

WDHD | Enteric Infections: Prevention & Management

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Be Aware: Enteric Infections Remain a Significant Public Health Problem, Everywhere



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There has been progress, particularly in low-income countries. Since 1990, an impressive number of 1.8 billion people have gained access to improved drinking-water sources⁽¹⁾. In the past 20 years, the annual death toll in children below the age of 5 years associated with diarrhea has been reduced from over 3 million to less than 1.5 million^(2,3). That still is nearly one in five deaths in this age group and that, of course, is still unacceptable. Enteric infections, however, do not occur only in developing countries. In the United States it is estimated that food borne agents cause 48 million cases of illness annually⁽⁴⁾, many characterized by diarrhea. An estimated 127,000 hospitalizations and 3,000 deaths were associated with diarrhea, including 300 in children. Progress due to the introduction of rotavirus vaccine has been recorded here as well⁽⁵⁾. There were some 16,000 deaths from diarrhea recorded in Europe in 2002⁽⁶⁾. German sources describe that one third of the total

population will have diarrhea at least once annually. Lastly, over 20% of travelers from the industrialized countries can expect suffering from diarrhea during a two-week stay in a developing country. Although a substantial decrease in incidence rate has recently been observed in this population⁽⁷⁾, the problem is still significant.

Obviously different strategies are indicated to reduce the incidence of diarrheal diseases and their impact in different parts of the world. [Improvement of the infrastructure will reduce the risk of children developing the disease in the first place]. Prevention in low-income countries continues to be primarily targeted on initiatives to ensure i) access to clean water and sanitation, ii) safety of food and iii) protection of environment. To this end, awareness programs will continue to play an important role. The World Gastroenterol-

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A Guest Editorial from the Editors of *e-WGN*



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Acute diarrhea is a major public health problem in both resource-limited countries and developed countries of the world. In the former acute diarrhea is the second highest cause of death (after pneumonia) in children under five, and it is likely that repeated enteric infections may be responsible for both growth and mental retardation in a sizeable number of children. The primary factor responsible for acute diarrhea is the lack of clean water with the existing water supplies frequently contaminated with fecal wastes. Acute diarrhea also affects individuals in more economically advanced countries in several distinct ways including: a) epidemically when the food-supply chain is broken (which often becomes newsworthy and is the subject of much 'headline' news) and becomes contaminated by one or more bacteria; and b) sporadically during travel to underdeveloped countries which is often referred to as 'Traveler's diarrhea'.

World Digestive Health Day (WDHD) - which has been held since its inauguration in 2004 on 29 May, the anniversary of the founding of the World Gastroenterology Organisation (WGO) - was established to emphasize to both the public and professionals the importance of a major digestive tract illness. The theme for this year's WDHD is the Prevention & Management of Enteric infections: the important role of clean water, clean food, clean environment. This year's WDHD will emphasize both the public health aspects of acute infec-

tious diarrheal diseases as well as the scientific issues regarding interaction between multiple infectious agents and the small and large intestine.

The gastrointestinal tract has the largest surface interface to the environment and as a result has the potential for exposure to viruses, bacteria, parasites and a large variety of toxins. Equally important is that the intestine (especially the colon) has an extremely large endemic population of bacterial organisms that are associated with health and can be altered in several disease situations. Molecular methodology has opened a new world for the study of the endogenous fecal flora. When challenged by pathogens, the defense mechanisms of our innate and adaptive immune systems may respond by induction of fluid secretion and propulsive muscular activity resulting in diarrhea (and hopefully expulsion of the pathogen that initiated the process). The resulting diarrhea especially in very young children often leads to dehydration and metabolic acidosis, and primary treatment of acute diarrhea is the use of oral rehydration solution (ORS) [View the WGO Global Guideline on Acute Diarrhea Now](#). ORS leads to enhanced fluid absorption primarily as a result of stimulation of glucose-stimulated Na and water absorption (via SGLT1) in the small intestine. Unfortunately, ORS usage world-wide is quite low (~30-35%) for many reasons, and concerted action is required to increase its use with the

expectation that enhanced use of ORS will lead to improved child health.

Over the past three decades there have been several efforts to alter the formulation of ORS to reduce diarrhea and accelerate improvement. The present ORS formulation is hypo-osmolar with the administration of zinc for 10 days. An alternative approach that shows considerable progress is the incorporation of so-called amylase-resistant starch (starch that is relatively resistant to amylase digestion) that will result in both liberation of glucose in the small intestine and the production of short-chain fatty acids in the colon - a dual-action ORS.

Many diarrheal diseases find their way to the human gut via contaminated water supplies and access to clean water or means for cleaning water are crucial for preventing spread of disease. Likewise, clean food, how to avoid contamination of food, and clean environments are key issues in large parts of the world. The causative agent in many cases of acute diarrhea has eluded identification. Advances in molecular biology is now providing new knowledge and new tools for identifying virus and bacteria and one such tool, a rapid test for the most common bacterial causes for acute diarrhea in the West, is highlighted by Dr. Eduardo Salazar-Lindo in the Research Review of the latest *e-WGN*. It is anticipated that significant improvement in the diagnosis and treatment of acute infectious diarrhea will occur during the coming decade.

PSG @ 50: Towards A More Socially Responsive Society Through Education, Environmental and Health Advocacy Programs

The Philippine Society of Gastroenterology (PSG), on the occasion of its golden anniversary, embarked on the process of redefining its future by examining the past accomplishments of the society and the current ongoing projects and advocacy programs geared towards the attainment of the society's vision-mission. As a society characterized by commitment to continuing medical education programs both for its 316 active members and the Filipino community in general, a strategic management workshop was conducted in July 2010, particularly to define the core values of the society, determine the challenges from its defined external and internal environment and the defined population that it serves and formulate strategies and action plan to attain the desired results. One of the goals identified was to empower the society by 2020 on relevant gastrointestinal health issues through education, environmental and health advocacy programs. The Civic Action Committee of the Society, in collaboration with the Committee on Councils and Committee on Research and Education identified two priority advocacy programs which are consistent not only with the goals identified, but also with the national health issues, particularly control of preventable diseases linked to poor sanitation and nutrition.

Cognizant of existing and future global environmental health issues, The "PSG GREENS-Gastroenterologists for Reforestation and Environmental Sustainability" and the "PSG POWS-Potable Water System" were conceptualized and realized. A Memorandum of Agreement was signed by the President of the PSG, Dr. Diana Alcantara-Payawal and the President of the De la Salle Health Sciences Institute (DLSHSI) Brother Augustine Boquer FSC, for a three year project that shall ensure that PSG GREENS and the DLSHSI OMTB (One Million Trees and Beyond) will 1) Protect a three hectare forest area for a period of three years; 2) Plant 3,000 seedlings for the 3 year period; and 3) Clear and maintain a three hectare forest for a period of three years.

