

10. DIARRHEAL DISEASE, ACUTE

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The recommendations on the evaluation and management of acute diarrheal disease in children were developed by summarizing the guidelines and recommendations of review articles (Hamilton, 1985; DeWitt, 1989; Fitzgerald, 1989; Walker-Smith, 1990; American Academy of Pediatrics [AAP], 1993; Laney and Cohen, 1993; Richards et al., 1993; World Health Organization [WHO], 1993; Northrup and Flanigan, 1994) and the April 1991 supplement to *The Journal of Pediatrics*, found in volume 118, number 4, part 2, which discussed the "Management of Acute Diarrheal Disease." The review articles were selected from a MEDLINE literature search on the key words diarrhea and gastroenteritis, looking for articles in the English language published between the years 1985 and 1995. Focused assessment of the literature with respect to specific areas of importance or disagreement among the reviews were then conducted which relied on reference lists in those review articles.

IMPORTANCE

Acute diarrheal disease is one of the most common presenting conditions in the pediatric population in the United States. Based on longitudinal studies conducted in Charlottesville, Virginia, Washington, D.C., and Winnipeg, Manitoba, done in the period from 1975 to 1980, the incidence of mild diarrheal illness during the first five years of life was estimated to be 6.5 to 11.5 episodes per child, resulting in 21.5 to 38 million episodes per year (Glass et al., 1991). The incidence of diarrheal illness is felt to be highest among children one to three years of age (Glass et al., 1991). The rate of diarrheal illness among children attending daycare centers may be two to three times higher than for other cohorts of children (Cohen, 1991; Northrup and Flanigan, 1994).

The incidence of a diarrheal illness leading to a physician visit was about 0.6 to 1.1 cases per child during the first five years of life based on data from the National Health Interview Survey for 1981 to 1985

and from the 1985 National Ambulatory Care Survey and the National Ambulatory Care Complement Survey (Glass and Cohen, 1991). Based on the National Hospital Discharge Survey for 1979 to 1984 and the McAuto data base of 1982-1985, hospitalization for diarrhea occurred among 1.4 percent of all children up to five years of age; this represented 10.6 percent of all hospitalizations of children in the United States, constituting 4.2 days per hospitalization (Glass and Cohen, 1991).

Based on the Multiple Cause of Death data files for 1973 to 1983, one child out of every 15,000 born in the United States died of complications associated with diarrhea such as dehydration, electrolyte abnormalities, shock, cardiac arrest, respiratory failure, prematurity, malnutrition, and bronchopneumonia (Glass et al., 1991). Another possible cause of death in children with diarrhea is hypoglycemia (Wapnir and Lebenthal, 1991). Deaths from diarrhea account for ten percent of preventable postneonatal infant deaths in the United States (Richards et al., 1993). Most deaths attributable to diarrhea occurred among infants less than one year of age (Glass et al., 1991). In the infant less than 36 months of age with diarrhea and fever, the risk of bacterial enteritis with bacteremia is felt high enough to warrant a septic work-up. The incidence of diarrheal illnesses is high, and the morbidity and mortality significant.

Northrup and Flanigan (1994) estimate the typical cost of care for inpatient parenteral therapy for an episode of acute diarrhea at \$2000 and \$200 for oral rehydration in an outpatient setting. Listernick et al. (1986) similarly found that oral rehydration cost about twelve percent as much as intravenous therapy. Considering the numbers of cases of acute diarrhea among children, the cost is high.

EFFICACY AND/OR EFFECTIVENESS OF INTERVENTIONS

Screening and Prevention

Though acute diarrheal illness is not a condition or symptom screened for in the United States health system, the health care provider in the provision of routine health supervision should inquire as to factors of high risk for episodes of diarrhea such as attendance in a child care center, frequent visits to a health care facility (e.g.,

for children with a chronic illness), or the presence of a compromised immune condition. In these high-risk situations, parents, and children who are old enough to understand, should be instructed on the importance of prevention of diarrheal episodes through good sanitation practices such as careful handwashing after toileting (DeWitt, 1989) and care in food preparation (Hamilton, 1985). In the infant, breastfeeding may also afford some degree of protection against infectious diarrheal events (Hamilton, 1985). In addition, various vaccines are presently undergoing development in an effort to prevent diarrhea caused by rotaviruses, typhoid fever, shigella, cholera, enterotoxigenic *E. coli*, and enteropathogenic *E. coli* (Levine, 1991).

