dehydrated patients [19-21].

- **Abdomen** — Abdominal pain out of proportion to typical gastroenteritis raises the possibility of a surgical emergency. Among patients with severe dysentery due to *Shigella*, intestinal obstruction was reported in 2.5 percent of hospitalized cases in one series [22]. Intussusception may present with acute bloody diarrhea and severe intermittent abdominal pain; in some cases a cylindrical abdominal mass is palpable. In young children, appendicitis may also present with diarrhea and abdominal pain. (See "Emergent evaluation of the child with acute abdominal pain".)

- **Central nervous system** — Moderate dehydration can lead to irritability; severe dehydration can lead to lethargy and coma. Encephalopathy and/or seizures can occur in the setting of severe disease due to *Shigella*, and less commonly in systemic *Salmonella* infection. The differential diagnosis of seizures in a child with diarrhea includes hypoglycemia, hyponatremia, hypernatremia, encephalopathy, meningitis, and febrile seizures. Meningeal signs may be absent in infants with meningitis; therefore any abnormal neurologic findings should raise suspicion for meningitis. (See "Bacterial meningitis in children older than one month: Clinical features and diagnosis", section on 'Clinical features'.)

**Diagnostic studies** — Most children with acute diarrhea do not require laboratory testing, although in complex cases some laboratory studies may be useful. Patients with seizures or altered consciousness should have glucose and electrolyte assessment if possible. Children with suspected pneumonia, sepsis, meningitis, urinary tract infection, or HIV infection should have the relevant investigations. Imaging studies are warranted for patients with acute abdominal findings on physical examination.

Microscopy can be used for presumptive diagnosis of two important causes of gastroenteritis. Cholera may be diagnosed using dark field microscopy to detect motile *Vibrios*, which appear as "shooting stars". In the setting of acute bloody diarrhea, direct microscopic evidence of *Entamoeba* trophozoites containing red blood cells is a sufficient diagnostic finding warranting treatment for amoebic dysentery (rather than shigellosis) (picture 3).

Microbiology laboratory evaluation, when available, is warranted for patients with invasive diarrhea who do not respond to empiric antibiotic therapy. Other judicious uses of microbiology data include surveillance to detect epidemics and evaluation of antimicrobial susceptibility patterns of selected pathogens.

In other cases, microbiological identification of specific pathogens in the setting of diarrhea is of uncertain significance, as several pathogens can often be found in the stool of children in resource-limited settings during both diarrheal illnesses and asymptomatic periods; diarrhea appears to be associated with a state of overall pathogen excess. As an example, in a study from Bangladesh that included 147 infants followed from birth until one year of age, an average of 5.6 and 3.3 pathogens were detected through polymerase chain reaction (PCR) in stools sampled during diarrheal
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**TREATMENT** — Treatment consists of correcting fluid and electrolyte losses, administering appropriate nutrition, and managing associated comorbid conditions. In the setting of invasive diarrhea, treatment of the underlying cause of illness is also necessary. The World Health Organization (WHO) provides guidelines for the management of diarrheal illness in resource-limited countries in "The Treatment of Diarrhea: A Manual for Physicians and Other Senior Health Workers" [24].

**Acute watery diarrhea**

**Fluid and electrolytes** — Fluid management consists of two phases: replacement and maintenance. The goal of replacement therapy is to replenish deficits in water and electrolytes lost. The replacement phase is continued until signs and symptoms of diarrhea are absent and the patient has urinated; ideally this is achieved during the first few hours of therapy. Maintenance therapy counters ongoing losses of water and electrolytes; this phase is continued until all symptoms resolve.

Most children with acute diarrhea should be treated with Oral Rehydration Solution (ORS), a mixture of water, salts, and glucose, in both the replacement and maintenance phase. For children with severe dehydration, the replacement phase should begin with intravenous fluids (IVF). The compositions of common oral and intravenous rehydration solutions are listed in the Table (**table 4**). (See "Oral rehydration therapy" and "Treatment of hypovolemia (dehydration) in children".)

Fluid loss in acute watery diarrhea can be isonatremic, hyponatremic, or hypernatremic. The advantage of correcting sodium imbalances with ORS is that the correction occurs relatively gradually, reducing the risk of the neurologic complications due to rapid shifts in osmolarity that may occur with intravenous fluids.

