



## World Gastroenterology Organisation practice guideline: **Acute diarrhea**

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## 1 Methodology and literature review

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WGO Guidelines summarize what is known as published in existing systematic reviews, evidence-based guidelines, and high-quality trials. This information is then appraised and configured to make the guideline as relevant and accessible as possible globally. Sometimes this means building cascades — different approaches designed to achieve the same ends. Each approach is different, because it tries to take account of resources, cultural preferences, and policies. WGO Guidelines are not systematic reviews based on a systematic and comprehensive review of all available evidence and guidelines. These global guidelines try to distinguish between geographical areas with differing resources and differing epidemiologies, and the guidelines are then translated into French, Mandarin, Portuguese, Spanish, and Russian to facilitate relevance and access.

A “graded evidence” service keeps track of evidence newly published since the date of publication of the guideline.

This guideline was written by the review team after a series of literature searches were carried out to establish what had changed since the WGO’s first position statement on the topic of acute diarrhea, published in 2002, at:

- <http://www.omge.org/globalguidelines/guide01/guideline1.htm>

Existing evidence was searched using a precise, rather than sensitive, syntax for each platform searched. Relevant guidelines were searched in the National Guidelines Clearinghouse platform at [www.ngc.org](http://www.ngc.org) and on the web sites of the major gastroenterology and cancer societies. Further searches were carried out in Medline and Embase on the Dialog-DataStar platform from 2002 onwards. A search in the Cochrane Library gathered all relevant systematic reviews and protocols.

The draft was edited by the chairperson of the review team and the librarian.

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## 2 Epidemiologic features

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In the year 2000, diarrheal diseases claimed an estimated 1.4 to 2.5 million lives; they are among the leading causes of death in children in developing countries. Both the incidence and the risk of mortality from diarrheal diseases are greatest among children younger than 1 year of age, and thereafter rates decline incrementally. Other direct consequences of diarrhea in children include malnutrition, diminished growth, and impaired cognitive development in resource-limited countries.

In industrialized countries, relatively few patients die from diarrhea, but it continues to be an important cause of morbidity and incurs substantial health-care costs (Table 1).

**Table 1** Epidemiology of acute diarrhea: developed versus developing countries.

Per year	Estimated episodes of acute diarrhea	Hospitalizations	Deaths
United States	375 million — 1.4 episodes per person per year  > 1.5 million child outpatient visits	900 000 total  200 000 children	6000 total  300 children
Worldwide	1.5 billion episodes  In developing countries, children < 3 y have 3 episodes per year		1.5–2 million children < 5 y

During the past three decades, factors such as the widespread distribution and use of oral rehydration solutions (ORS), improved rates of breastfeeding, improved nutrition, better sanitation and hygiene, and increased coverage of measles immunization have contributed to a consistent decline in the mortality rate in developing countries (Table 2).

**Table 2** Estimates of mortality from diarrheal diseases among children in developing countries.

Publication	Year of estimate	Year of publication	Deaths per year (× 1 000 000)
Rohde JE. Selective primary health care: strategies for control of disease in the developing world. XV. Acute diarrhea. <i>Rev Infect Dis</i> 1984;6:840–54.	1976	1984	5
Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: a review of active surveillance data. <i>Bull World Health Organ</i> 1982;60:605–13.	1982	1982	4.6
Institute of Medicine. The prospects of immunizing against rotavirus. In: <i>New vaccine development: diseases of importance in developing countries, vol. 2</i> . Washington, DC: National Academy Press, 1986: D13-11-12.	1986	1986	3.5
Martines J, Phillips M. Diarrheal diseases. In: Jamison D, Mosley W, Measham A, Bobadilla J, editors. <i>Disease control priorities in developing countries</i> . New York: Oxford University Press, 1993: 91–116.	1990	1990	3.2
Bern C, Martines J, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. <i>Bull World Health Organ</i> 1992;70:705–14.	1992	1992	3.3

World Bank. World development report: investing in health. New York: World Bank, 1993.	1993	1993	2.5
Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors. Global Burden of Disease Study. Lancet 1997;349:1436–42.	1997	1997	2.4–2.9
Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. Bull World Health Organ 2003;81:197–204.	2000	2003	2.1–4.7
Parashar U, Hummelman E, Bresee J, et al. Global illness and deaths caused by rotavirus disease in children. Emerg Infect Dis 2003;9:565–72.	2000	2003	1.7–3.0
World Health Organization. Global burden of disease estimates 2001. Geneva: WHO, 2002.	2001	2002	1.4
Murray C, Lopez A, Mathers C, et al. The Global Burden of Disease 2000 project: aims, methods, and data sources. Geneva: World Health Organization, 2001.			
World Health Organization. World health report 2003: shaping the future. Geneva: World Health Organization, 2003.	2002	2003	1.6

The morbidity from diarrhea has remained relatively constant during the past two decades, with each child under 5 years of age experiencing an average of three annual episodes. ORS and nutritional improvements probably have a greater impact on mortality rates than the incidence of diarrhea (Fig. 1). Interventions such as breastfeeding and improved sanitation are expected to affect mortality and morbidity simultaneously.

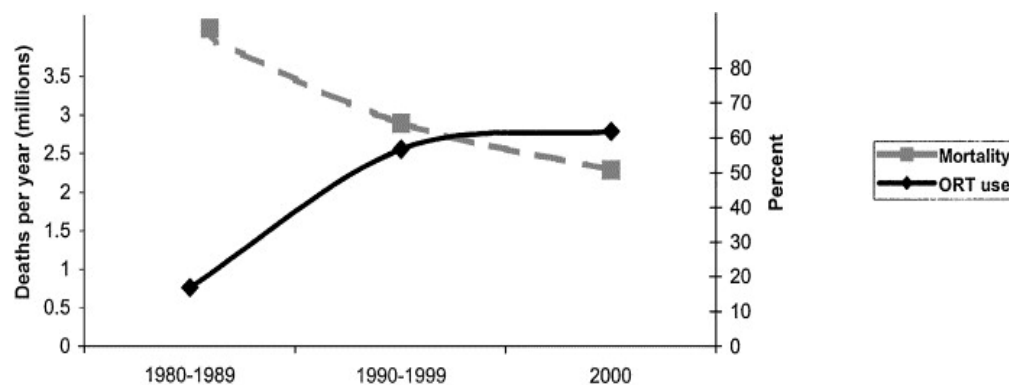


Fig. 1 Inverse association between coverage rates of oral rehydration solution (ORS) use and rates of mortality from diarrhea in various countries.

### 3 Causative agents and pathogenic mechanisms (Fig. 2)

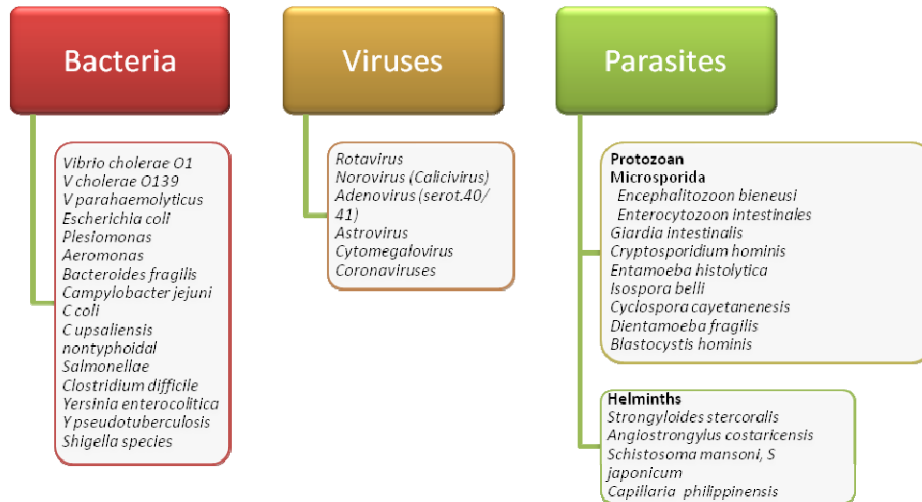


Fig. 2 Overview of causative agents in diarrhea.

#### 3.1 Bacterial agents

In developing countries, enteric bacteria and parasites are more prevalent than viruses and typically peak during the summer months.

**Diarrheagenic *Escherichia coli*.** All forms cause disease in children in the developing world, but enterohemorrhagic *E. coli* (EHEC, including *E. coli* O157:H7) causes disease more commonly in the developed countries.

- Enterotoxigenic *E. coli* (ETEC) — traveler's diarrhea, diarrhea in infants and children in developing countries.
- Enteropathogenic *E. coli* (EPEC) — children < 2 years; chronic diarrhea in children; rarely causes disease in adults.
- Enteroinvasive *E. coli* (EIEC) — bloody mucoid diarrhea; fever is common.
- Enterohemorrhagic *E. coli* (EHEC) — bloody diarrhea; severe hemorrhagic colitis and the hemolytic uremic syndrome in 6–8%; cattle are the predominant reservoir.
- Enteroaggregative *E. coli* (EAaggEC) — watery diarrhea in young children; persistent diarrhea in children and adults with human immunodeficiency virus (HIV).

