

## Acute Infectious Diarrhea in Children

**Introduction:** Diarrhea is a worldwide health problem and one of the most common problems seen by the primary care physician in the United States. Complaints arising from the gastrointestinal tract are exceeded only by acute respiratory disease and skin problems. Diarrheal illness is responsible for 10% of all hospitalizations during the first five years of life.

**Pathophysiology:** Most diarrheal disease is noninflammatory and primarily affects the small intestine. Diarrhea may be broadly classified as secretory or malabsorptive (osmotic), depending on whether stool output continues or ceases, respectively, in the fasting patient.

Over 10L of fluid per day are secreted and absorbed by the normal adult gut. In the small intestine, fluid secretion occurs by the extrusion of chloride ion from the cells of the villus crypt; this extrusion is mediated by cyclic adenosine monophosphate (AMP). Absorption of fluid occurs at the cells of the villus tip. The balance between fluid secretion and absorption is upset in secretory diarrhea, and the resultant loss of water and electrolytes in the stool can be rapid and massive. The stool sodium concentration is high in secretory diarrheas (60 to 120 mEq per L) and, in severe cases, approaches the serum sodium concentration.

In malabsorptive diarrhea, damage to the intestinal microvillus membrane leads to malabsorption of luminal solute, with osmotic loss of free water into the gut lumen. The stool sodium concentration is usually low (30 to 40 mEq per L). Luminal osmolality has important therapeutic implications, which are discussed later in this article.

Stool losses of bicarbonate and potassium occur in both secretory and malabsorptive diarrhea.

**Etiology:** A variety of pathogens can cause acute infectious diarrhea in children (Table 1), and even more organisms may be responsible for diarrhea in immunocompromised hosts. In the United States, 30 to 40 percent of episodes of acute gastroenteritis in children are caused by viruses and 20 to 30 percent are caused by bacteria or parasites; no etiologic agent can be identified in as many as 40 percent of cases.

In addition to acute infectious gastroenteritis, the differential diagnosis of vomiting and diarrhea in children includes other infections, such as otitis media and sepsis, as well as noninfectious causes, including intestinal obstruction, toxic ingestions and inflammatory and allergic conditions.

Table I: Pathogens That Cause Acute Infectious Diarrhea in Children				
<b>Viruses</b>	<b>Bacteria</b>			<b>Parasites</b>
Rotavirus	Toxigenic	Cytotoxic	Invasive	<i>Giardia lamblia</i>
Enteric adenovirus	<i>Vibrio cholerae</i>	Clostridium difficile	Shigella species	<i>Entamoeba histolytica</i>
	Enterotoxigenic	Shigella species	Salmonella species	Cryptosporidium species
	<i>Escherichia coli</i>		<i>Y. enterocolitica</i>	Strongyloides stercoralis
	Shigella species	Adherent	<i>Campylobacter jejuni</i>	
	<i>Yersinia enterocolitica</i>	Enteropathogenic E. coli	<i>Vibrio parahaemolyticus</i>	
	<i>Aeromonas</i> species	Enterohemorrhagic E. coli	<i>Campylobacter fetus</i>	
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**Viruses:** Worldwide, rotavirus is the most common single pathogen identified in children with severe diarrhea. This pathogen accounts for 35 percent of hospitalizations for acute diarrheal illness. Infection probably occurs via fecal-oral transmission and is most common in children six months to two years of age. By the time they reach four years of age, most children are immune to the syndrome of severe dehydrating rotaviral diarrhea. In this country, the disease may occur at any time of the year, but it has a distinct pattern of winter seasonality, with peaks occurring in the Southwest in the fall and sweeping across the country toward the Northeast by late winter to spring.

Rotavirus invades and lyses the absorptive cells of the villus tip of the small intestinal epithelium, causing decreased absorption and depletion of brush-border disaccharidases with consequent carbohydrate malabsorption. Typically, rotavirus causes a self-limited syndrome with an incubation period of one to three days. Vomiting may occur for up to three days, and watery diarrhea may occur for three to eight days. The vomiting and diarrhea are often accompanied by fever and upper respiratory signs. Dehydration can be severe.

Other viral agents also cause acute infectious diarrhea in children. The pathogenesis and clinical syndromes of these infections are similar to those of rotavirus infection. However, adenovirus infection tends to cause a more prolonged diarrhea, and Norwalk virus infection often occurs in the setting of epidemic outbreaks.