Stool potassium losses commonly result in hypokalemia. This most often manifests with muscle weakness, though in more severe cases may be complicated by paralytic ileus and/or arrhythmia. Among 140 patients who died following rehydration therapy in Bangladesh, hypokalemia was a proximate cause of death in 9 percent of cases [25]. Potassium losses are generally replaced using ORS, though some isotonic intravenous fluids contain higher amounts of potassium to replace these losses.

The approach to fluid and electrolyte management depends on the degree of dehydration:

- **No signs of dehydration** — According to the WHO classification, patients with no overt signs of dehydration are <5 percent dehydrated; they do not require a replacement phase and can begin maintenance therapy (**table 3**). Such patients usually do not require hospital admission and may be sent home after a brief period of observation to verify that they are tolerating oral maintenance fluids. Ideally ORS is administered for maintenance fluids to counter ongoing fluid and electrolyte losses.

  If the stool output is modest, ORS may not be necessary and ongoing feeding along with supplemental fluids may be sufficient. Acceptable supplemental fluids are listed in the Table (**table 5**). In general, patient thirst should be sufficient to guide the volume of ORS administered; children under two years should receive approximately 50 to 100 mL of ORS for each episode of diarrhea or vomiting and children over two years should receive 100 to 200 mL of ORS for each episode. All children over the age of six months should also receive zinc therapy. (See 'Vitamins and minerals' below.)

- **Some dehydration** — According to the WHO classification this category includes children with 5 to 10 percent dehydration (**table 3**). These children require replacement therapy with ORS in a supervised setting (**table 6**). If ongoing stool losses are profound, these losses can be added to the initial amount of fluids given over the first four hour period. Ideally stool output is measured by collecting stool using a cholera cot (**picture 4**). Alternatively, stool output can be estimated as 10 to 20 mL/kg of body weight for each diarrheal stool.

  Observed fluid replacement and frequent reassessment of hydration status are essential for patients in this category. Replacement fluids should be continued under supervision until all the initial signs of dehydration are absent and the patient has urinated. This may require more fluids than initially estimated. Once dehydration has been corrected, maintenance fluids to counter ongoing losses can be managed as for patients with no signs of
oral rehydration or progress to severe dehydration; this occurs in approximately 3 to 5 percent of patients [26]. Such patients require management as outlined for severe dehydration below.

- Severe dehydration — According to the WHO classification, this category includes children with >10 percent dehydration (table 3). Severe dehydration is a medical crisis and should be managed urgently with intravenous fluids in a hospital setting. However, patients with severe malnutrition should not receive intravenous fluids, as discussed below. (See Malnourished children below.)

The goal of rehydration with intravenous fluids is to stabilize the circulation immediately. This requires that isotonic fluids be administered as quickly as possible, often through multiple sites of intravenous access. For resource-limited settings the WHO recommends that a bolus of isotonic crystalloid fluid of 30 mL/kg given over 30 (or one hour in infants <12 months), followed by additional isotonic fluids to correct the bulk of the remaining deficit, by giving 70 mL/kg of isotonic crystalloid over 2.5 hours (or 5 hours for infants). It is critical that these crystalloid fluids such as Ringers’ Lactate solution or normal saline be used [24]. Colloids, blood products, or hypotonic fluids can be harmful and should NOT be administered since these may cause fluid shifts which exacerbate fluid loss in the cellular compartment.

ORS should be initiated in addition to intravenous fluids as soon as the patient can drink, since commercial isotonic intravenous fluid solutions primarily replace water and sodium but do not replace glucose, potassium, or other electrolyte losses. If seizures are present (and hypoglycemia is suspected), a rapid bolus of intravenous glucose should be given followed by addition of 5 percent glucose to the intravenous fluid. Some locally prepared isotonic intravenous fluids (termed “cholera saline”) contain higher amounts of potassium to replace potassium losses, but these fluids are not available in many clinical settings.

In settings where intravenous fluids are not available or intravenous access cannot be established, patients can be resuscitated by administration of fluids via nasogastric tube; such patients should be monitored for abdominal distension. Intraosseous administration of fluids is also a possible alternative. If neither of these approaches is possible, fluids may be administered by mouth directly at a rate of 20 mL/kg/hour for up to six hours. These are suboptimal therapies due to the risk of aspiration, but are preferable to the alternative of no fluid therapy. Comatose patients receiving oral fluids should be monitored for vomiting and aspiration, in which case the rate of administration should be slowed until fluids are tolerated.