***Campylobacter*** is prevalent in adults and is one of the most frequently isolated bacteria from the feces of infants and children in developing countries.

- Asymptomatic infection is very common in developing countries and is associated with the presence of cattle close to dwellings.
- Infection is associated with watery diarrhea and on occasion dysentery (acute bloody diarrhea).

- Peak isolation rates are found in children 2 years of age and younger.
- Guillain–Barré syndrome is a rare complication.
- Poultry is an important source of *Campylobacter* infections in developed countries.
- The presence of an animal in the cooking area is a risk factor in developing countries.

#### ***Shigella* species.**

- There are 160 million infections annually in developing countries, primarily in children.
- It is more common in toddlers and older children than in infants.
- *S. sonnei* — mildest illness; seen most commonly in developed countries.
- *S. flexneri* — dysenteric symptoms and persistent illness; most common in developing countries.
- *S. dysenteriae* type 1 (Sd1) — produces Shiga toxin, as does EHEC. It has caused devastating epidemics of bloody diarrhea with case-fatality rates approaching 10% in Asia, Africa, and Central America.

#### ***Vibrio cholerae*.**

- Many species of *Vibrio* cause diarrhea in developing countries.
- *V. cholerae* serogroups O1 and O139 cause rapid and severe depletion of volume.
- In the absence of prompt and adequate rehydration, hypovolemic shock and death can occur within 12–18 h after the onset of the first symptom.
- Stools are watery, colorless, and flecked with mucus.
- Vomiting is common; fever is rare.
- In children, hypoglycemia can lead to convulsions and death.
- There is a potential for epidemic spread; any infection should be reported promptly to the public health authorities.

#### ***Salmonella*.**

- All serotypes (> 2000) are pathogenic for humans.
- Infants and the elderly appear to be at the greatest risk.
- Animals are the major reservoir for *Salmonellae*.
- There is an acute onset of nausea, vomiting, and diarrhea that may be watery or dysenteric.
- Fever develops in 70% of affected children.
- Bacteremia occurs in 1–5%, mostly in infants.
- Enteric fever — *Salmonella typhi* or *paratyphi* A, B, or C (typhoid fever).
- Diarrhea (with or without blood) develops, and fever lasting 3 weeks or more.

### **3.2 Viral agents**

In industrialized countries, viruses are the predominant cause of acute diarrhea and show distinct winter seasonality.

#### **Rotavirus.**

- Leading cause of severe, dehydrating gastroenteritis among children.
- One-third of diarrhea hospitalizations and 500 000 deaths worldwide each year.

- Nearly all children in both industrialized and developing countries have been infected with rotavirus by the time they are 3–5 years of age. Neonatal infections are a common occurrence, but are often asymptomatic.
- The incidence of clinical illness peaks in children between 4 and 23 months of age.
- Rotavirus is associated with gastroenteritis of above-average severity.

#### **Human caliciviruses (HuCVs).**

- Belong to the family *Caliciviridae*, the noroviruses and sapoviruses.
- Previously called “Norwalk-like viruses” and “Sapporo-like viruses.”
- Noroviruses are the most common cause of outbreaks of gastroenteritis, affecting all age groups.
- Sapoviruses primarily affect children.
- May be the second most common viral agent after rotavirus, accounting for 4–19% of episodes of severe gastroenteritis in young children.

#### **Adenovirus.**

- Adenovirus infections most commonly cause illness of the respiratory system. However, depending on the infecting serotype and especially in children, they may also cause gastroenteritis.

### **3.3 Parasitic agents**

*Giardia intestinalis*, *Cryptosporidium parvum*, *Entamoeba histolytica*, and *Cyclospora cayatanensis* most commonly cause acute diarrheal illness in children.

- These agents account for a relatively small proportion of cases of infectious diarrheal illnesses among children in developing countries.
- Uncommon in the developed world — usually restricted to travelers.
- *G. intestinalis* has a low prevalence (approximately 2–5%) among children in developed countries, but as high as 20–30% in developing regions.
- *Cryptosporidium* and *Cyclospora* are common among children in developing countries; frequently asymptomatic.

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## **4 Clinical manifestations and diagnosis**

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Despite clinical clues, determining the causative agent of diarrhea in an individual patient on the basis of clinical grounds alone is usually difficult (Figs. 3, 4; Table 3).

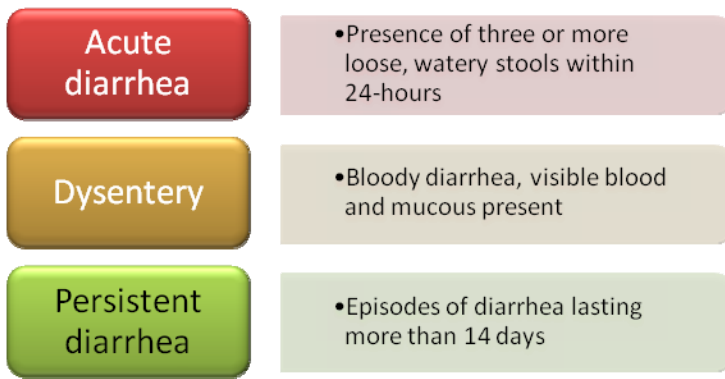


Fig. 3 Episodes of diarrhea can be classified into three categories.

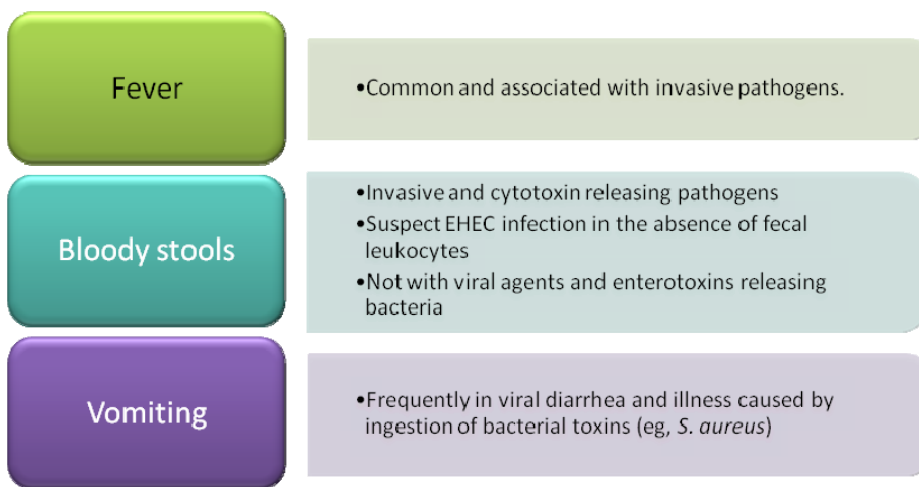


Fig. 4 Linking the main symptoms to the causes of acute diarrhea. EHEC, enterohemorrhagic *Escherichia coli*.



**Table 3** Clinical features of infection with selected diarrheal pathogens.

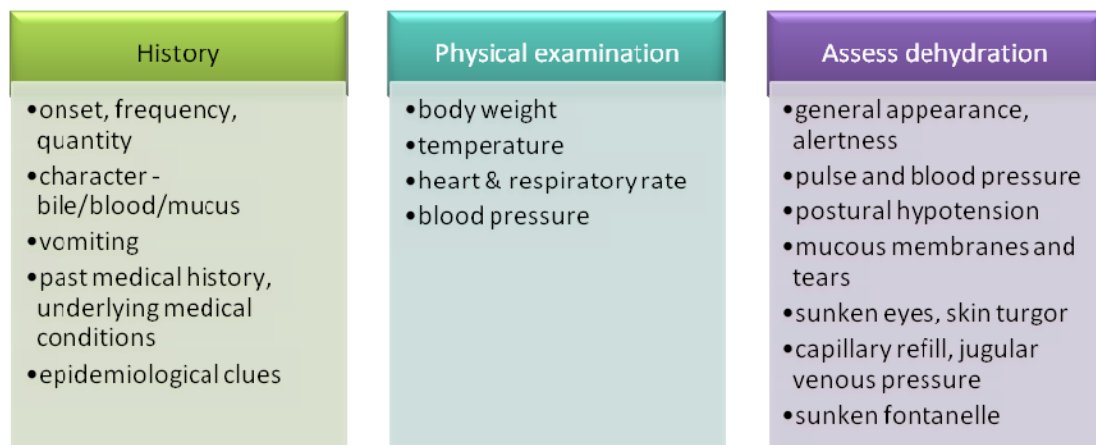
Clinical features	Pathogens											
	<i>Shigella</i>	<i>Salmonella</i>	<i>Campylobacter</i>	<i>Yersinia</i>	<i>Norovirus</i>	<i>Vibrio</i>	<i>Cyclospora</i>	<i>Cryptosporidium</i>	<i>Giardia</i>	<i>Entamoeba histolytica</i>	<i>Clostridium difficile</i>	Shiga toxin-producing <i>E. coli</i> (including O157:H7)
Abdominal pain						V	V	V		O	O	
Fever					V	V	V	V		O	O	A
Fecal evidence of inflammation				O		V		O		V		N
Vomiting and/or nausea		O	O	O		V	O	O	O	V		O
Heme-positive stool	V	V	V	O		V					O	
Bloody stool	O	O	O	O		V				V	O	

Key: common: O = occurs, V= variable; not common: A= atypical, N= often not.