Diagnosis

The presence of diarrhea, that is "stools that are abnormally frequent and liquid" (DeWitt, 1989), is established through assessment of the history and the gross examination of a stool sample when available. The health care provider should assess the child's hydration status and the likelihood of sepsis. The health care provider should also determine the etiology of the diarrheal episode, whether viral, bacterial, parasitic, or noninfectious, and the possible need for further intervention, such as the need for antimicrobial agents or public health referral. In most cases in which shock is not present or sepsis is not suspected, however, the episode of diarrhea will be brief and self-limited; the health care provider may reserve more exhaustive etiologic evaluation for the child who does not respond to standard hydration (Richards et al., 1993; Northrup and Flanigan, 1994).

The presence and severity of diarrhea must first be established. The health care provider should inquire as to (1) the date of onset, (2) the consistency and character of the stool, whether voluminous, watery, mucousy, or bloody, and (3) the frequency of stools (DeWitt, 1989). A precise definition of diarrhea is not available; it is assessed in comparison to the individual child's normal frequency, consistency, and volume of stools. The degree of oral intake of fluids is also important to determine, as is the degree of urinary output (DeWitt, 1989; Fitzgerald, 1989). The clinician should also inquire as to the child's

affect and the presence of fever, abdominal pain, tenesmus, or vomiting (DeWitt, 1989; Northrup and Flanigan, 1994). Other useful information would include past or present antibiotic use, contact persons with similar symptoms, attendance in a child care setting, recent diet history, recent travel history, recent exposure to livestock or other animals, and history of chronic illness, specifically sickle cell anemia or immunocompromise (DeWitt, 1989; Northrup and Flanigan, 1994). If available, the stool should be examined, especially for presence of gross blood (Northrup and Flanigan, 1994). The physical examination should focus on assessing hydration status as noted below and also on the possibility of sepsis (Baraff et al., 1993), especially in children under three years old. The vital signs should be measured and recorded (DeWitt, 1989). The weight should be recorded (DeWitt, 1989). Information gathering with regard to specific etiology may be postponed until the child's hydration status is stabilized, unless it relates directly to management of fluids and electrolytes or diagnosing sepsis.

Because much of the morbidity and mortality of acute diarrhea are caused by problems of hydration and electrolyte imbalance, the hydration status of the child with diarrhea must be immediately assessed through elements of the history and physical examination. In the World Health Organization Management of the Patient with Diarrhea chart, the assessment of dehydration is based on the factors shown in Table 10.1 (AAP, 1993; WHO, 1993):

Table 10.1
WHO Factors For Assessing Hydration Status

| FACTORS | DEGREE OF DEHYDRATION | | |
|-------------------|------------------------------|--|--|
| | MINIMAL | MILD-TO-MODERATE | SEVERE |
| General condition | Well, alert | *Restless, irritable | *Lethargic or unconscious; floppy |
| Eyes | Normal | Sunken | Very sunken and dry |
| Tears | Present | Absent | Absent |
| Mouth and tongue | Moist | Dry | Very dry |
| Thirst | Drinks normally, not thirsty | *Thirsty, drinks eagerly | *Drinks poorly or not able to drink |
| Skin pinch | Skin goes back quickly | *Skin goes back slowly | *Skin goes back very slowly |
| <u>DECISION</u> | No signs of dehydration | *≥ 2 of above signs, including at least one "key" sign | *≥ 2 of above signs, including at least one "key" sign |