Malnourished children — The mortality of children with diarrhea and severe malnutrition may exceed 50 percent; this can be reduced to less than 10 percent using a standardized approach incorporating management of dehydration, nutrition, hypoglycemia, and treatment of common concomitant infections [9]. In severely malnourished patients, important clinical signs of dehydration may be masked by kwashiorkor and sepsis.

In general, the approach to rehydration in patients with severe malnutrition should be conservative because of the risk of fluid overload, while the approach to possible concomitant infection should be aggressive. Intravenous fluids should be used only in patients with overt shock, and a specialized approach to the composition and administration of ORS is required [17,24]. The WHO recommends the use of reduced osmolality ORS in malnourished children. All patients with severe malnutrition and diarrhea should be started on empiric broad spectrum antibiotics immediately, as well as appropriate nutritional therapy [17,24]. These areas are covered in detail separately. (See "Severe malnutrition in children in resource-limited countries: Treatment").

Nutrition — The goal of nutritional management for patients without malnutrition is to encourage sufficient feeding both during and after the diarrheal illness episode to prevent development of malnutrition and chronic enteropathy.

Infants with diarrhea should be encouraged to breastfeed as much as possible [24]. Infants that are not breastfed should be encouraged to continue to take undiluted formula at least every three hours, in addition to ORS. For infants with dehydration, this should start once rehydration is completed. Milk intolerance is a rare cause of diarrhea in resource-limited countries; this diagnosis should not be applied unless milk refeeding causes a prompt increase in stool volume,
between children who received "early" refeeding (within 12 hours of the start of rehydration) or "late" refeeding (after 12 hours from the start of rehydration) with respect to the number of participants who needed unscheduled intravenous fluids, experienced episodes of vomiting, or developed persistent diarrhea. The mean length of hospital stay was also similar. Therefore, early refeeding does not appear to increase the risk of these complications in the setting of acute diarrheal illness; further study is needed for evaluation of other parameters such as duration of diarrhea and effect on weight gain.

As long as diarrhea persists, foods high in energy content and micronutrients should be offered at frequent intervals (at least six meals a day). After diarrhea resolves, at least one extra meal per day should be continued for a minimum of two weeks, or until the patient regains normal weight-for-height.

In children with severe malnutrition, nutritional therapy is part of a specific and comprehensive management approach. This is discussed in detail elsewhere. (See "Severe malnutrition in children in resource-limited countries: Treatment and prevention".)

**Vitamins and minerals**

**Zinc** — Several studies have demonstrated that zinc supplementation reduces the severity and duration of diarrhea and reduces the incidence of subsequent episodes of diarrhea for several months. Based on these studies, the WHO recommends zinc for children under 5 years of age with diarrhea (10 mg/day for children under 6 months and 20 mg/day for children 6 months to 5 years, each for 10 days). (See "Zinc deficiency and supplementation in children and adolescents".)

**Vitamin A** — Children with diarrhea in resource-limited countries are at high risk of vitamin A deficiency and should receive high dose supplementation with vitamin A. Patients with signs of xerophthalmia, severe malnutrition, or a history of measles should receive a three dose series of repeated treatments for vitamin A deficiency. (See "Overview of vitamin A").

**Antibiotics** — Antibiotics are not indicated for most children with acute watery diarrhea; suspected cholera is an important exception in which antibiotic therapy is useful.

In the absence of culture for diagnosis of cholera, a presumptive diagnosis can be made by darkfield microscopy, rapid dipstick, or clinical suspicion (e.g., based on history of acute vomiting and voluminous watery diarrhea in the setting of a choleric outbreak). Rehydration therapy is the most critical element in the reducing the mortality; appropriate antibiotics selected based on local resistance patterns are a useful adjunctive therapy and significantly reduce the fluid requirements and duration of illness in severe cases (table 7). (See "Overview of cholera")

**Other therapies** — The mainstays of treatment for children with diarrhea in resource-limited countries are correction of fluid and electrolyte losses, appropriate nutritional care, and treatment of associated comorbid conditions. No additional therapies have well established benefits and some are potentially harmful. Children with acute diarrhea should NOT receive antimotility agents or antiemetics. Antimotility agents (loperamide, diphenoxylate-atropine, and tincture of opium) prolong some bacterial infections and may cause fatal paralytic ileus in children. Antiemetics (chlorpromazine, prochlorperazine, promethazine, and metoclopramide) have sedating effects that can interfere with rehydration and may cause extrapyramidal reactions and respiratory depression.