On October 10, 2010 (10-10-10), the 50th anniversary of the society, the two projects were undertaken by the Civic Action Committee chaired by Dr. Hilda Dina Gonzales with five members: Drs. Cirilo Chan, Teresita Gamutan, Russellini Magdaong, Yvonne Mina and Digna Pena. Together with students and academic staff volunteers from DLSHSI and the DENR (Dept of Environment and Natural Resources), the PSG 1st Vice President Dr. Marceliano Aquino Jr. the PSG Secretary, Dr. Joseph Bocobo and the Chair and four members of the Civic Action Committee, one thousand seedlings of plant species tuai, kalingag, dita, tamayuan, batiro and malagiting giting were planted on a cleared area of land in the steep Mount Palay-Palay in Mt. Palay Palay National Park Ternate, Cavite. This area will be maintained and nurtured as stipulated in the MOA signed by PSG with DLSHSI. PSG commits itself to sustain this advocacy and on February 26, 2011 another 1000



ogy Organisation selection of the topic for the WDHD is timely: On July 28, 2010 the United Nations General Assembly declared access to clean water and sanitation a human right. As demonstrated from the abovementioned U.S. report, food safety also is very relevant in industrialized countries. Vaccines will increasingly play a role in prevention, although the 'dream cocktail' immunizing against a majority of pathogens remains in the distant future. Prophylactic medication such as non-absorbable antibiotics, for example, are reserved for select groups of high-risk travelers⁽⁸⁾.

With respect to management of diarrhea in the developing world, reducing deaths "depends largely on delivering life-saving treatment of low-osmolarity oral rehydration salts and zinc tablets"⁽³⁾. However, only 39 per cent of children with diarrhea receive the recommended treatment, and limited trend data suggest that there has been little progress since 2000^(3,9). Important barriers have been identified, thus it now must be the time "to revitalize efforts to reduce diarrhea mortality

worldwide"⁽⁹⁾, using updated oral rehydration solution recommendations. The World Gastroenterology Organisation has recently published practice guidelines on Acute Diarrhea developed by a review team chaired by Prof. Michael Farthing⁽¹⁰⁾. It describes not only treatment options for all parts of the world, particularly industrialized nations, but also offers algorithms for clinical and laboratory evaluation.

Gastroenterologists worldwide as 'Global Guardians of Digestive Health' are expected to support the global fight against enteric infections on May 29 and throughout the year. The objective of WDHD 2011 is to focus attention on the prevention and management of diarrheal diseases, to improve child survival in developing countries and also to reduce morbidity and mortality in the industrialized world. Special attention will be given to at risk travelers.

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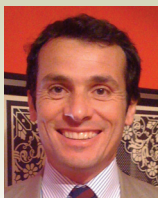
seedlings of the species *Rhizophora* were planted in the mangrove area in Calatagan Batangas, a province in the Southern Tagalog region of the Philippines. In attendance were the President of the PSG, Dr. Diana Payawal, the 1st and 2nd Vice Presidents, Dr. Marceliano Aquino Jr. and Dr. Marichona Naval respectively, as well as the PRO and Chair of the Civic action Committee, Dr. Hilda Dina Gonzales and two members, Drs. Gamutan and Magdaong. They were joined by 17 volunteers composed of nurses and academic staff from DLSHSI, and the local police officials of the community. This mangrove area will be monitored and if necessary, more trees will be replanted. The society plans to embark on regular tree planting sessions yearly and to invite more members of the society to participate in this noble and enjoyable undertaking.

Realizing that the society should have a more active and concrete role in the prevention of treatable diseases such as water-borne illnesses, the PSG POWS was conceptualized. With the help of an experienced Community Health Program Coordinator, Dr. Estrella Gonzaga, the society identified a depressed area in General Aguinaldo, Cavite to be the first recipient of this lofty and humble project. The community of Catmon in Barangay Batas Dao, General Aguinaldo Cavite consist mostly of families belonging to the economic Class C and D (poor and very poor). Due to the long distance of the community from the main road, the local water district cannot provide them potable water for consumption. Although the community has two rivers, the roads are generally non passable especially during rainy season. The same group that planted the trees in Mt. Palay Palay proceeded to the remote community

for a simple turnover ceremony of the artesian well to the members of the local barangay officials who were very appreciative of the efforts of the society. To this date, the artesian well, which was subjected to divination and water analysis for potability, provides a steady supply of water for this depressed community. PSG, through the current PRO and Chair of the Civic Action Committee, Dr. Frederick Dy, will duplicate the project in the indigenous community of the Aetas in Pampanga, a province in Central Luzon.

As we unite and move towards one direction, each of the officers and members of the Philippine Society of Gastroenterology, in collaboration with the Philippine Society of Digestive Endoscopy and the Hepatology Society of the Philippines commit to live our society's vision-mission for the welfare of the people that we serve.

Zinc as Multipotent Agent in the Treatment of Acute Diarrhea



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Despite significant improvements in the treatment of acute diarrhea in children, it continues to pose a daunting public health challenge, especially in developing countries. Worldwide, acute diarrhea affects 3 to 5 billion children each year, and recent estimates suggest that nearly 3% of neonatal mortality and 17% of under-five child mortality is attributable to the disease. Asia and Africa have still an alarmingly high incidence of childhood diarrhea⁽¹⁻²⁾. Substantial progress has been made in the treatment of acute diarrhea in children, with the introduction of reduced-osmolarity oral rehydration solution (ORS) and zinc supplementation. At present, the World Health Organization (WHO) and United Nations Children's Fund (UNICEF) jointly recommended that zinc supplementation should be provided at a dose of 10–20 mg per day for 10–14 days, and that this was efficacious in significantly reducing severity of diarrhea and duration of the episode⁽³⁾. Zinc is now included in the WHO essential medicine list for diarrhea treatment, and in the 2008 Copenhagen Consensus, a group of leading global economists, ranked zinc supplementation as the most effective intervention for advancing human development⁽⁴⁾. Zinc is now increasingly used in the treatment of acute diarrhea in developing countries where it is responsible for saving more than 400,000 lives a year⁽⁵⁾. Even more evidences have demonstrated that zinc supplementation has a considerable beneficial effect on the clinical course of acute diarrhea, and more recently the mechanisms of action of zinc are becoming clearer⁽⁶⁾. As reported in a recent systemic review, zinc supplementation reduced the mean duration of acute diarrhea by approximately 20%, and persistent diarrhea by 15–30%⁽⁶⁾. Another systemic review of the effects of zinc for diarrhea treatment was designed to meet the needs of the Lives Saved Tool (LiST). In LiST, increases in coverage of an intervention result in a reduction of one or more causes of mortality. The mentioned review was designed to develop estimates of the effect of an intervention in reducing death due to diarrhea and reported that zinc for the treatment of diarrhea will reduce diarrhea mortality by 23%. In addition, zinc has been shown to decrease diarrhea prevalence in both 24-hour and 2-week recall survey⁽⁷⁾. One study was of major interest as it measured the impact on stool output, the most objective marker of severity and a useful proxy indicator for risk of dehydration, in 286 hospitalized children with acute diarrhea and dehydration⁽⁸⁾. In the zinc treated children, the total stool output was reduced by 31% (95% CI 1% to 52%) compared to the placebo group. Introduction of zinc to community programs resulted in increased use of ORS, decreased use of unnecessary antibiotics, and a reduced need for medical visits

for acute diarrhea⁽⁹⁾. A recent study evaluating the therapeutic impact of supplementation with zinc, zinc plus vitamin A, and a combination of micronutrients and vitamins (i.e., zinc, iron, copper, selenium, vitamin B12, folate and vitamin A) on diarrhea in children showed that supplementation with a combination of micronutrients and vitamins was not superior to zinc alone, confirming the clinical benefit of zinc in children with diarrhea⁽¹⁰⁾. All studies showed that the effect of zinc did not vary significantly with age, or the nutritional status assessed by anthropometry. The effects were not dependent upon the type of zinc salts used: zinc sulfate, zinc acetate or zinc gluconate. There was little gain in efficacy when the commonly used 20 mg daily dose of elemental zinc was increased to 30–40 mg daily⁽¹¹⁾.