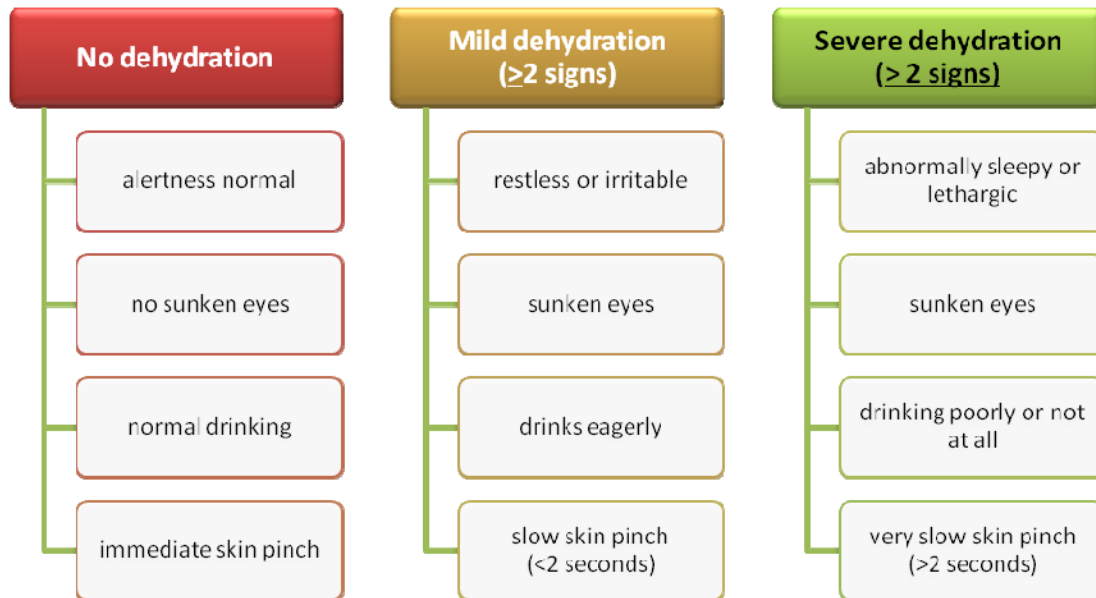
#### 4.1 Clinical evaluation

The initial clinical evaluation of the patient (Fig. 5) should focus on:

- Assessing the severity of the illness and the need for rehydration (Fig. 6)
- Identifying likely causes on the basis of the history and clinical findings



**Fig. 5** Evaluation of the acute diarrhea patient.



**Fig. 6** Levels of dehydration in children with acute diarrhea.

*Cautionary note:* 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; the child may appear to be drifting into unconsciousness. In some infants and children, the eyes normally appear somewhat sunken. It is helpful to ask the mother if the child's eyes are normal or more sunken than usual. The skin pinch is less useful in infants or children with marasmus or kwashiorkor, or obese children. Other signs that may be altered in children with severe malnutrition are described in section 8.1 of the World Health Organization 2005 Guideline (see reference list).

Signs of dehydration in adults:

- Pulse rate > 90
- Postural hypotension
- Supine hypotension and absence of palpable pulse
- Dry tongue
- Sunken eyeballs
- Skin pinch

## 4.2 Laboratory evaluation

For acute enteritis and colitis, maintaining adequate intravascular volume and correcting fluid and electrolyte disturbances take priority over the identification of the causing agent. Stool cultures are usually unnecessary for immunocompetent patients who present within 24 hours after the onset of acute, watery diarrhea. Microbiologic investigation is indicated in patients who are dehydrated or febrile or have blood or pus in their stool.

Epidemiologic clues to infectious diarrhea can be found by evaluating the incubation period, history of recent travel, unusual food or eating circumstances, professional risks, recent use of antimicrobials, institutionalization, and HIV infection risks.

Stool analysis and culture costs can be reduced by improving the selection and testing of the specimens submitted on the basis of interpreting the case information —

such as patient history, clinical aspects, visual stool inspection, and estimated incubation period (Figs. 7–9).

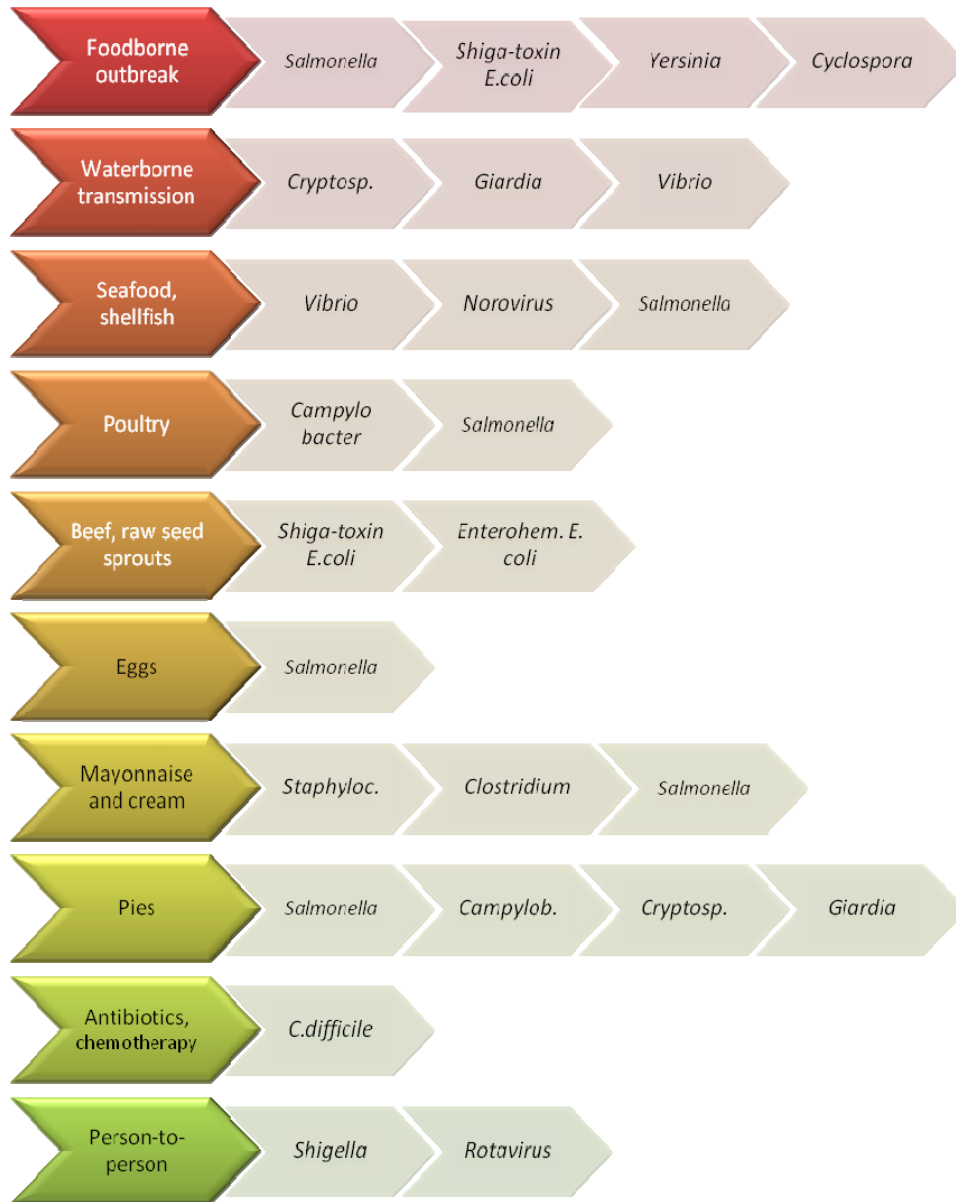
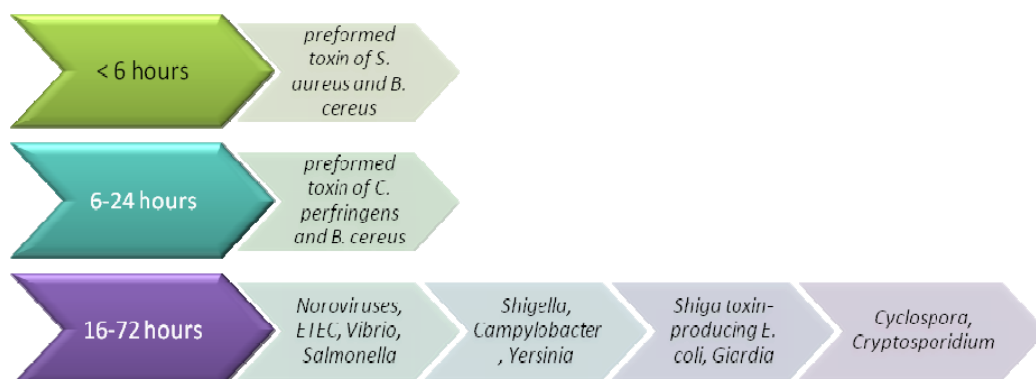
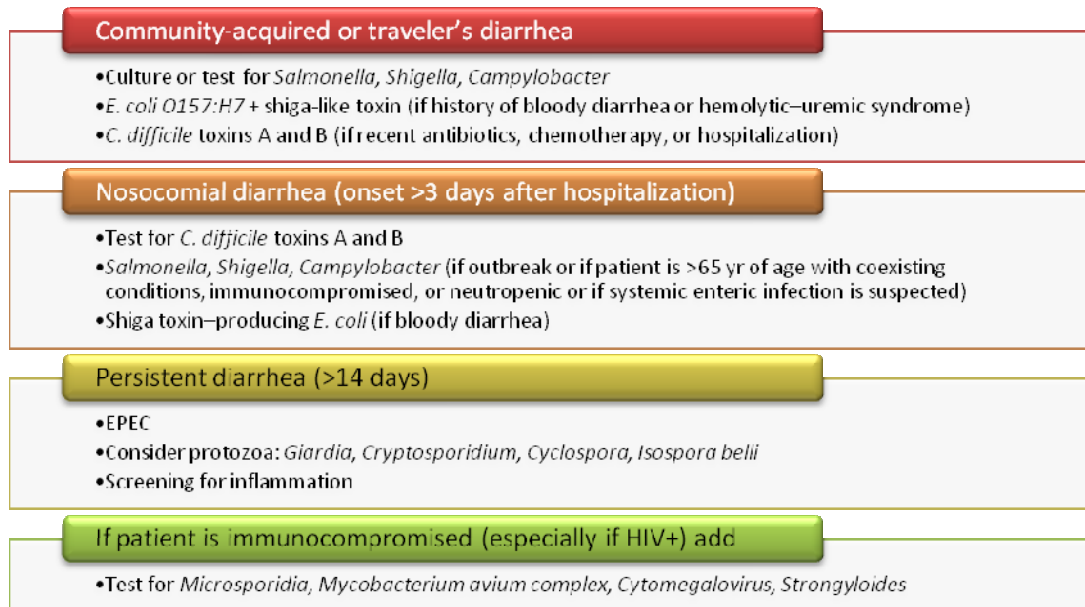