**Invasive diarrhea** — Treatment consists of invasive diarrhea requires correction of fluid and electrolyte losses, appropriate nutritional care, and treatment of the underlying cause of illness. The management of fluids and nutrition is as described in the preceding sections. (See 'Acute watery diarrhea' above.)

Empiric antibiotic therapy for acute bloody diarrhea should be targeted against Shigella species. Antimicrobial treatment of Shigella gastroenteritis reduces the duration of fever and diarrhea, decreases the duration of bacterial shedding, and may reduce the risk of life threatening complications of infection such as bacteremia. (table 2) (See "Shigella infection: Treatment and prevention in children", section on 'Antibiotic therapy'.)

For children with bloody diarrhea that does not remit within two days of starting empiric antibiotics for shigellosis, antibiotic-resistant infection or an alternative infectious etiology should be considered. Amoebic dysentery due to the...
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Hemolytic uremic syndrome — Shigella dysenteriae serotype 1 produce Shiga toxin, which is associated with hemolytic uremic syndrome. In patients with Shigellosis treated with appropriate antibiotics, there is no increase in toxin production or risk of HUS [34]. This is in contrast to Shiga-toxin producing E. coli, for which retrospective and prospective observational studies have reported an increased risk of HUS with the administration of antibiotics during the bloody diarrhea phase. (See "Clinical manifestations, diagnosis and treatment of enterohemorrhagic Escherichia coli (EHEC) infection", section on 'Treatment' and "Shigella infection: Clinical manifestations and diagnosis", section on 'Hemolytic-uremic syndrome'.)

PREVENTION — The institution of the appropriate interventions in childhood diarrhea is aimed at reducing subsequent episodes of diarrhea, malnutrition, and delays in physical and mental development. In addition to the interventions above, WHO recommendations to prevent diarrhea include:

- Exclusive breastfeeding until age six months, and continued breastfeeding with complementary foods until two years of age. Complementary feeding may be considered in younger infants if growth is inadequate.
- The consumption of safe food and water. If available, water brought to a rolling boil for at least five minutes is optimal for preparing food and drinks for young children.
- Handwashing after defecating, disposing of a child's stool, and before preparing meals.
- The use of latrines; these should be located more than 10 meters and downhill from drinking water sources.

Immunizations — The WHO Strategic Advisory Group of Experts has recommended that rotavirus vaccine for infants be included in all national immunization programs, and strongly recommended the introduction of this vaccine in countries where diarrheal deaths account for ≥10 percent of mortality among children aged <5 years [35]. (See "Rotavirus vaccines for infants".)

Cholera vaccines are commercially available in some countries, but at this time they are not widely utilized in areas where cholera is endemic. (See "Overview of cholera", section on 'Prevention'.)

SUMMARY

- Diarrhea is the passage of loose or watery stools at least three times in a 24 hour period. Diarrheal illness is the second leading cause of child mortality; among children younger than five years it causes 1.5 to 2 million deaths annually. Diarrheal illness may consist of acute watery diarrhea, invasive (bloody) diarrhea, or chronic diarrhea (persistent ≥14 days) (table 1). (See 'Introduction' above.)
- The approach to the child with diarrhea includes classification of the type of diarrheal illness, assessing and correcting fluid and electrolyte losses, administering appropriate nutrition, and managing associated co-morbid conditions. (See 'Clinical assessment' above.)
- The degree of dehydration should be assessed at presentation based on physical signs and symptoms (table 3). Fluid management consists of two phases: replacement and maintenance (table 5 and table 6 and table 4). The goal of replacement therapy is to replenish deficits in water and electrolytes lost. This phase is continued until all signs and symptoms of diarrhea are absent and the patient has urinated. Maintenance therapy counters ongoing losses of water and electrolytes; this phase is continued until all symptoms resolve. (See 'Hydration status' above and 'Fluid and electrolytes' above.)
- In general, the approach to rehydration in patients with severe malnutrition should be conservative because of the risk of fluid overload; intravenous fluids should be used only in patients with overt shock. All patients with severe malnutrition and diarrhea should be started on empiric broad spectrum antibiotics immediately, as well as appropriate nutritional therapy. (See 'Malnourished children' above and "Severe malnutrition in children in resource-limited countries: Treatment".)