Although most studies reported positive effects elicited by zinc in the treatment of childhood acute diarrhea, some negative results have recently been published⁽¹²⁻¹³⁾. This discrepancy could be due to such factors as differences in the study design, nutritional and/or zinc status, age, race, sex, and the causative pathogen. A recent review and meta-analysis on the effect of zinc supplementation in prevention of diarrhea showed that zinc supplementation has a modest beneficial association (9% reduction) with incidence of diarrhea, a stronger beneficial association (19% reduction) with prevalence of diarrhea and occurrence of multiple diarrheal episodes (28% reduction). The authors described a significant heterogeneity across the studies for these associations. Age, continent of study origin, zinc salt and risk of bias contributed significantly to between studies heterogeneity. Finally, zinc supplementation did not show statistically significant benefit in reducing the incidence of persistent diarrhea, dysentery or mortality⁽¹⁴⁾. Other problems could derive from the fact that most of the data came from studies of children living in developing countries, and data from industrialized countries are needed.

Zinc is one of the most important trace elements for human health. It serves over 300 biological functions and elicits effects on multiple systems, including the gastrointestinal tract⁽¹⁶⁾. Zinc is not stored in the body, so its level is determined by the balance of dietary intake, absorption, and losses. A zinc deficiency state may exist in children with acute diarrhea as a result of intestinal loss, and chronic zinc deficiency may increase susceptibility to diarrhea^(6,16). Zinc is a multipotent agent at intestinal level and its positive action in acute diarrhea derives from several possible mechanisms: first, zinc regulates intestinal fluid transport and mucosal

integrity; second, zinc plays a substantive role in immunity; third, zinc can modify expression of genes encoding several zinc-dependent enzymes, like metalloproteases cytokines and uroguanylin; fourth, zinc may modulate oxidative stress⁽⁶⁾. Lastly, zinc is able to resist its potential loss in diarrhea. Few other substances exert such a variety of beneficial effects in the intestine. Zinc is safe, well accepted, easily administered, and inexpensive. As an adjunct to ORS, zinc has the potential to improve the management of acute diarrhea, determined by different mechanisms, at affordable costs. An universal zinc-containing super-ORS has been proposed^(3,17,18), and we have recently demonstrated the efficacy of a new hypotonic ORS containing zinc and prebiotics in the treatment of Italian ambulatory children with acute diarrhea⁽¹⁹⁾.

To conclude, clinical trials, reviews and meta-analyses strongly demonstrated that zinc reduces diarrhea duration, stool output, and stool frequency in children in developing countries. Recently, several *in vitro* observations have increased our knowledge of cellular mechanisms elicited by zinc that could support its use in the treatment of acute diarrhea. Most importantly, however, more clinical studies are necessary to better define its role in the treatment of acute diarrhea in western countries and to explore the selective effects of zinc against specific pathogens responsible for diarrhea.

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Frequently Asked Questions On Travelers' Diarrhea

Who gets travelers' diarrhea?

Travelers' diarrhea (TD) is the most common illness affecting travelers. Each year between 20%-50% of international travelers, an estimated 10 million persons, develop diarrhea. The onset of TD usually occurs within the first week of travel but may occur at any time while traveling, and even after returning home. The most important determinant of risk is the traveler's destination. High-risk destinations are the developing countries of Latin America, Africa, the Middle East, and Asia. Persons at particular high-risk include young adults, immunosuppressed persons, persons with inflammatory-bowel disease or diabetes, and persons taking H-2 blockers or antacids. Attack rates are similar for men and women. The primary source of infection is ingestion of fecally contaminated food or water.

What are common symptoms of travelers' diarrhea?

Most TD cases begin abruptly. The illness usually results in increased frequency, volume, and weight of stool. Altered stool consistency also is common. Typically, a traveler experiences four to five loose or watery bowel movements each day. Other commonly associated symptoms are nausea, vomiting, diarrhea, abdominal cramping, bloating, fever, urgency, and malaise. Most cases are benign and resolve in 1-2 days without treatment. TD is rarely life-threatening. The natural history of TD is that 90% of cases resolve within 1 week, and 98% resolve within 1 month.

What causes travelers' diarrhea?

Infectious agents are the primary cause of TD. Bacterial enteropathogens cause approximately 80% of TD cases. The most common causative agent isolated in countries surveyed has been enterotoxigenic *Escherichia coli* (ETEC). ETEC produce watery diarrhea with associated cramps and low-grade or no fever. Besides ETEC and other bacterial pathogens, a variety of viral and parasitic enteric pathogens also are potential causative agents.

What preventive measures are effective for travelers' diarrhea?

Travelers can minimize their risk for TD by practicing the following effective preventive measures:

- Avoid eating foods or drinking beverages purchased from street vendors or other establishments where unhygienic conditions are present
- Avoid eating raw or undercooked meat and seafood
- Avoid eating raw fruits (e.g., oranges, bananas, avocados) and vegetables unless the traveler peels them.

If handled properly well-cooked and packaged foods usually are safe. Tap water, ice, unpasteurized milk, and dairy products are associated with increased risk for TD. Safe beverages

include bottled carbonated beverages, hot tea or coffee, beer, wine, and water boiled or appropriately treated with iodine or chlorine.

Is prophylaxis of travelers' diarrhea recommended?

CDC does not recommend antimicrobial drugs to prevent TD. Studies show a decrease in the incidence of TD with use of bismuth subsalicylate and with use of antimicrobial chemoprophylaxis. Several studies show that bismuth subsalicylate taken as either 2 tablets 4 times daily or 2 fluid ounces 4 times daily reduces the incidence of travelers' diarrhea. The mechanism of action appears to be both antibacterial and antisecretory. Use of bismuth subsalicylate should be avoided by persons who are allergic to aspirin, during pregnancy, and by persons taking certain other medications (e.g., anticoagulants, probenecid, or methotrexate). In addition, persons should be informed about potential side effects, in particular about temporary blackening of the tongue and stool, and rarely ringing in the ears. Because of potential adverse side effects, prophylactic bismuth subsalicylate should not be used for more than 3 weeks.

Some antibiotics administered in a once-a-day dose are 90% effective at preventing travelers' diarrhea; however, antibiotics are not recommended as prophylaxis. Routine antimicrobial prophylaxis increases the traveler's risk for adverse reactions and for infections with resistant organisms. Because antimicrobials can increase a traveler's susceptibility to resistant bacterial pathogens and provide no protection against either viral or parasitic pathogens, they can give travelers a false sense of security. As a result, strict adherence to preventive measures is encouraged, and bismuth subsalicylate should be used as an adjunct if prophylaxis is needed.