**Bacteria:** Bacterial agents may cause diarrhea by several mechanisms, with some pathogens acting by more than one mechanism.

Toxigenic bacteria elaborate an enterotoxin that binds to specific receptors on the small bowel mucosa to cause a secretory diarrhea. The classic example is cholera, in which enterotoxin secreted by the gram-negative bacillus *Vibrio cholerae* stimulates cyclic AMP production and net fluid secretion by the small intestinal epithelium. In the United States, the most common toxigenic bacteria is enterotoxigenic *Escherichia coli*, which is also the most frequent cause of traveler's diarrhea.

Cytotoxic pathogens produce substances that cause cell damage and inflammation, primarily in the colon. The cytotoxin-mediated diarrhea of *Clostridium difficile* infection is often associated with use of antimicrobial agents.

Other bacterial pathogens damage the epithelium of both the small and large intestine by tightly adhering to the mucosal surface.

Invasive bacteria act primarily in the colon by first colonizing the lumen, then adhering to and invading the mucosa, where they multiply and elicit an acute inflammatory reaction. This effect results in the clinical picture of dysentery, with fever, abdominal pain, tenesmus, and blood and pus in the stool.

**Parasites:** Infection with enteric parasites can cause a prolonged clinical syndrome, which may be dysenteric, as with invasive *Entamoeba histolytica* disease. The pathogenic mechanisms of *Giardia lamblia* and Cryptosporidium species are not known.

**Clinical Evaluation of the Child with Acute Infectious Diarrhea:** The diagnosis of diarrhea is usually evident from the history. However, the specific etiology may be elusive.

## A. History

1. **General Information:** It is important to know the age of the child and whether or not there has been fever, vomiting, pain or the presence of other symptoms. It is also often helpful to know whether or not other family members or patient contacts have been affected.
2. **Specific Information:** Most of the specific information that would be useful involve the stool and urine patterns. It is helpful to know the duration, frequency, volume, color, odor, mucous content, blood content, and water content of the stools. In order to assess hydration it is important to know what type and how much fluids have been ingested and the frequency and volume of the urine output. In most cases these have to be estimated, but the mother or caretaker can tell if there have been any appreciable changes. Although **seizures** can occur with any infection they are more characteristic of Shigellosis.

## B. Physical Examination

Since diarrhea can be a symptom of several disease processes, a complete physical examination should be done, however, emphasis should be focused on three questions.

1. **What is the child's general appearance?** Much can be gained from the assessment of the child's general appearance. Does the child look ill or toxic? What is the level of activity?
2. **What is the state of hydration?** Careful examination of the skin, mucous membranes, eyes, and fontanelles for signs of dehydration is of major importance.
3. **Is there a focus of infection?** Children, particularly small infants, can have diarrhea associated with foci of infection other than in the gastrointestinal tract. Is there an infection that needs antibiotic treatment?

### C. Laboratory Examination

If there is a suspicion of bacterial or parasitic infection, or if the child is more ill than would be expected from a common viral diarrhea; then further information about the disease can be gathered from selected initial laboratory tests.

The following *initial* laboratory test may prove helpful:

1. **Stool analysis for blood, ova, parasites, white blood cell, pH and reducing substances.** These tests can be accomplished relatively quickly and may help in the decision as to whether or not the diarrhea is due to infection or some other etiology. Inflammatory diarrheas are more likely to be associated with the presence of blood and microscopic exam may show the presence of leukocytes. (Wrights Stain). Few cells are usually seen in the toxigenic diarrheas. The presence of eosinophils should raise suspicion of allergy or parasitic infection. A low pH (less than 6) and reducing substances are seen in carbohydrate malabsorption. The Rotazyme (R) test is useful in detecting the presence of rotavirus and stool cultures are necessary to identify specific bacterial organisms.
2. **Electrolytes and BUN.** These studies should be obtained when it is necessary to determine the fluid and electrolyte status.
3. **Complete Blood Count.** The CBC is usually of little help but may be useful in recognizing the presence of bacterial infection.

In persistent or chronic diarrhea the laboratory evaluation will become more important and an extensive laboratory workup may be necessary.

### Treatment of the Child with Acute Diarrhea

#### A. Dietary Management

The cornerstone of treatment of diarrhea is the replacement of the fluids and electrolytes being lost through the gastrointestinal tract. If vomiting is not a problem, the oral route is preferred. Almost all children with 5% or less dehydration can be rehydrated and maintained on oral fluids. Rarely, a child with as much as 10% dehydration can be managed orally. The remainder will require hospitalization and parenteral fluid and electrolyte therapy.