*key signs of dehydration

Based on these five factors the child is assessed as not dehydrated, as having some dehydration (50-100 milliliters per kilogram estimated fluid deficit), or as having severe dehydration (greater than 100 ml/kg fluid deficit (WHO, 1993). Northrup and Flanigan (1994) similarly distinguish between mild (10-40 milliliters/kilogram fluid deficit), moderate (50-90 ml/kg), and severe (100-130 ml/kg) levels of dehydration based on the above and the factors shown in Table 10.2:

Table 10.2
Northrup and Flanigan Factors For Assessing Hydration Status

| FACTORS | DEGREE OF DEHYDRATION | | |
|---------------------------|-----------------------|----------------------|--------------------|
| | MILD | MODERATE | SEVERE |
| Anterior fontanelle | Normal | Depressed | Severely depressed |
| Radial pulse | Full | Full-weak | Feeble or absent |
| Pulse rate | Normal | Elevated | Vary rapid |
| Peripheral blood pressure | Normal | Within normal limits | Low or absent |

Fitzgerald (1989) also mentions increased urine specific gravity, decreased urine output, and an increased ratio of blood urea nitrogen to creatinine as signs of dehydration. DeWitt (1989) lists similar criteria but also mentions serum electrolytes with high sodium and low bicarbonate as being consistent with dehydration. DeWitt (1989) also advises a urine culture if excessive white blood cells are seen on the urinalysis.

The possibility of sepsis must also be considered, particularly in infants and in the presence of fever, blood in the stool, and other dysenteric signs and symptoms (Finkelstein et al., 1989; Baraff et al., 1993). If there is any suspicion of sepsis or bacteremia, a sepsis evaluation should be performed (Baraff et al., 1993). (See Chapter 12 for the general approach to the child with possible bacteremia or sepsis.)

Though in most cases of acute diarrhea, determining the specific etiology is unimportant, (Richards et al., 1993; Northrup and Flanigan, 1994) in a few cases, such as when sepsis is suspected or when the clinical course is prolonged, establishing the etiologic agent may be useful in terms of treatment. Initially, the clinician may make a presumptive etiologic determination based on characteristic clinical and epidemiologic patterns (Northrup and Flanigan, 1994). Fitzgerald (1989) and Northrup and Flanigan (1994) recognize two clinical patterns of acute diarrhea. The first is secretory or enterotoxigenic diarrhea characterized by watery diarrhea, sometimes with vomiting and fever but without significant cramping, without blood or leukocytes in the stool. Secretory or enterotoxigenic diarrhea may be caused by enterotoxigenic *Echerichia coli*, *Vibrio cholera*, *Giardia lamblia*, *Cryptosporidium*, Rotavirus, and Norwalk-like virus and organisms associated with food poisoning such as *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium perfringens* (Northrup and Flanigan, 1994). The second is inflammatory diarrhea characterized by mucous in the stools, fever, cramps, abdominal pain, often myalgias and arthralgias, and blood and leukocytes in the stool; the inflammatory diarrheas include *Shigella*, invasive *E. coli*, *Salmonella*, *Campylobacter*, *C. difficile*, and *Entameba histolytica* (Northrup and Flanigan, 1994).

Fitzgerald (1989) also lists clinical characteristics for viral diarrheas:

1. low grade temperature elevation
2. vomiting
3. pale, large volume, acidic stools
4. no occult blood
5. rapid development of dehydration.

The factors for bacterial diarrheas are:

1. abrupt onset
2. fever greater than 101°F
3. no vomiting
4. blood in stool
5. dark mucoid stools
6. toxic appearance
7. low serum albumin

Clinical features specific to each of the viral, bacterial, and parasitic diarrheas may be found in the above cited reviews (Hamilton, 1985; DeWitt, 1989; Fitzgerald, 1989; Laney and Cohen, 1993; Northrup and Flanigan, 1994) as well as other sources (Blacklow and Greenberg, 1991; Guerrant and Bobak, 1991; Pickering, 1991).