What treatment measures are effective for travelers' diarrhea?

TD usually is a self-limited disorder and often resolves without specific treatment; however, oral rehydration is often beneficial to replace lost fluids and electrolytes. Clear liquids are routinely recommended for adults. Travelers who develop three or more loose stools in an 8-hour period—especially if associated with nausea, vomiting, abdominal cramps, fever, or blood in stools—may benefit from antimicrobial therapy. Antibiotics usually are given for 3-5 days. Currently, fluoroquinolones are the drugs of choice. Commonly prescribed regimens are 500 mg of ciprofloxacin twice a day or 400 mg of norfloxacin twice a day for 3-5 days. Trimethoprim-sulfamethoxazole and doxycycline are no longer recommended because of the high level of resistance to these agents. Bismuth subsalicylate also may be used as treatment: 1 fluid ounce or 2 262 mg tablets every 30 minutes for up to eight doses in a 24-hour period, which can be repeated on a second day. If diarrhea

10 Eating & Drinking Tips While Traveling

Diseases from food and water are the leading cause of illness in travelers.

Follow these tips for safe eating and drinking

- Wash your hands often with soap and water, especially before eating. If soap and water are not available, use an alcohol-based hand gel (with at least 60% alcohol).
- In areas where water is contaminated, travelers should not brush their teeth with tap water.
- Drink only bottled or boiled water, or carbonated (bubbly) drinks in cans or bottles.
- Avoid tap water, fountain drinks, and ice cubes. If this is not possible, learn how to make water safer to drink.
- Water on the surface of a beverage can or bottle may also be contaminated. Therefore, the area of a can or bottle that will touch the mouth should be wiped clean & dry.
- Do not eat food purchased from street vendors.
- Make sure food is fully cooked.
- Avoid dairy products, unless you know they have been pasteurized.
- Some fish are not guaranteed to be safe even when cooked because of the presence of toxins in their flesh.
- Infants younger than 6 months should either be breast-fed or be given powdered commercial formula prepared with boiled water.

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persists despite therapy, travelers should be evaluated by a doctor and treated for possible parasitic infection.

When should antimotility agents not be used to treat travelers' diarrhea?

Antimotility agents (loperamide, diphenoxylate, and paregoric) primarily reduce diarrhea by slowing transit time in the gut, and, thus, allows more time for absorption. Some persons believe diarrhea is the body's defense mechanism to minimize contact time between gut pathogens and intestinal mucosa.

In several studies, antimotility agents have been useful in treating travelers' diarrhea by decreasing the duration of diarrhea. However, these agents should not be used by travelers with fever or bloody diarrhea, because they can increase the severity of disease by delaying clearance of causative organisms. Because antimotility agents are now available over the counter, their injudicious use is of concern. Adverse complications (toxic megacolon, sepsis, and disseminated intravascular coagulation) have been reported as a result of using these medications to treat diarrhea.



World Gastroenterology Organisation practice guideline:
Acute diarrhea

March 2008

Review team:

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1 Methodology and literature review

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 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.

2 Epidemiologic features

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	900 000 total	6000 total
	> 1.5 million child outpatient visits	200 000 children	300 children
Worldwide	1.5 billion episodes		1.5–2 million children < 5 y
	In developing countries, children < 3 y have 3 episodes per year		

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 ($\times 1\,000\,000$)
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</i> , vol. 2. 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.

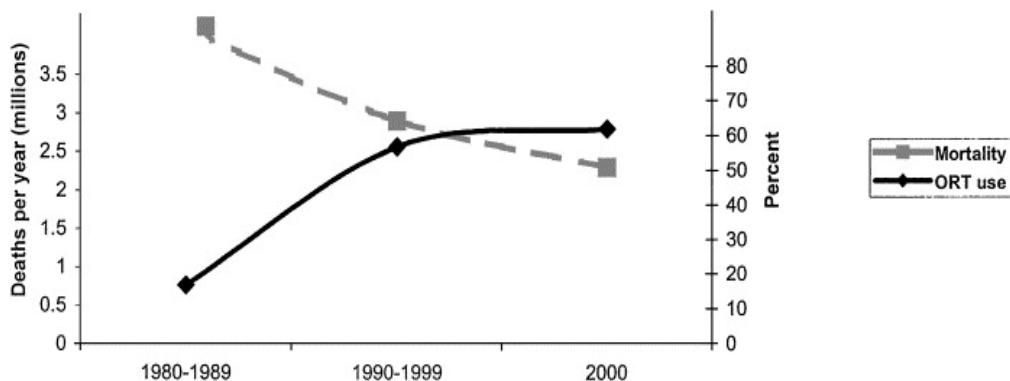


Fig. 1 Inverse association between coverage rates of oral rehydration solution (ORS) use and rates of mortality from diarrhea in various countries.

3 Causative agents and pathogenic mechanisms (Fig. 2)

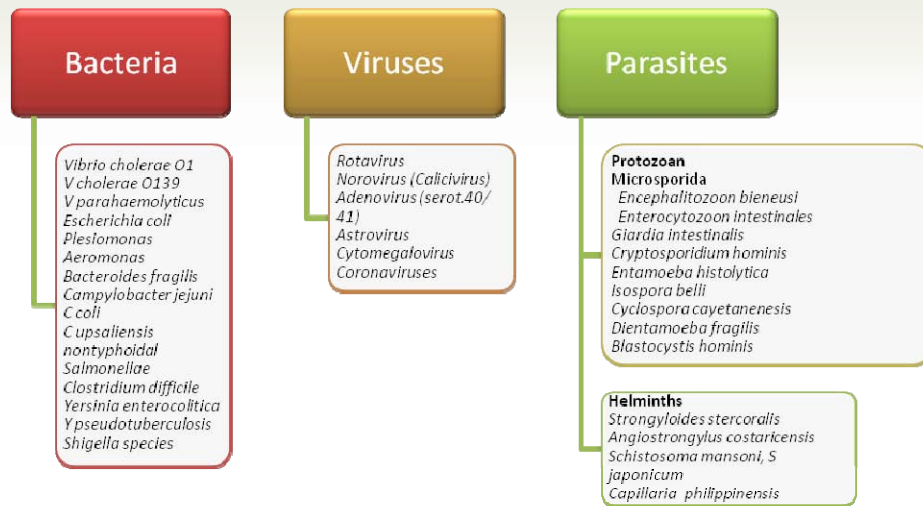


Fig. 2 Overview of causative agents in diarrhea.

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 cayetanensis* 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.

4 Clinical manifestations and diagnosis

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).

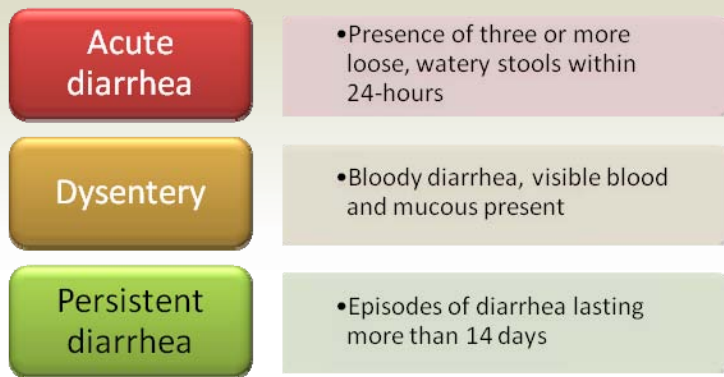


Fig. 3 Episodes of diarrhea can be classified into three categories.