Fig. 7 Patient history details and causes of acute diarrhea.



**Fig. 8** The incubation period and likely causes of diarrhea.



**Fig. 9** A fecal specimen should be obtained for analysis in cases of severe, bloody, inflammatory, or persistent diarrhea, or if an outbreak is suspected.

(Screening usually refers to noninvasive fecal tests.) The identification of a pathogenic bacterium, virus, or parasite in a stool specimen from a child with diarrhea does not indicate in all cases that it is the cause of illness.

Certain laboratory studies may be important when the underlying diagnosis is unclear or diagnoses other than acute gastroenteritis are possible.

Measurement of serum electrolytes is only required in children with severe dehydration or with moderate dehydration and an atypical clinical history or findings. Hypernatremic dehydration requires specific rehydration methods — irritability and a doughy feel to the skin are typical manifestations and should be sought specifically.

### 4.3 Prognostic factors and differential diagnosis (Fig. 10)

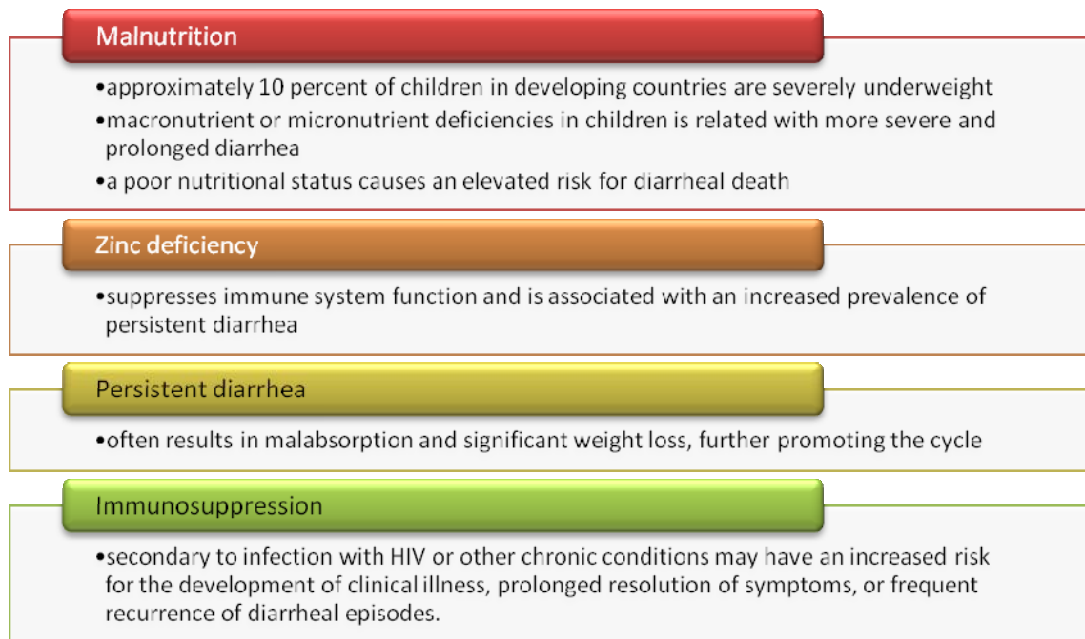


Fig. 10 Prognostic factors in children.

Differential diagnosis of acute diarrhea in children:

- Meningitis
- Bacterial sepsis
- Pneumonia
- Otitis media
- Urinary tract infection

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## 5 Treatment options and prevention

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### 5.1 Rehydration

Oral rehydration therapy (ORT) is the administration of fluid by mouth to prevent or correct dehydration that is a consequence of diarrhea. ORT is the standard for efficacious and cost-effective management of acute gastroenteritis, also in developed countries.

Oral rehydration solution (ORS) is the fluid specifically developed for ORT. A more effective, lower-osmolality ORS (with reduced concentrations of sodium and glucose, associated with less vomiting, less stool output, and a reduced need for intravenous infusions in comparison with standard ORS) has been developed for global use (Table 4). The hypotonic WHO-ORS is also recommended for use in treating adults and children with cholera. ORT consists of:

- Rehydration — water and electrolytes are administered to replace losses.
- Maintenance fluid therapy (along with appropriate nutrition).

In children who are in hemodynamic shock or with abdominal ileus, ORT may be contraindicated. For children who are unable to tolerate ORS via the oral route (with persistent vomiting), nasogastric feeding can be used to administer ORS.

Global ORS coverage rates are still less than 50%, and efforts must be made to improve coverage.

**Table 4** Oral rehydration solution (ORS) constituents

	mmol/L
Sodium	75
Chloride	65
Glucose, anhydrous	75
Potassium	20
Citrate	10
Total osmolarity	245

Rice-based ORS is superior to standard ORS for adults and children with cholera, and can be used to treat such patients wherever its preparation is convenient. Rice-based ORS is not superior to standard ORS in the treatment of children with acute noncholera diarrhea, especially when food is given shortly after rehydration, as is recommended to prevent malnutrition.

## 5.2 Supplemental zinc therapy, multivitamins, and minerals

For all children with diarrhea: 20 mg zinc for 14 days.

Zinc deficiency is widespread among children in developing countries. Micronutrient supplementation — supplementation treatment with zinc (20 mg per day until the diarrhea ceases) reduces the duration and severity of diarrheal episodes in children in developing countries.

Supplementation with zinc sulfate (2 mg per day for 10–14 days) reduces the incidence of diarrhea for 2–3 months. It helps reduce mortality rates among children with persistent diarrheal illness. Administration of zinc sulfate supplements to children suffering from persistent diarrhea is recommended by the WHO.

All children with persistent diarrhea should receive supplementary multivitamins and minerals each day for 2 weeks. Locally available commercial preparations are often suitable; tablets that can be crushed and given with food are least costly. These should provide as broad a range of vitamins and minerals as possible, including at least two recommended daily allowances (RDAs) of folate, vitamin A, zinc, magnesium, and copper (WHO 2005).

As a guide, one RDA for a child aged 1 year is:

Folate	50 µg
Zinc	20 mg
Vitamin A	400 µg
Copper	1 mg
Magnesium	80 mg

### 5.3 Diet

The practice of withholding food for > 4 hours is inappropriate. Food should be started 4 hours after starting ORT or intravenous fluid. The notes below apply to adults and children unless age is specified.

Give:

- An age-appropriate diet — regardless of the fluid used for ORT/maintenance
- Infants require more frequent breastfeedings or bottle feedings — special formulas or dilutions unnecessary
- Older children should be given appropriately more fluids
- Frequent, small meals throughout the day (six meals/day)
- Energy and micronutrient-rich foods (grains, meats, fruits, and vegetables)
- Increasing energy intake as tolerated following the diarrheal episode

Avoid:

- Canned fruit juices — these are hyperosmolar and can aggravate diarrhea.