Epidemiologic data demonstrate that in 50 to 75 percent of stool specimens an enteropathogen is identified (Cohen, 1991). When the etiology of acute diarrhea is established the most common cause is viral, followed by bacterial and then parasitic etiologies (Fitzgerald, 1989; Cohen, 1991; Laney and Cohen, 1993). Rotavirus is the cause of diarrhea in up to 25 percent of children with diarrhea in the outpatient setting and in up to 50 percent of young children requiring hospitalization for diarrhea and dehydration (Cohen, 1991). Blacklow and Greenberg (1991) state that Rotavirus is "responsible for 30 to 60 percent of all cases of severe watery diarrhea in young children." Northrup and Flanigan (1994) cite a median of 34 percent for Rotavirus among children less than 2 years of age requiring hospitalization for diarrhea and dehydration. Rotavirus occurs most commonly in the fall in

the southwest United States and in the late winter and spring in the northeast United States, especially among children between 3 months and 15 months of age, and may be spread by both fecal-oral and respiratory routes (Blacklow and Greenberg, 1991; Northrup and Flanigan, 1994). Norwalk virus tends to occur in outbreaks among children older than 6 years of age and adults (Northrup and Flanigan, 1994). Infection with Norwalk virus is usually from a common source rather than person-to-person (Laney and Cohen, 1993). Both Rotavirus and Norwalk virus have short incubation periods of 1 to 3 days; duration of symptoms is 5 to 7 days for Rotavirus and 1 to 2 days for Norwalk virus (Blacklow and Greenberg, 1991; Northrup and Flanigan, 1994). Enteric adenoviruses are another common cause of acute diarrhea, especially in children less than two years of age (Blacklow and Greenberg, 1991; Laney and Cohen, 1993). Enteric adenoviruses have been found in 2 to 22 percent of cases of diarrhea from studies from various parts of the world (Blacklow and Greenberg, 1991). Enteric adenoviruses have a 8 to 10 day incubation period and a 5 to 12 day duration (Blacklow and Greenberg, 1991; Northrup and Flanigan, 1994). Enteric adenovirus infection is usually passed by the fecal-oral (Laney and Cohen, 1993) or person-to-person route (Blacklow and Greenberg, 1991). Other viruses that may cause acute episodes of diarrhea include pestivirus, astrovirus, calicivirus, parvovirus, and non-group A rotavirus (Cohen, 1991). Despite some epidemiologic differences noted after the fact, it is difficult to delineate between viral etiologies of acute diarrhea upon initial presentation.

Bacterial causes of acute diarrhea are less common. Among the invasive bacterial enteritides, *Salmonella* is the most common bacterial cause of diarrhea in the United States (Laney and Cohen, 1993). *Salmonella* infections are most common in infants younger than 6 months (Cohen, 1991) and also among those with acquired immunodeficiency syndrome, sickle cell anemia, and reticuloendothelial dysfunction and is acquired through contaminated foods, in particular meat, dairy, and poultry products (Northrup and Flanigan, 1994). The incubation period for *Salmonella* is 2 to 3 days, and the duration of illness about 2 to 3 days. *Shigella* is the second most common bacterial cause of diarrhea in

the United States identified among children 6 months to 10 years of age (Cohen, 1991; Laney and Cohen, 1993) and is uncommon in infants less than six months of age (Cohen, 1991). *Shigella* may be transmitted from person to person in child care (Laney and Cohen, 1993; Northrup and Flanigan, 1994) or other group settings (Northrup and Flanigan, 1994). *Shigella* may, in fact, be the most common etiology of bacterial diarrhea in the child care setting (Cohen, 1991). *Campylobacter* is most frequent among children less than 1 year of age and among young adults (Laney and Cohen, 1993). Incubation is for 1 to 7 days; the *campylobacter* is most commonly transmitted by the fecal-oral route (Laney and Cohen, 1993). *Aeromonas* species, particularly in Australia, and *Plesiomonas shigelloides* are also associated with acute diarrhea (Cohen, 1991). Acute diarrhea caused by *Yersinia enterocolitica*, though common in Europe and Canada, is uncommon in the United States (Cohen, 1991; Northrup and Flanigan, 1994) and is more likely in the child less than 5 years of age (Laney and Cohen, 1993; Northrup and Flanigan, 1994). *Yersinia* outbreaks are usually associated with contaminated foods, particularly milk and milk products (Cohen, 1991). Though not common, enterohemorrhagic *E. coli* has significant epidemiologic association with the hemolytic uremic syndrome which is characterized by microangiopathic hemolytic anemia, uremia, and thrombocytopenia (Laney and Cohen, 1993).