*References*

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- Antibiotics are not indicated for most children with acute watery diarrhea; suspected cholera is an important exception in which antibiotic therapy is warranted (table 7). (See 'Antibiotics' above.)

- Treatment of invasive diarrhea includes the same approach to fluids, electrolytes, and nutrition as in acute watery diarrhea. In addition, empiric antibiotic therapy with activity against *Shigella* species should be initiated. (See 'Invasive diarrhea' above and "Shigella infection: Treatment and prevention in children".)

- Preventive measures for acute diarrhea among children in resource-limited settings include breastfeeding, consumption of safe food and water, adherence to hygienic practices, and vaccination against rotavirus infection. (See 'Prevention' above.)

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REFERENCES


Topic 13956 Version 13.0
## Major etiologies of childhood diarrhea in developing countries

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<thead>
<tr>
<th>Syndrome</th>
<th>Etiologic agents</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute watery diarrhea</strong></td>
<td>Rotavirus</td>
<td>Leading cause of gastroenteritis in children younger than two years.</td>
</tr>
<tr>
<td></td>
<td>Enterotoxigenic <em>Escherichia coli</em> (ETEC)</td>
<td>Leading cause of gastroenteritis in older children and adults</td>
</tr>
<tr>
<td></td>
<td><em>Vibrio cholerae</em> O1 and O139</td>
<td>Associated with endemic and epidemic disease. Vomiting and voluminous &quot;rice-water diarrhea&quot; in severe cases.</td>
</tr>
<tr>
<td></td>
<td>Cryptosporidium</td>
<td>Common in infants (younger than one year) even in the absence of HIV; infrequently seen in older children.</td>
</tr>
<tr>
<td></td>
<td>Norovirus</td>
<td>Abrupt onset of vomiting and diarrhea with low grade fever.</td>
</tr>
<tr>
<td><strong>Invasive diarrhea</strong></td>
<td>Shigella spp.</td>
<td>Leading cause of invasive diarrhea. <em>S. dysenteriae</em> serotype I produces Shiga-toxin and is associated with epidemics of severe disease. Complications include toxic megacolon, rectal prolapse, intestinal perforation, seizures, encephalopathy and sepsis.</td>
</tr>
<tr>
<td></td>
<td>Nontyphoidal <em>Salmonella enterica</em></td>
<td>Several serotypes cause gastroenteritis. Infants, elderly, and immunocompromised at increased risk for disseminated infection.</td>
</tr>
<tr>
<td></td>
<td>Campylobacter spp.</td>
<td>Predominantly <em>C. jejuni</em> and <em>C. coli</em>. May mimic appendicitis. Complications include Guillain-Barré syndrome.</td>
</tr>
<tr>
<td></td>
<td>Enteroinvasive <em>Escherichia coli</em> (EIEC)</td>
<td>EIEC are closely related to Shigella and cause a syndrome essentially identical to shigellosis.</td>
</tr>
<tr>
<td></td>
<td>Enterohemorrhagic <em>Escherichia coli</em> (EHEC)</td>
<td>EHEC produce Shiga toxin identical to that produced by <em>S. dysenteriae</em> serotype I, associated with increased risk of hemolytic uremic syndrome.</td>
</tr>
<tr>
<td></td>
<td><em>Entamoeba histolytica</em></td>
<td><em>E. histolytica</em> is a protozoal organism which causes intestinal infection which may be indistinguishable from Shigella and other bacteria. Rare complications include extraintestinal infections, most commonly hepatic abscess.</td>
</tr>
</tbody>
</table>

Graphic 50975 Version 3.0
### Antibiotics for suspected shigellosis in developing settings