Reduction in intake of complex foods including milk is usually necessary during the rehydration process. The primary intake should be oral rehydration solutions. As the diarrhea resolves food can be gradually added to the diet. Since intolerance to lactose frequently develops following acute diarrheal disease, milk should be withheld for several days (3-5 days) or replaced with a non-lactose milk substitute such as a soy based formula. The fluid and electrolyte content of various rehydration fluids are listed in Table II.

Table II Composition of Oral Rehydration Solutions						
MEg/L						
Solution	Na+	K+	CL-	Base	Sugar	Osmolality
WHO Oral Rehydration	90	20	80	HCO <sub>3</sub>	Glucose 2%	310
Rehydralyte	75	20	65	Citrate	Glucose 2 1/2%	305
INFALYTE	50	20	40	HCO <sub>3</sub>	Glucose 2%	200
PEDIALYTE	45	20	35	Citrate	Glucose 2 1/2%	250
GATORADE	21	3	17	Phosphate	Glucose plus Sucrose 4.6%	330
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Other "clear liquids" should be used cautiously. Most are hyperosmolar and have unacceptably low sodium concentrations. Gatorade comes the closest.

### B. Specific Antibiotic Therapy

Since most diarrhea in children is not due to bacterial infection, antibiotic therapy is usually not indicated or needed. However, when a specific bacterial or parasitic organism is identified, specific antibiotic or antiparasitic therapy may be indicated. The following chart summarizes current recommendations regarding this therapy.

<u>Organism</u>	<u>Drug</u>	<u>Dose</u>
E. Coli	Trimethoprim-sulfa	8 mg/kg/day X 5 days
Shigella	or	
Salmonella*	Ampicillin	80 mg/kg/day X 5 days
Campylobacter**	Erythromycin	40 mg/kg/day X 5 days
Giardia	Furazolidone	5 mg/kg/day X 7 days
	or	
	Metronidazole	15 mg/kg/day X 7 days

\*Treatment may prolong the carrier state

\*\*Treatment not proven to reduce illness but may reduce spread.

### C. Non-specific Therapy

1. **Antiemetics.** Vomiting is a frequent occurrence during the early phase of gastroenteritis. Usually this is transient and ceases after oral foods are discontinued. If it is felt that temporary relief is necessary, suppositories will usually suffice. Promethazine (Phenergan 12.5, 25 and 50 mg), chlorperazine (Compazine 2 1/2, 5 and 25 mg) are among the most commonly used rectal suppositories. Children should be given the lowest recommended dose that is effective. If the vomiting is persistent or if there is associated central nervous system symptoms the medication should not be used and further evaluation of the problem should be accomplished.

2. **Anticholinergics.** Atropine, scopolamine, hyoscyamine and belladonna which are components of several antidiarrheal medications serve as anti-spasmodics to help control hypermotility and hypersecretion of the gastrointestinal tract. They may provide some relief to any age patients but should be used primarily in older children and adults in whom the symptoms can be more reliably monitored. They should be used only with caution in infants. They might potentially worsen bacterial diarrhea.
3. **Absorbants.** Substances such as kaolin, pectin, and polycarbophil serve to absorb intestinal fluid thereby providing more mass to the bowel movement. They can provide some reduction in frequency of bowel movement, however, they have no direct benefit in reducing fluid loss or shortening the duration of illness. Again, they are probably more efficacious in older children and adults.
4. **Opiates.** Opium and its derivatives act directly on the smooth muscle of the gut to increase tone and decrease motility. The most commonly used opiates include opium, paregoric (camphorated opium tincture) and diphenoxylate (Lomotil®). They are most useful for treatment of cramping and tenesmus but may potentially worsen the course of bacterial diarrhea. These drugs are safer and more efficacious in school-aged children and diarrhea in smaller children and infants.
5. **Other Drugs.** (Pepto-Bismol®) (Bismuth subsalicylate) is an across-the-counter medication for "upset stomach" and diarrhea. Its mechanism of action is not clear but it has been recently found to be useful in the treatment of "traveler's diarrhea" which is usually due to toxigenic E. Coli.

**Note:** Emetrol® is an oral solution (mint flavored) containing balanced amounts of levulose (fructose) and dextrose (glucose) and orthophosphoric acid with hydrogen hyperactive G.I. tract to control both nausea and vomiting by reducing smooth-muscle contraction.