Probiotics are specific defined live microorganisms, such as *Lactobacillus* GG (ATCC 53103), which have demonstrated health effects in humans. Controlled clinical intervention studies and meta-analyses support the use of specific probiotic strains and products in the treatment and prevention of rotavirus diarrhea in infants. However, all effects are strain-specific and need to be verified for each strain in human studies. Extrapolation from the results of even closely related strains is not possible, and significantly different effects have been reported.

### 5.4 Nonspecific antidiarrheal treatment

None of these drugs addresses the underlying causes of diarrhea. Antidiarrheals have no practical benefits for children with acute/persistent diarrhea. Antiemetics are usually unnecessary in acute diarrhea management.

Antimotility:

- Loperamide is the agent of choice for adults (4–6 mg/day; 2–4 mg /day for children > 8 y).
  - Should be used mostly for mild to moderate traveler’s diarrhea (without clinical signs of invasive diarrhea).
  - Inhibits intestinal peristalsis and has mild antisecretory properties.
  - Should be avoided in bloody or suspected inflammatory diarrhea (febrile patients).
  - Significant abdominal pain also suggests inflammatory diarrhea (this is a contraindication for loperamide use).
  - Loperamide is not recommended for use in children < 2 y.

Antisecretory agents:

- Bismuth subsalicylate can alleviate stool output in children or symptoms of diarrhea, nausea, and abdominal pain in traveler's diarrhea.
- Racecadotril is an enkephalinase inhibitor (nonopiate) with antisecretory activity, and is now licensed in many countries in the world for use in children. It has been found useful in children with diarrhea, but not in adults with cholera.

Adsorbents:

- Kaolin-pectin, activated charcoal, attapulgite
  - Inadequate proof of efficacy in acute adult diarrhea

## 5.5 Antimicrobials

Antimicrobial therapy is not usually indicated in children. Antimicrobials are reliably helpful only for children with bloody diarrhea (most likely shigellosis), suspected cholera with severe dehydration, and serious nonintestinal infections (e.g., pneumonia). Antiprotozoal drugs can be very effective for diarrhea in children, especially for *Giardia*, *Entamoeba histolytica*, and now *Cryptosporidium*, with nitazoxanide.

In adults, the clinical benefit should be weighed against the cost, the risk of adverse reactions, harmful eradication of normal intestinal flora, the induction of Shiga toxin production, and the increase of antimicrobial resistance.

Antimicrobials are to be considered the drugs of choice for empirical treatment of traveler's diarrhea and of community-acquired secretory diarrhea when the pathogen is known (Fig. 11).

Considerations with regard to antimicrobial treatment:

- Consider antimicrobial treatment for:
  - Persistent *Shigella*, *Salmonella*, *Campylobacter*, or parasitic infections.
  - Infections in the aged, immunocompromised patients, and patients with impaired resistance, sepsis, or with prostheses.
  - Moderate/severe traveler's diarrhea or diarrhea with fever and/or with bloody stools — quinolones (co-trimoxazole second choice).
- Nitazoxanide is an antiprotozoal and may be appropriate for *Cryptosporidium* and other infections, including some bacteria.
- Rifaximin is a broad-spectrum, nonabsorbed antimicrobial agent that may be useful.





Fig. 11 Antimicrobial agents for the treatment of specific causes of diarrhea.

\*\* Tinidazole can also be given in a single dose (50 mg/kg orally; maximum dose 2 g). Ornidazole can be used in accordance with the manufacturers' recommendations.

N.B.:

- Erythromycin is hardly used for diarrhea today. Azithromycin is widely available and has the convenience of single dosing. For treating most types of common bacterial infection, the recommended azithromycin dosage is 250 mg or 500 mg once daily for 3–5 days. Azithromycin dosage for children can range (depending on body weight) from 5 mg to 20 mg per kilogram of body weight per day, once daily for 3–5 days.
- Quinolone-resistant *Campylobacter* is present in several areas of South-East Asia (e.g., in Thailand) and azithromycin is then the appropriate treatment.
- Treatment for amebiasis should, ideally, include diloxanide furoate following the metronidazole, to get rid of the cysts that may remain after the metronidazole treatment.
- All doses shown are for oral administration. If drugs are not available in liquid form for use in young children, it may be necessary to use tablets and estimate the doses given in this table.
- Selection of an antimicrobial should be based on the sensitivity patterns of strains of *Vibrio cholerae* O1 or O139, or *Shigella* recently isolated in the area.
- An antimicrobial is recommended for patients older than 2 years with suspected cholera and severe dehydration.
- Alternative antimicrobials for treating cholera in children are TMP-SMX (5 mg/kg TMP + 25 mg/kg SMX, b.i.d. for 3 days), furazolidone (1.25 mg/kg, q.i.d. for 3 days), and norfloxacin. The actual selection of an antimicrobial will depend on the known resistance/sensitivity pattern of

*V. cholerae* in the region, which requires the availability of a well-established and consistent surveillance system.

- For adults with acute diarrhea, there is good evidence that an ultrashort course (one or two doses) of ciprofloxacin or another fluoroquinolone reduces the severity and shortens the duration of acute traveler's diarrhea. This area is still controversial; use should be limited to high-risk individuals or those needing to remain well for short visits to a high-risk area.

## 5.6 Prevention

Water, sanitation, and hygiene:

- Safe water
- Sanitation: houseflies can transfer bacterial pathogens
- Hygiene: hand washing

Safe food:

- Cooking eliminates most pathogens from foods
- Exclusive breastfeeding for infants
- Weaning foods are vehicles of enteric infection

Micronutrient supplementation: the effectiveness of this depends on the child's overall immunologic and nutritional state; further research is needed.

Vaccines:

- *Salmonella typhi*: two typhoid vaccines currently are approved for clinical use. No available vaccine is currently suitable for distribution to children in developing countries.
- *Shigella* organisms: three vaccines have been shown to be immunogenic and protective in field trials. Parenteral vaccines may be useful for travelers and the military, but are impractical for use in developing countries. More promising is a single-dose live-attenuated vaccine currently under development in several laboratories.
- *V. cholerae*: oral cholera vaccines are still being investigated, and their use is recommended only in complex emergencies such as epidemics. Their use in endemic areas remains controversial. In traveler's diarrhea, oral cholera vaccine is only recommended for those working in refugee or relief camps, since the risk of cholera for the usual traveler is very low.
- ETEC vaccines: the most advanced ETEC vaccine candidate consists of a killed whole cell formulation plus recombinant cholera toxin B subunit. No vaccines are currently available for protection against Shiga toxin-producing *E. coli* infection.
- Rotavirus: in 1998, a rotavirus vaccine was licensed in the USA for routine immunization of infants. In 1999, production was stopped after the vaccine was causally linked to intussusception in infants. Other rotavirus vaccines are being developed, and preliminary trials are promising. Currently, two vaccines have been approved: a live oral vaccine (RotaTeq™) made by Merck for use in children, and GSK's Rotarix™.

Measles immunization can substantially reduce the incidence and severity of diarrheal diseases. Every infant should be immunized against measles at the recommended age.

## 6 Clinical practice

### 6.1 Adults (Fig. 12)

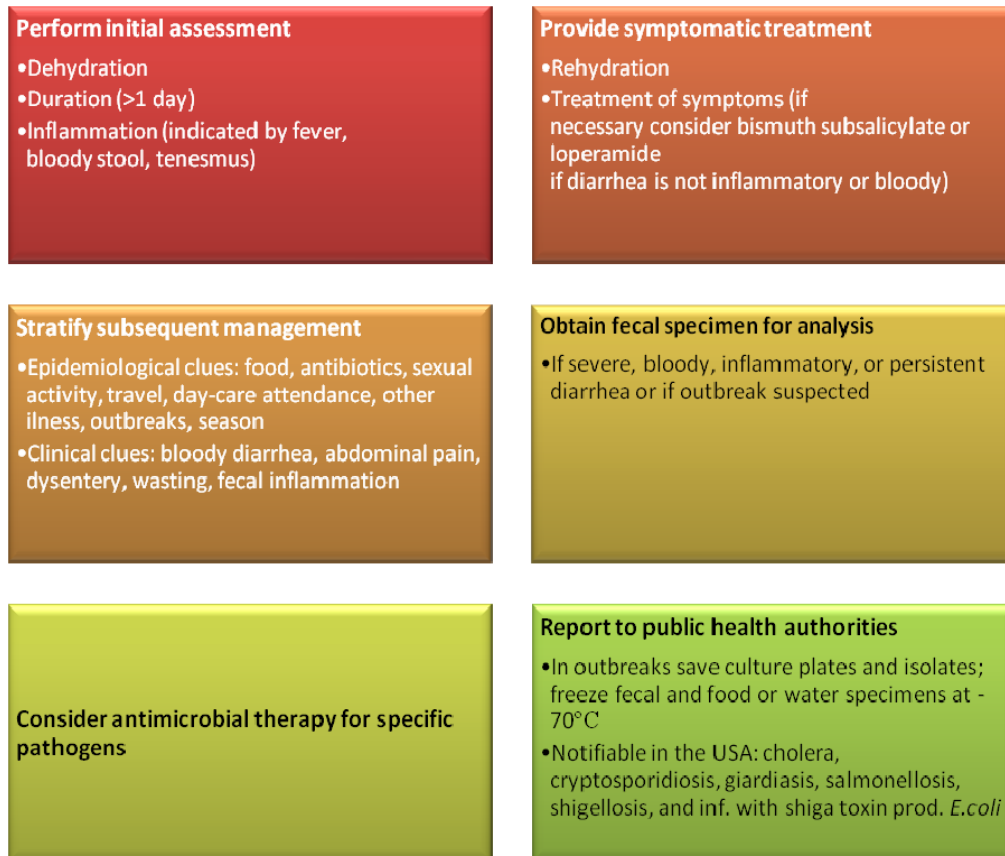


Fig. 12 The approach in adults with acute diarrhea.