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Route</th>
<th>Typical pediatric dose</th>
<th>Comment(s)</th>
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</thead>
<tbody>
<tr>
<td><strong>Preferred agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Oral</td>
<td>30 mg/kg/day (divided twice daily) for 3 days</td>
<td>Multi-dose therapy is preferred.</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Oral</td>
<td>15 mg/kg initial dose (day 1)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>10 mg/kg/day (daily, day 2-5)</td>
<td></td>
</tr>
<tr>
<td><strong>Alternative agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>IM/IV</td>
<td>50-100 mg/kg/day (divided four times daily) for 2-5 days</td>
<td>Ceftriaxone is the preferred empiric therapy for severe infections and infections refractory to other therapies.</td>
</tr>
<tr>
<td>Pivmecillinam</td>
<td>PO</td>
<td>80 mg/kg/day (divided four times daily) for 5 days</td>
<td></td>
</tr>
</tbody>
</table>

Resistance to amoxicillin, trimethoprim-sulfamethoxazole, and chloramphenicol (original first-line therapies) is too widespread to justify their empiric use for invasive diarrhea in developing countries.


Graphic 66147 Version 2.0
Acute watery diarrhea

Watery stools of <14 days duration, with no visible blood constitutes acute watery diarrhea.

(A) Green watery stool. Green colored stool, often seen in rotavirus gastroenteritis.

(B) Rice water stool. White colored stool characteristic of severe cholera.

Graphic 52564 Version 2.0
Invasive diarrhea

The appearance of frank blood in the stool constitutes invasive diarrhea.
(A) Melenic stool with abundant mucous.
(B) Watery stool with blood and mucous.
(C) Bloody, mucoid stool.

Graphic 64377 Version 1.0
## WHO guidelines for assessment of dehydration

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Predicted degree of dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None (&lt;5 percent)</td>
</tr>
<tr>
<td>General appearance</td>
<td>Well, alert</td>
</tr>
<tr>
<td>Eyes</td>
<td>Normal</td>
</tr>
<tr>
<td>Thirst</td>
<td>Drinks normally, not thirsty</td>
</tr>
<tr>
<td>Skin pinch</td>
<td>Goes back quickly</td>
</tr>
<tr>
<td>Estimated fluid deficit</td>
<td>&lt;50 mL/kg</td>
</tr>
</tbody>
</table>


Graphic 68271 Version 4.0
Trophozoites of *E. histolytica* with ingested erythrocytes stained with trichrome.


Graphic 57615 Version 3.0
### Composition (mEq/L) of common solutions used for rehydration

<table>
<thead>
<tr>
<th>Route</th>
<th>Solution</th>
<th>Na+</th>
<th>K+</th>
<th>Cl⁻</th>
<th>HCO₃⁻</th>
<th>Citrate</th>
<th>Ca++</th>
<th>Glucose/carbohydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td>Normal saline</td>
<td>154</td>
<td>-</td>
<td>154</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ringer's Lactate</td>
<td>130</td>
<td>4</td>
<td>111</td>
<td>28</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ringer's Lactate + 5 percent dextrose</td>
<td>130</td>
<td>4</td>
<td>109</td>
<td>28</td>
<td>-</td>
<td>3</td>
<td>278</td>
</tr>
<tr>
<td></td>
<td>Cholera saline</td>
<td>133</td>
<td>13</td>
<td>98</td>
<td>48</td>
<td>-</td>
<td>-</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>Cholera saline (&quot;Dhaka solution&quot;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>Standard ORS</td>
<td>90</td>
<td>20</td>
<td>80</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>111</td>
</tr>
<tr>
<td></td>
<td>Hypo-osmolar ORS</td>
<td>75</td>
<td>20</td>
<td>65</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>ReSoMal* (Reduced Osmolarity ORS for Malnourished Children)</td>
<td>45</td>
<td>40</td>
<td>76</td>
<td>-</td>
<td>7</td>
<td>-</td>
<td>125</td>
</tr>
</tbody>
</table>

ORS is reviewed in detail separately. (See "Oral rehydration therapy").

ORS: oral rehydration solution(s).
* Also contains Mg 6 mmol/L, Zn 300 umol/L, Cu 45 umol/L.