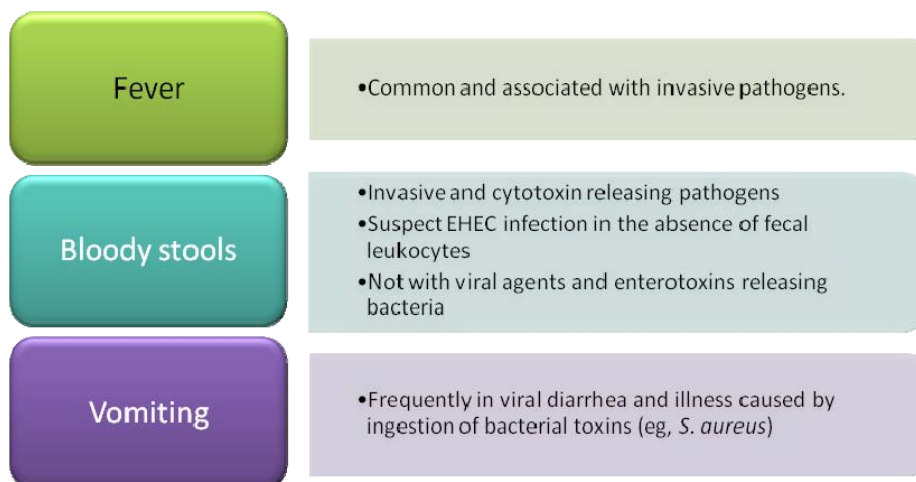


Fig. 4 Linking the main symptoms to the causes of acute diarrhea. EHEC, enterohemorrhagic *Escherichia coli*.

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

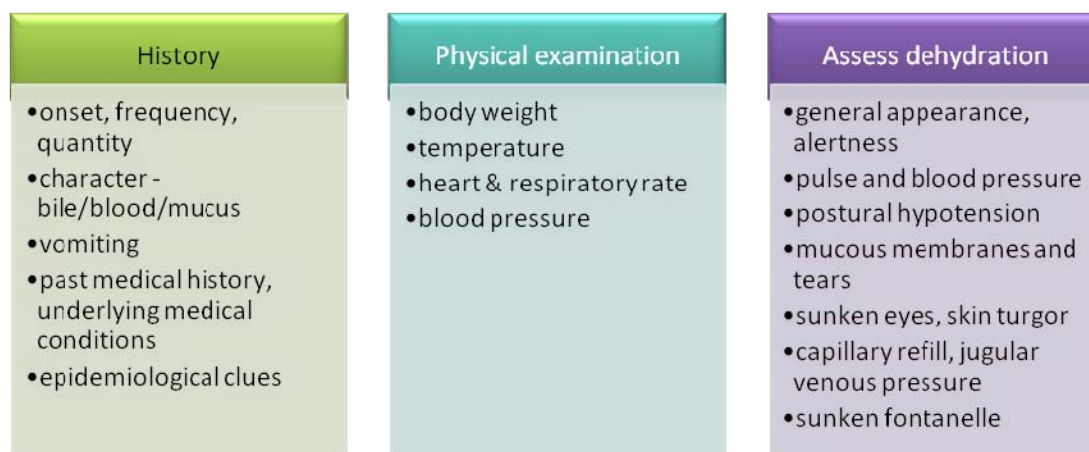


Fig. 5 Evaluation of the acute diarrhea patient.

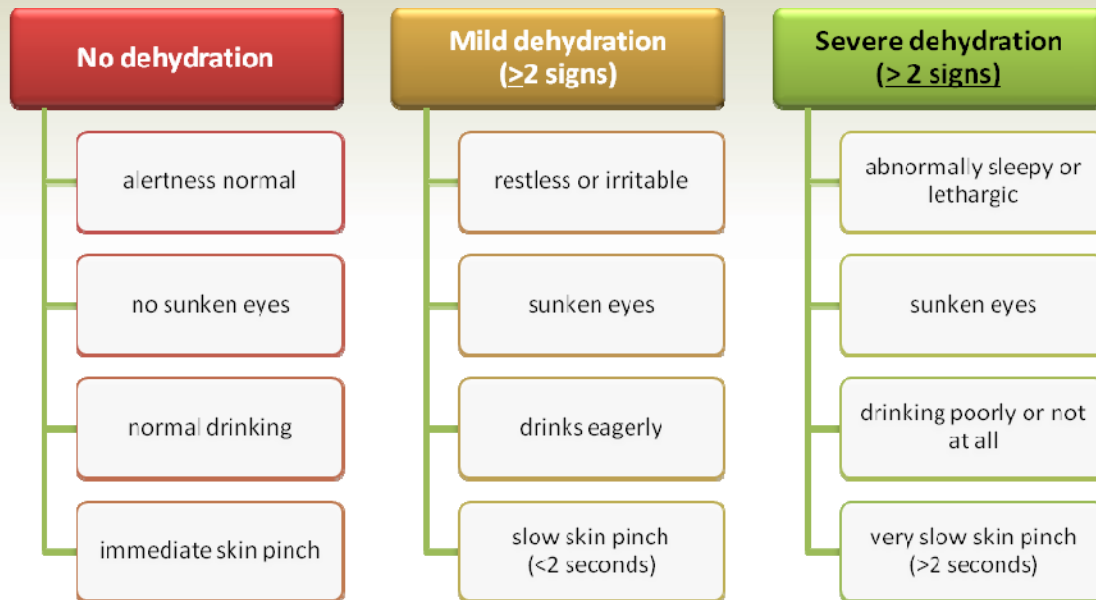


Fig. 6 Levels of dehydration in children with acute diarrhea.

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.

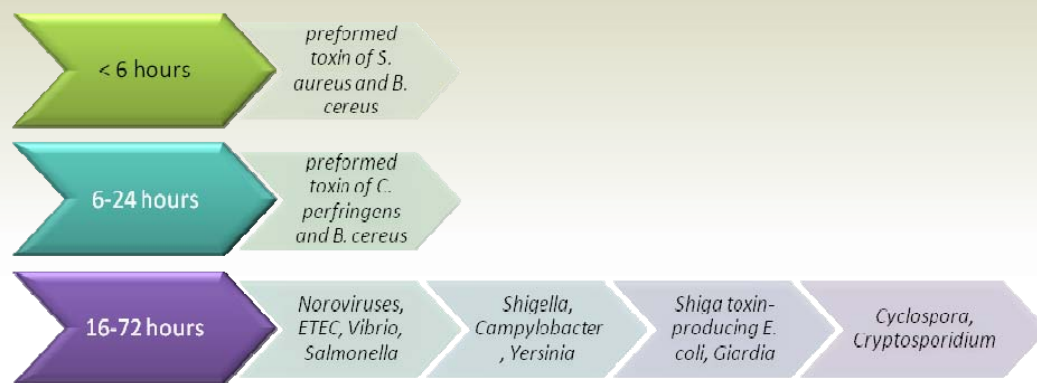


Fig. 8 The incubation period and likely causes of diarrhea.