### 6.2 Children (Figs. 13–15)

In 2004, WHO and UNICEF revised their recommendations for the management of diarrhea, including zinc supplementation as an adjunct therapy to oral rehydration. Since then, the recommendations have been adopted by more than 40 countries throughout the world. In countries where both the new ORS and zinc have been introduced, the rate of ORS usage has dramatically increased.

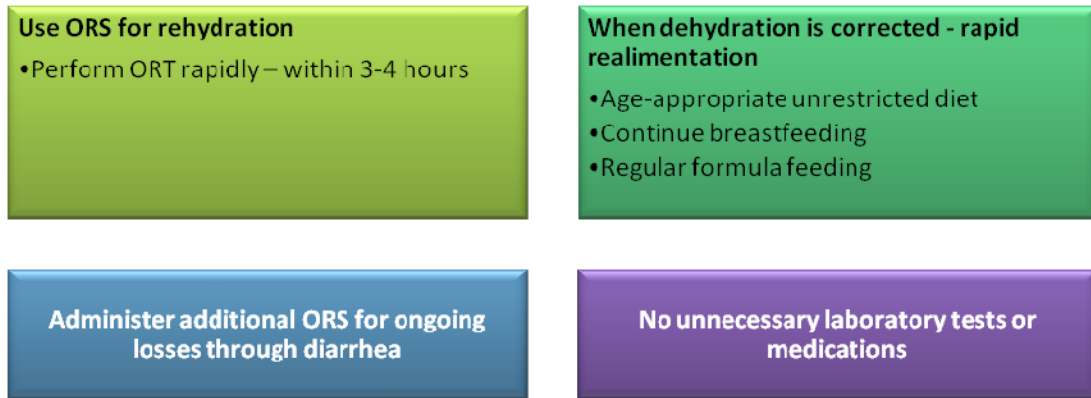


Fig. 13 Principles of appropriate treatment for children with diarrhea and dehydration.

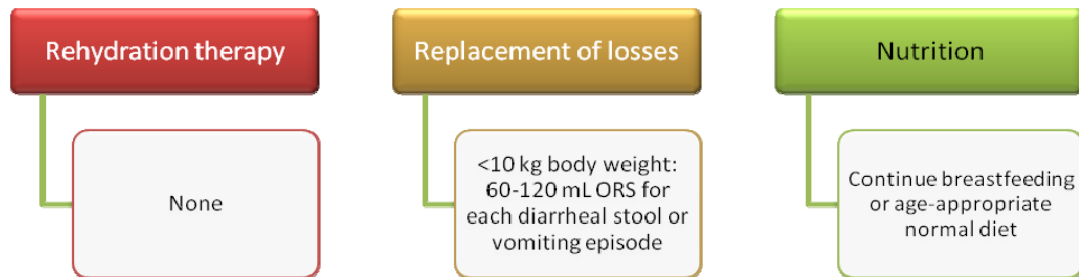


Fig. 14 Treatment for children based on the degree of dehydration.  
a Minimal or no dehydration.

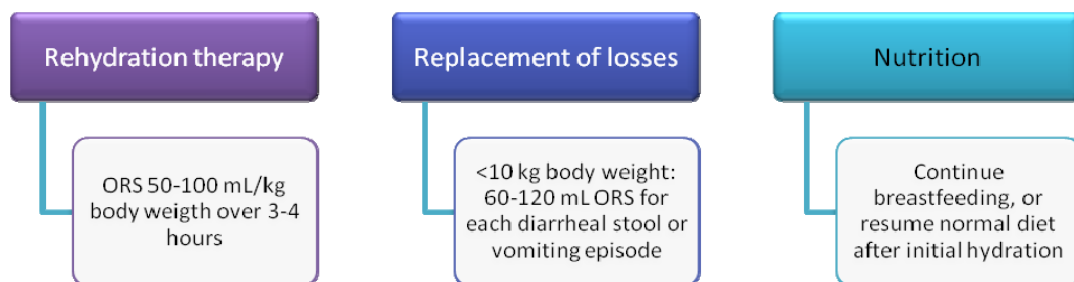


Fig. 14b Mild to moderate dehydration. Note: if vomiting is persistent, the patient (child or adult) will not take ORS and is likely to need intravenous fluids.

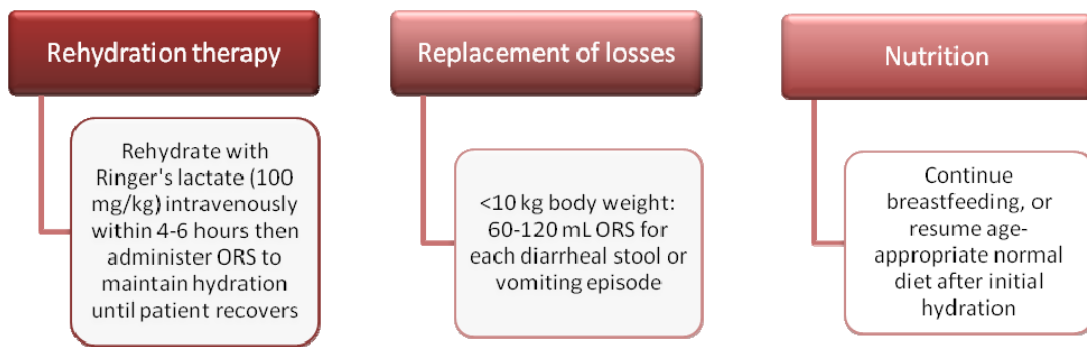


Fig. 14c Severe dehydration.

*Cautionary note.* Treating a patient with severe dehydration due to infectious diarrhea with 5% dextrose with 1/4 normal saline is unsafe. Severe dehydration occurs, usually as a result of bacterial infection (cholera, ETEC), which usually leads to more sodium loss in feces (60–110 mmol/L). A 1/4 normal saline solution contains Na 38.5 mmol/L, and this does not balance the sodium losses. Intravenous infusion with 5% dextrose with 1/4 normal saline will thus lead to severe hyponatremia, convulsion, and loss of consciousness. Five percent dextrose with 1/2 standard normal saline can only be used when Ringer's lactate is not available.

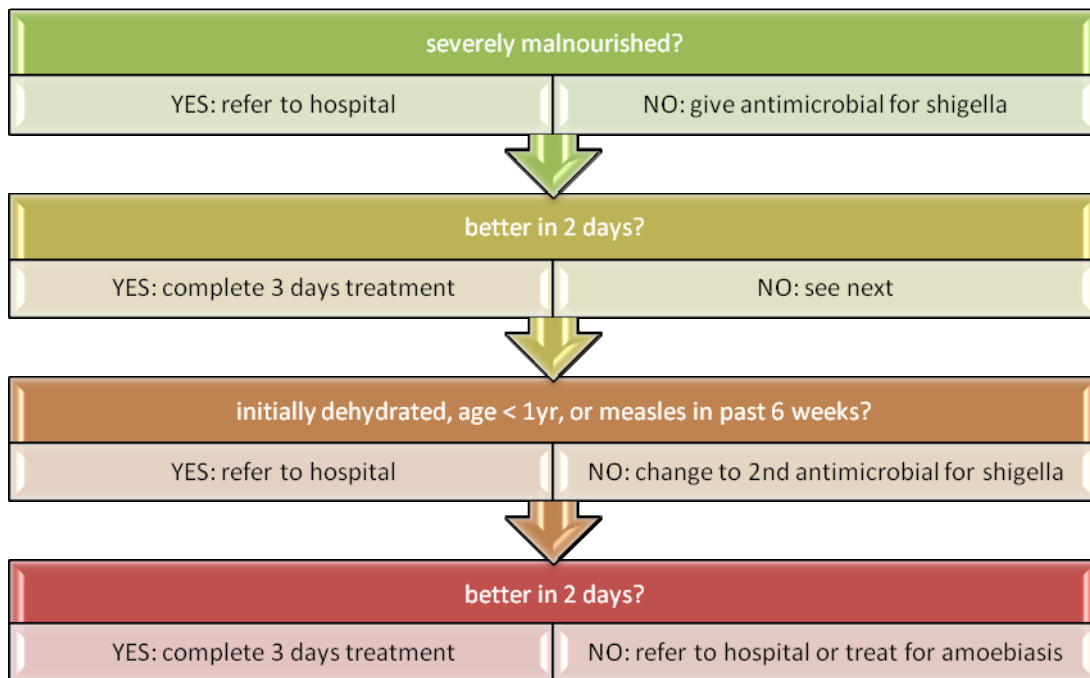


Fig. 15 The therapeutic approach to acute bloody diarrhea (dysentery) in children. The main principles are: treatment of dehydration; stool cultures and microscopy to guide therapy; and frequent smaller meals with higher protein intakes.