Fluids for patients without signs of dehydration

<table>
<thead>
<tr>
<th>Acceptable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral rehydration solution (optimal for both repletion and maintenance)</td>
</tr>
<tr>
<td>Salted drinks (salted rice water or salted yogurt drink)</td>
</tr>
<tr>
<td>Broth/soup (salted vegetable or meat soup)</td>
</tr>
<tr>
<td>Water</td>
</tr>
<tr>
<td>Rice water</td>
</tr>
<tr>
<td>Coconut water (unsweetened)</td>
</tr>
<tr>
<td>Weak tea (unsweetened)</td>
</tr>
<tr>
<td>Fresh fruit juice (unsweetened)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unacceptable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonated beverages</td>
</tr>
<tr>
<td>Sweetened juices</td>
</tr>
<tr>
<td>Coffee</td>
</tr>
<tr>
<td>Medicinal teas or infusions</td>
</tr>
</tbody>
</table>

Fluids containing salt should be encouraged. Unacceptable fluids include carbonated beverages and sweetened juices; the sugar in these fluids may worsen diarrhea. Coffee and medicinal teas or infusions are also unacceptable since they can have diuretic and purgative effects.


Graphic 82172 Version 4.0
Replacement fluid volume for patients with moderate volume depletion by age and weight

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Replacement fluid volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 months</td>
<td>&lt;5 kg</td>
<td>200 to 400 mL</td>
</tr>
<tr>
<td>4 to 12 months</td>
<td>5 to 8 kg</td>
<td>400 to 600 mL</td>
</tr>
<tr>
<td>1 to 2 years</td>
<td>8 to 11 kg</td>
<td>600 to 800 mL</td>
</tr>
<tr>
<td>2 to 4 years</td>
<td>11 to 16 kg</td>
<td>800 to 1200 mL</td>
</tr>
<tr>
<td>5 to 14 years</td>
<td>16 to 30 kg</td>
<td>1200 to 2200 mL</td>
</tr>
<tr>
<td>&gt;14 years</td>
<td>&gt;30 kg</td>
<td>2200 to 4400 mL</td>
</tr>
</tbody>
</table>

Patients with moderate volume depletion are estimated to have lost 5 to 10 percent of their body weight (ie, 50 to 100 mL of fluid per kg). The total fluid deficit should be repleted within the first three to four hours of presentation.

If weight is known, 100 mL/kg of fluid can be administered. Ongoing losses, if severe, should be incorporated into replacement phase. Fluids should never be restricted. For infants <6 months receiving standard oral rehydration solutions (ORS), provide an additional 100 to 200 mL of water; this is not needed for patients receiving hypo-osmolar ORS.

**Cholera cots**

These devices, in which patients may defecate directly into a collection bucket, facilitate the rapid measurement of ongoing fluid losses and management of epidemics. Inexpensive hand decontamination between examinations may be facilitated by using a portable locally prepared hand sanitizer with at least 60 percent ethanol or isopropenol and an emollient such as 3 percent glycerol[1].

Reference:


Graphic 70839 Version 1.0
## Oral antibiotics for suspected cholera

<table>
<thead>
<tr>
<th>Class</th>
<th>Antibiotic</th>
<th>Typical pediatric dose*</th>
<th>Adult dose</th>
<th>Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tetracyclines</strong></td>
<td>Doxycycline</td>
<td>4-6 mg/kg (single dose)</td>
<td>300 mg (single dose)</td>
<td>Antibiotic resistance to all tetracyclines is common[^1]. Empiric use is appropriate in epidemics caused by documented susceptible isolates. Not recommended for pregnant women and children less than 8 years.</td>
</tr>
<tr>
<td></td>
<td>Tetracycline</td>
<td>50 mg/kg/day in four equally divided doses, for three days</td>
<td>500 mg four times per day for three days</td>
<td></td>
</tr>
<tr>
<td><strong>Macrolides</strong></td>
<td>Azithromycin</td>
<td>20 mg/kg (single dose)</td>
<td>1 g (single dose)</td>
<td>Single dose azithromycin is preferred therapy[^2]. Rare reports of macrolide resistance.</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>40 mg/kg/day in four equally divided doses, for three days</td>
<td>500 mg four times per day for three days</td>
<td></td>
</tr>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td>Ciprofloxacin</td>
<td>20 mg/kg (single dose)</td>
<td>1 g (single dose)</td>
<td>Reduced susceptibility to fluoroquinolones has been reported in Asia and Africa[^2,3]. Not recommended for pregnant women and children less than 8 years.</td>
</tr>
</tbody>
</table>

* Not to exceed maximum dose.

**References:**

Contributor Disclosures

Jason B Harris, MD, MPH Consultant/Advisory Boards: Scientific Advisory Committee [Cholera (Oral cholera vaccine)].

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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