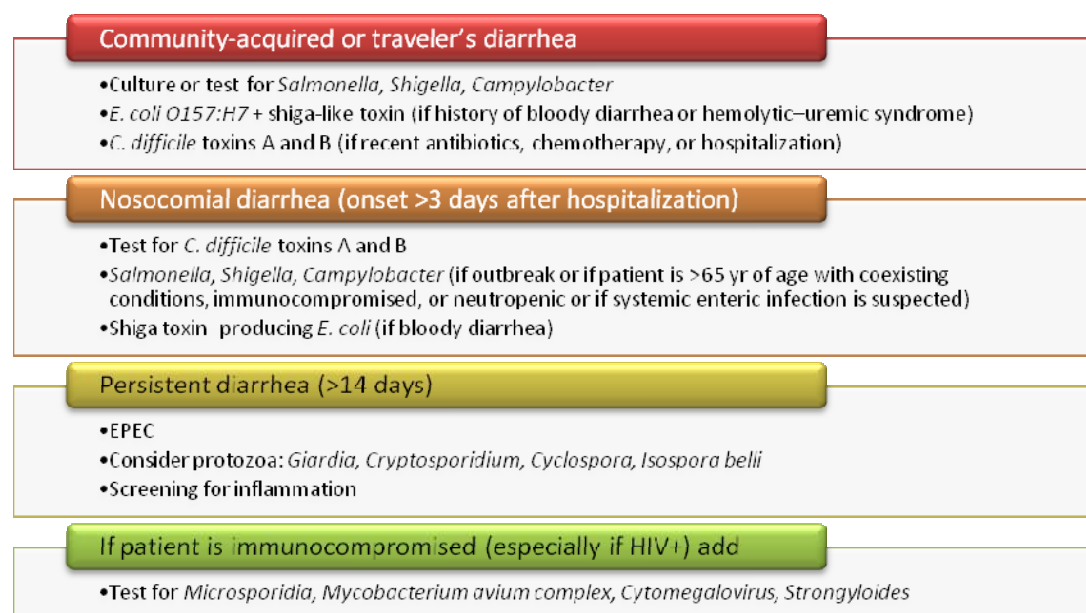


Fig. 9 A fecal specimen should be obtained for analysis in cases of severe, bloody, inflammatory, or persistent diarrhea, or if an outbreak is suspected.

(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)

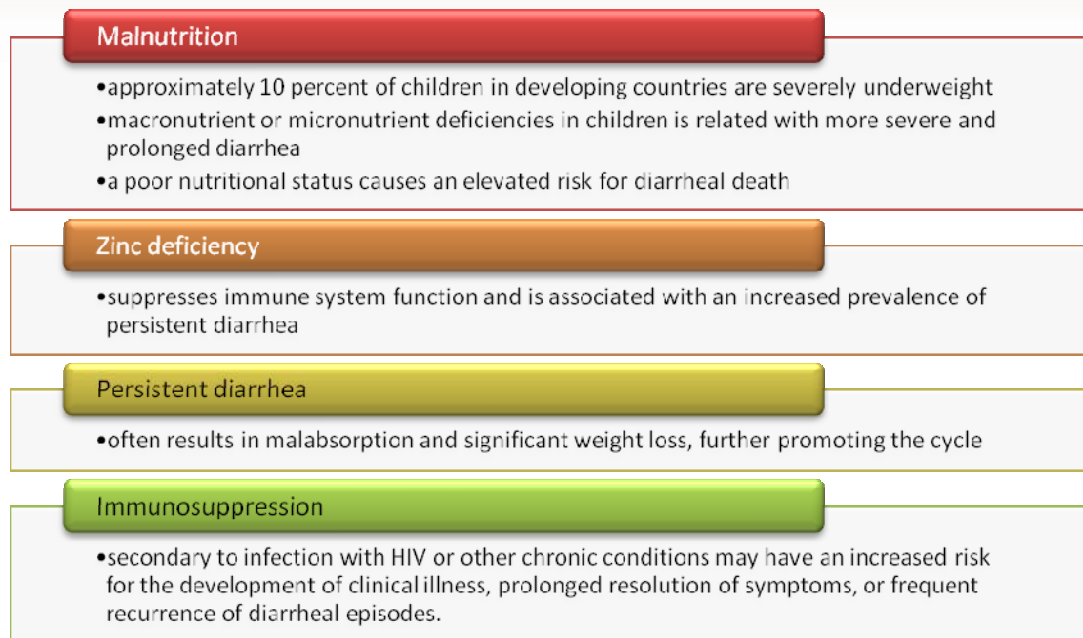


Fig. 10 Prognostic factors in children.

Differential diagnosis of acute diarrhea in children:

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

5 Treatment options and prevention

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, attapulgit
 - 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.

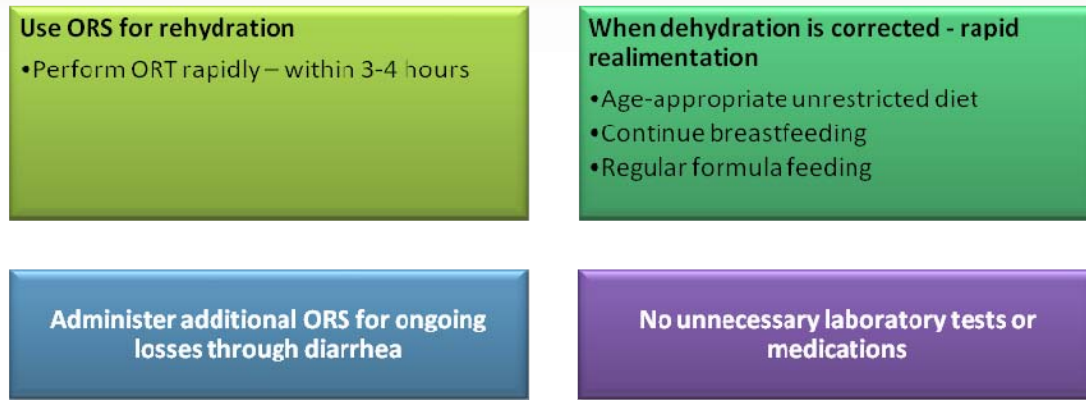


Fig. 13 Principles of appropriate treatment for children with diarrhea and dehydration.

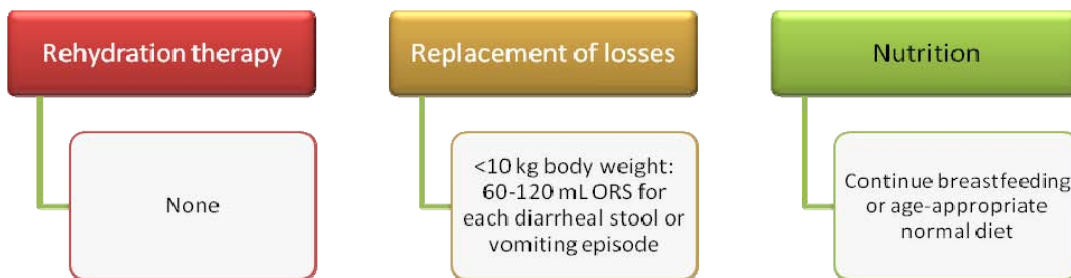


Fig. 14 Treatment for children based on the degree of dehydration.
a Minimal or no dehydration.