### 6.3 Home management of acute diarrhea

With ORS, uncomplicated cases of diarrhea in children can be treated at home, regardless of the etiologic agent. Caregivers need proper instructions regarding signs of dehydration, when children appear markedly ill, or do not respond to treatment. Early intervention and administration of ORS reduces dehydration, malnutrition, and other complications and leads to fewer clinic visits and potentially fewer hospitalizations and deaths.

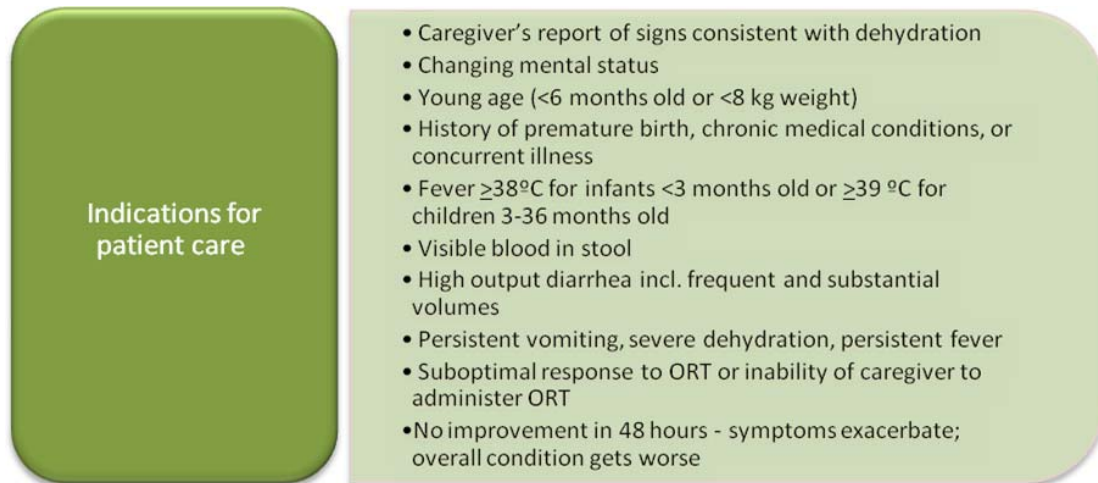


Fig. 16 Indications for in-patient care.

Self-medication in otherwise healthy adults is safe. It relieves discomfort and social dysfunction. There is no evidence that it prolongs the illness.

In adults who can maintain their fluid intake, ORS does not provide any benefits. It does not reduce the duration of diarrhea or the number of stools. In developed countries, adults with acute watery diarrhea should be encouraged to drink fluids and take in salt in soups and salted crackers. Nutritional support with continued feeding improves outcomes in children.

Among hundreds of over-the-counter products promoted as antidiarrheal agents, only loperamide and bismuth subsalicylate have sufficient evidence of efficacy and safety.

Principles of self-medication:

- Maintain adequate fluid intake.
- Consumption of solid food should be guided by appetite in adults — small light meals.
- Antidiarrheal medication with loperamide (flexible dose according to loose bowel movements) may diminish diarrhea and shorten the duration.
- Antimicrobial treatment is reserved for prescription only in residents' diarrhea or for inclusion in travel kits (add loperamide).

Family knowledge about diarrhea must be reinforced in areas such as prevention, nutrition, ORT/ORS use, zinc supplementation, and when and where to seek care (Fig. 16). Where feasible, families should be encouraged to have ORS ready-to-mix packages and zinc (syrup or tablet) readily available for use, as needed.

## 6.4 Cascades

A cascade is a hierarchical set of diagnostic or therapeutic techniques for the same disease, ranked by the resources available. Cascades for acute diarrhea are shown in Figs. 17–19.

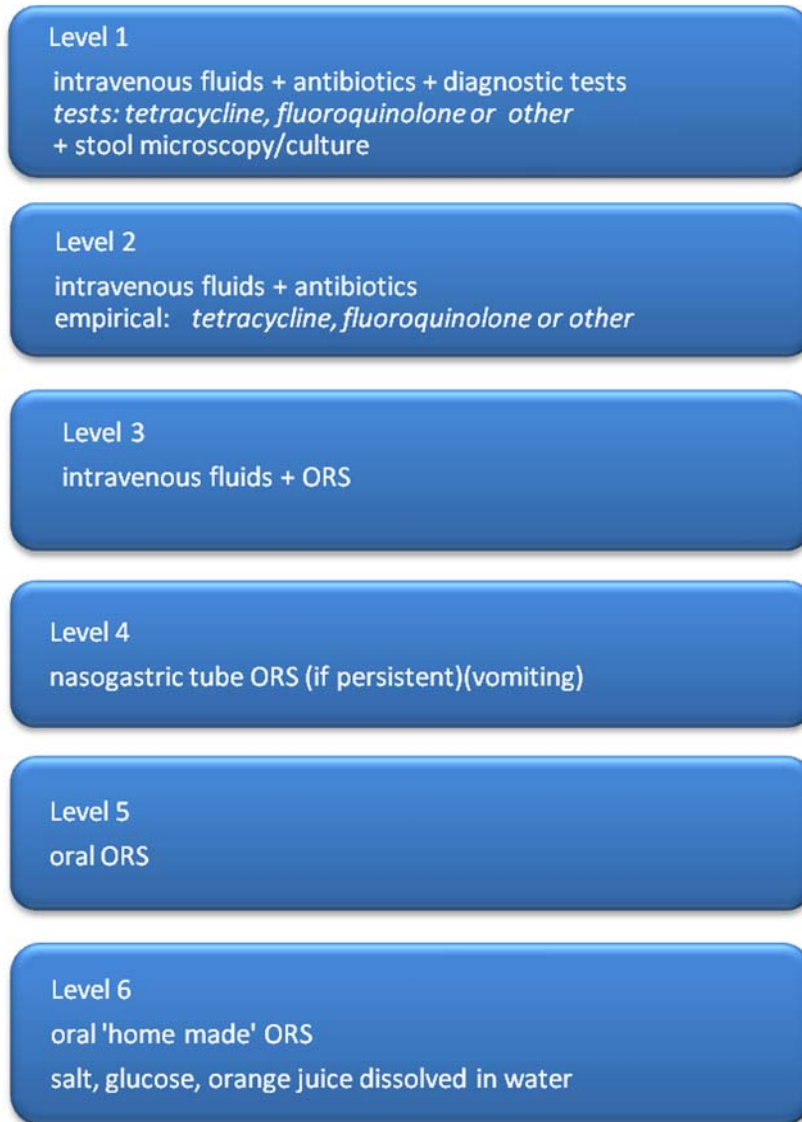


Fig. 17 Cascade for acute watery diarrhea – cholera-like, with severe dehydration.

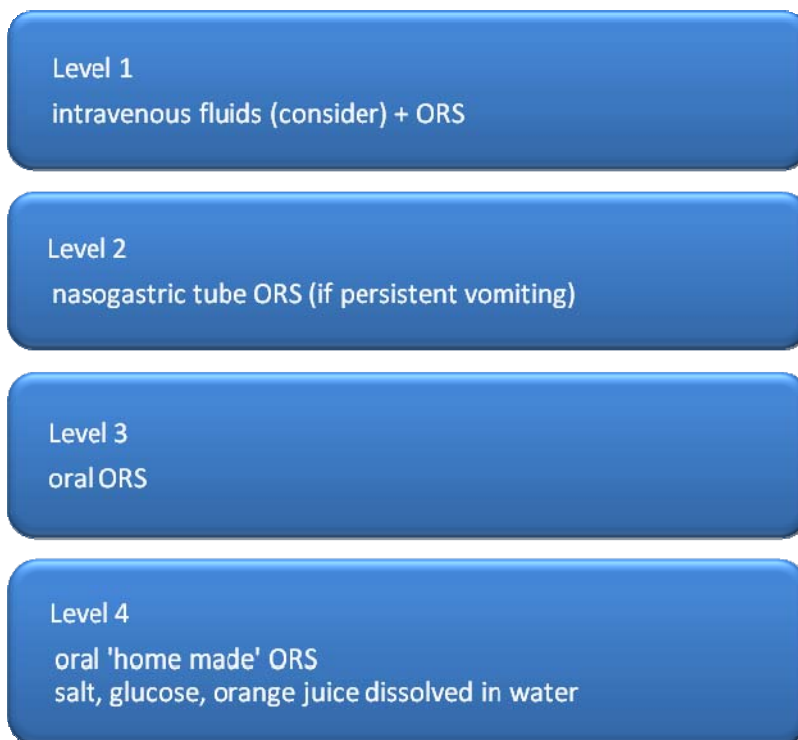
### Cautions:

- If facilities for referral are available, patients with severe dehydration (at risk of acute renal failure or death) should be referred to the nearest facility with intravenous fluids (levels 5 and 6 cannot replace the need for referral in case of severe dehydration).
- Levels 5 and 6 must be seen as interim measures and are better than no treatment if no intravenous facilities are available.