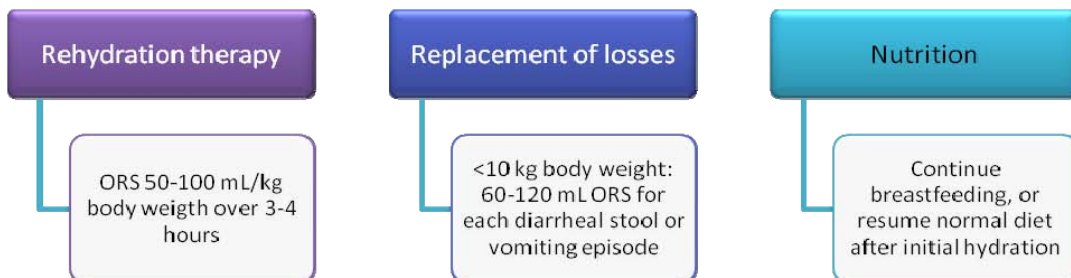


Fig. 14b Mild to moderate dehydration. Note: if vomiting is persistent, the patient (child or adult) will not take ORS and is likely to need intravenous fluids.



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.

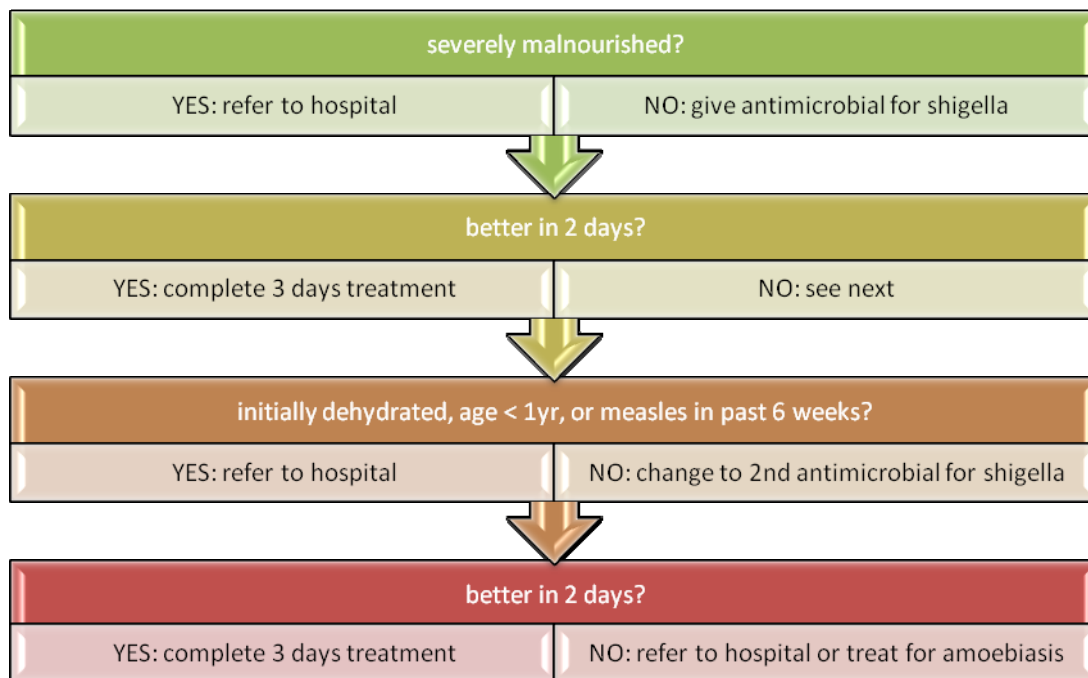


Fig. 15 The therapeutic approach to acute bloody diarrhea (dysentery) in children. The main principles are: treatment of dehydration; stool cultures and microscopy to guide therapy; and frequent smaller meals with higher protein intakes.

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.

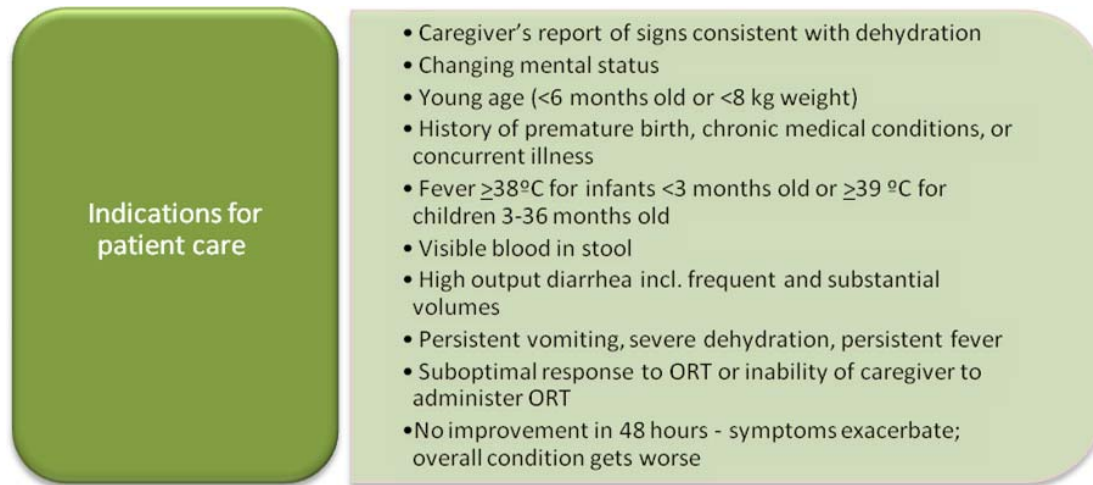


Fig. 16 Indications for in-patient care.

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.

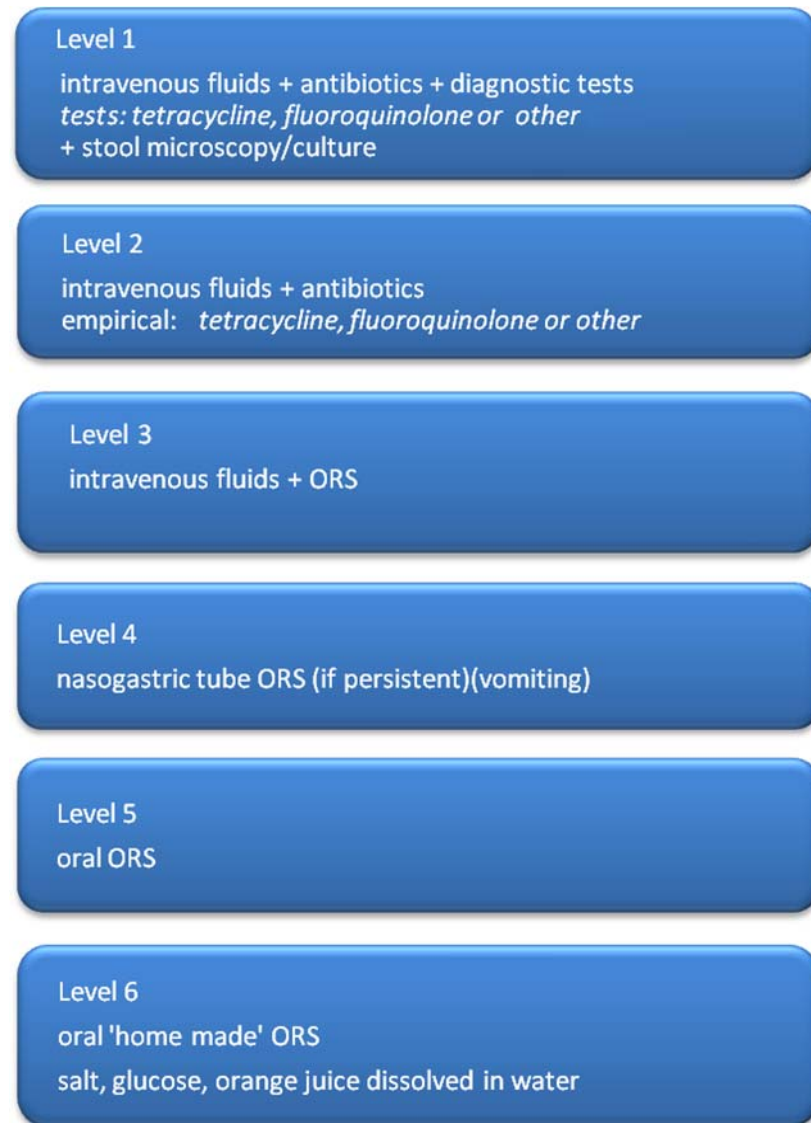


Fig. 17 Cascade for acute watery diarrhea – cholera-like, with severe dehydration.

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).

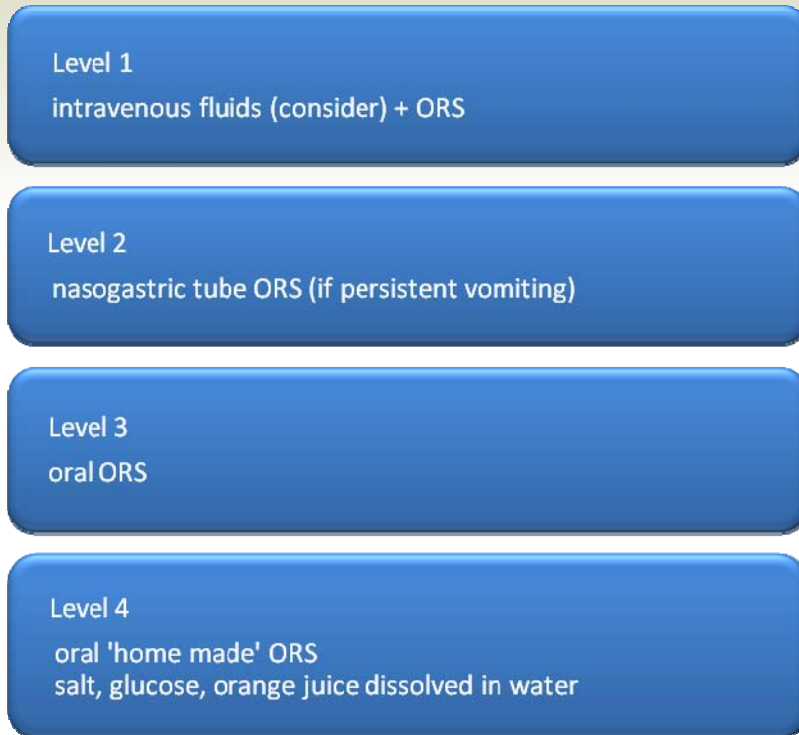


Fig. 18 Cascade for acute watery diarrhea, mild/moderate, with mild/moderate dehydration.

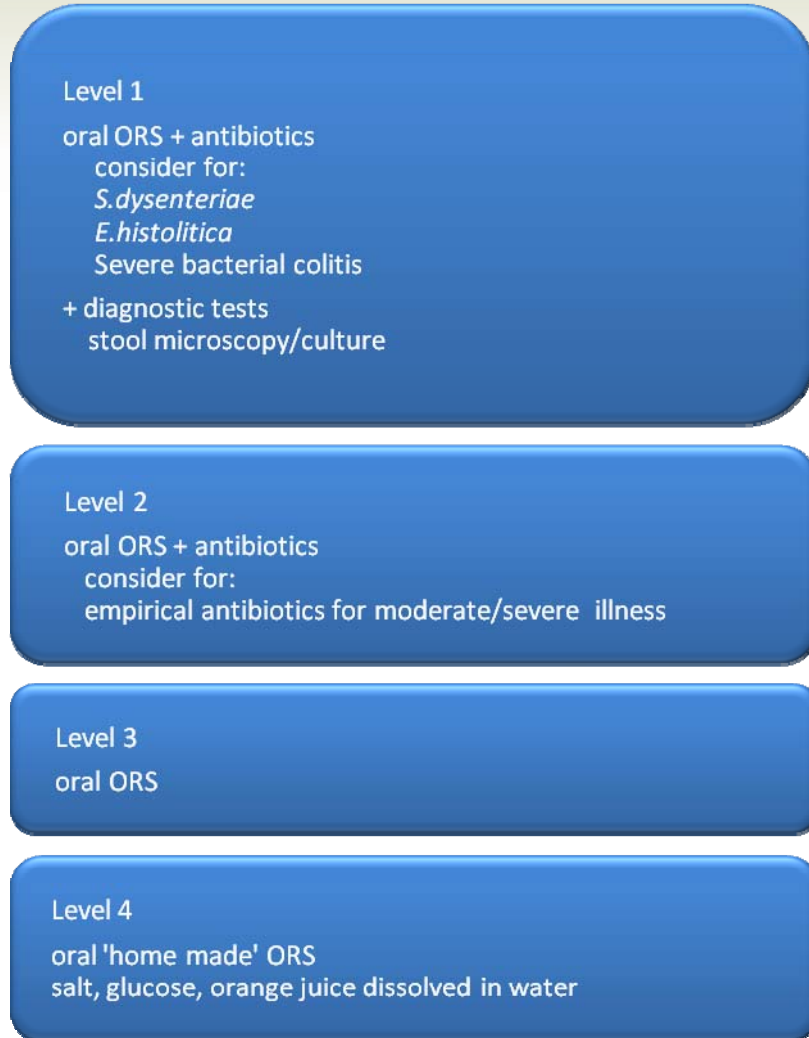


Fig. 19 Acute bloody diarrhea, with mild/moderate dehydration.

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) in Dhaka, Bangladesh.

7 Automatic searches, guidelines, and further reading

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, 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. 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).

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7.3 Further reading

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Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;367:1747–57 (PMID).

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8 Useful web sites

- 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

- 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
- 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) 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:
<http://www.icddr.org/activity/index.jsp?activityObjectID=448>

9 Queries and feedback

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>