- When intravenous facilities are used, it must be ensured that needles are sterile and that needles and drip sets are never reused, to avoid the risk of hepatitis B and C.
- Do not diagnose moderate dehydration as severe dehydration and thus initiate referral for intravenous feeding because oral rehydration is more time-consuming. It is in the mother's interest to avoid the unnecessary complications that may be associated with using intravenous therapy.

*Notes:*

- Tetracycline is not recommended in children.
- Nasogastric (NG) feeding is not very feasible for healthy and active older children, but it is suitable for malnourished, lethargic children.
- NG feeding requires skilled staff.
- Often, intravenous fluid treatment is more easily available than NG tube feeding.
- NG feeding (ORS and diet) is especially helpful in long-term severely malnourished children (anorexia).



**Fig. 18** Cascade for acute watery diarrhea, mild/moderate, with mild/moderate dehydration.



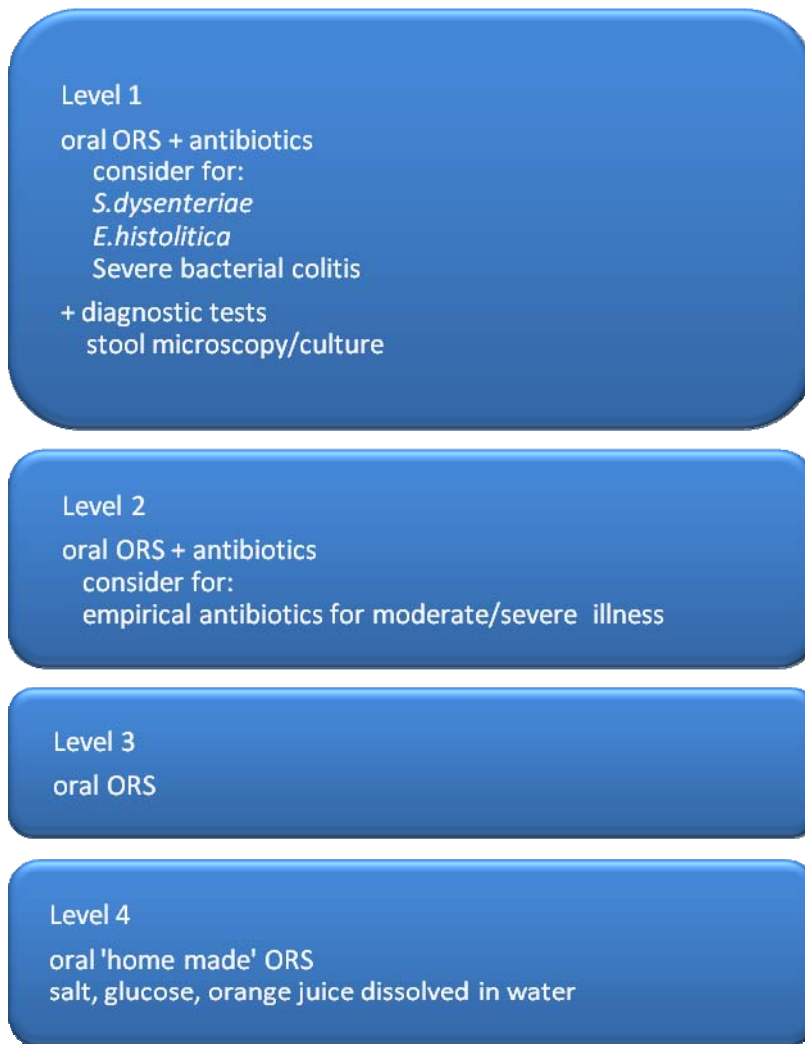


Fig. 19 Acute bloody diarrhea, with mild/moderate dehydration.

### Acknowledgment

The World Gastroenterology Organization's Acute Diarrhea Guideline Team is especially grateful for help and advice from Prof. Niklaus Gyr (Basle, Switzerland) and Prof. N.H. Alam of the International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) in Dhaka, Bangladesh.

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## 7 Automatic searches, guidelines, and further reading

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### 7.1 Introduction and automatic searches for PubMed

This section and the list of web sites following provide the best options for obtaining further information and help about acute diarrhea. PubMed/Medline, at [www.pubmed.org](http://www.pubmed.org), is the best source for keeping up to date with new evidence for acute diarrhea. The two links below are preprogrammed automatic searches in PubMed for evidence-based acute diarrhea from the last 3 years (link no. 1) and from the last 3 months (link no. 2)

- Link 1: Published research on acute diarrhea in the last 3 years  
[Click here to launch the search](#)
- Link 2: Published research on acute diarrhea in the last 3 months  
[Click here to launch the search](#)

### 7.2 Guidelines and consensus statements

The best general source for acute diarrhea guidelines is the National Guidelines Clearing House at: [www.ngc.org](http://www.ngc.org). Free subscriptions are available for notification every time a new evidence-based acute diarrhea guideline becomes available.

Centers for Disease Control and Prevention. [Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy](#). Atlanta, GA: Centers for Disease Control and Prevention — Federal Government Agency [U.S.]. 2003 Nov 21.

Cincinnati Children's Hospital Medical Center. [Evidence-based clinical care guideline for acute gastroenteritis \(AGE\) in children aged 2 months through 5 years](#). Cincinnati, OH: Cincinnati Children's Hospital Medical Center — Hospital/Medical Center, 1999 (revised 2005 Oct 31; reviewed 2006 May).

Manatsathit S, Dupont HL, Farthing M, et al. Guideline for the management of acute diarrhea in adults. *J Gastroenterol Hepatol* 2002;17(Suppl):S54–71 (PMID: 12000594).

UNICEF/WHO. Clinical management of acute diarrhea: UNICEF/WHO Joint Statement, May 2004 ([http://www.who.int/child-adolescent-health/New\\_Publications/CHILD\\_HEALTH/ISBN\\_92\\_4\\_159421\\_7.pdf](http://www.who.int/child-adolescent-health/New_Publications/CHILD_HEALTH/ISBN_92_4_159421_7.pdf)).

Wingate D, Phillips SF, Lewis SJ, et al. Guidelines for adults on self-medication for the treatment of acute diarrhoea. *Aliment Pharmacol Ther* 2001;15:773–82 (PMID: 11380315).

World Health Organization. Production of zinc tablets and zinc oral solutions: guidelines for programme managers and pharmaceutical manufacturers. Geneva: World Health Organization ([http://www.who.int/child-adolescent-health/publications/CHILD\\_HEALTH/ISBN\\_92\\_4\\_159494\\_2.htm](http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/ISBN_92_4_159494_2.htm)).

World Health Organization. The treatment of diarrhea: a manual for physicians and other senior health workers, 4th rev. ed. Geneva: World Health Organization, 2005 ([http://www.who.int/child-adolescent-health/New\\_Publications/CHILD\\_HEALTH/ISBN\\_92\\_4\\_159318\\_0.pdf](http://www.who.int/child-adolescent-health/New_Publications/CHILD_HEALTH/ISBN_92_4_159318_0.pdf)).

### 7.3 Further reading

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- Lawn JE, Wilczynska-Ketende K, Cousens SN. Estimating the causes of 4 million neonatal deaths in the year 2000. *Int J Epidemiol* 2006;35:706–18 (PMID).
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- Wang HH, Shieh MJ, Liao KF. A blind, randomized comparison of racecadotril and loperamide for stopping acute diarrhea in adults. *World J Gastroenterol* 2005;11:1540–3 (PMID: 15770734).
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## 8 Useful web sites

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- WHO links on the control of diarrheal diseases:  
<http://www.who.int/topics/diarrhoea/en/>  
[http://www.who.int/child-adolescent-health/New\\_Publications/CHILD\\_HEALTH/WHO\\_FCH\\_CAH\\_06.1.pdf](http://www.who.int/child-adolescent-health/New_Publications/CHILD_HEALTH/WHO_FCH_CAH_06.1.pdf)

- Centers for Disease Control links on the control of diarrheal disease:  
<http://www.cdc.gov/ncidod/dpd/parasiticpathways/diarrhea.htm>  
[http://www.cdc.gov/ncidod/dbmd/diseaseinfo/travelersdiarrhea\\_g.htm](http://www.cdc.gov/ncidod/dbmd/diseaseinfo/travelersdiarrhea_g.htm)
- The Institute for OneWorldHealth, a non-profit pharmaceutical company that has diarrheal disease as a key focus:  
<http://www.oneworldhealth.org/diseases/diarrhea.php>
- The International Center for Diarrheal Disease Research, Bangladesh (ICDDR, B) has a SUZY project (Scaling Up Zinc Treatment for Young Children with Diarrhea). Zinc in childhood diarrhea is a key research theme for the ICDDR, B:  
<http://www.icddr.org/activity/index.jsp?activityObjectID=448>

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## 9 Queries and feedback

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The Practice Guidelines Committee welcomes any comments and queries that readers may have. Do you feel we have neglected some aspects of the topic? Do you think that some procedures are associated with extra risk? Tell us about your own experience. You are welcome to click on the link below and let us know your views.

<mailto:guidelines@worldgastroenterology.org>