Among those bacteria causing enterotoxigenic diarrhea, some toxins are ingested by the child while others are produced in the infected intestine. Ingestion of toxin in the case of *S. aureus* or *B. cereus* leads to a brief duration of diarrhea after a short incubation period of 1 to 6 hours (Northrup and Flanigan, 1994). *C. perfringens* is found in contaminated foods and leads typically to not more than a three-day bout of severe diarrhea following a 8 to 12 hour incubation period (Northrup and Flanigan, 1994). Enterotoxigenic *E. coli* and *V. cholerae* cause a secretory diarrhea of 3 to 7 day duration (Northrup and Flanigan, 1994). *C. difficile* leading to pseudomembranous colitis is associated with antibiotic use and may spread from patient to patient (Northrup and Flanigan, 1994). Other possible bacterial enteropathogens include *Vibrio parahaemolyticus* and non-O1 *Vibrio* serogroups (Cohen, 1991).

Parasitic causes of acute diarrhea are even less common. Among parasitic causes, *Giardia lamblia* is the most common (Cohen, 1991). The prevalence of giardiasis is highest among infants and toddlers, with an increased incidence in children attending child care centers (Cohen, 1991). In child care settings, 21 to 26 percent of children may be asymptomatic carriers of *Giardia* (Laney and Cohen, 1993). *Giardia* is transmitted via the fecal-oral or person-to-person route (Laney and Cohen, 1993; Northrup and Flanigan, 1994). *Cryptosporidium* is a relatively common parasitic diarrheal illness in developing countries and is passed by the fecal-oral route and via person-to-person transmission (Northrup and Flanigan, 1994). The duration of cryptosporidial diarrhea is about 2 weeks (Northrup and Flanigan, 1994). *Cryptosporidium* is relatively common in the child care setting (DeWitt, 1989). Both *Cryptosporidium* and *Giardia* are more common among children with immune compromise (Northrup and Flanigan, 1994).

Laboratory diagnosis of specific etiologic agents of acute diarrhea is usually not necessary (Richards et al., 1993; Northrup and Flanigan, 1994) except (1) where sepsis is an issue, (2) in those rare cases in which antibiotic therapy is being considered, and (3) in cases that may require public health intervention, as with outbreaks of salmonella. Sepsis may be considered in cases with dysenteric symptoms such as blood in the stool or fever. Microscopic examination of the stool, if positive for erythrocytes and leukocytes and associated with fever, may suggest campylobacter, yersinia, salmonella, or shigella infection (Northrup and Flanigan, 1994). Despite the association with bacterial enteritides, the presence of fecal leukocytes does not necessarily predict a positive stool culture nor the need for antibiotics (Richards et al., 1993). DeWitt (1989) states that the probability of having a positive stool culture given stool leukocytes on microscopic examination is 70 percent; and, given a positive stool culture, the probability of stool leukocytes on examination is 90 percent. DeWitt (1985) indicated that fecal leukocyte determination or stool polymorphonuclear test should be reserved for children with diarrhea of abrupt onset, frequency of greater than four stools a day, and no vomiting before the onset of diarrhea. Positive fecal leukocyte determination, in addition to those

three factors, led to a sensitivity in detecting a positive stool culture of 74 percent and a specificity of 94 percent. The sensitivity and specificity of using fecal leukocyte alone was 85 percent and 88 percent, but DeWitt (1985) stated that performing a fecal leukocyte determination on all children with diarrhea was not practical. The presence of erythrocytes without leukocytes suggests entamoeba, and the lack of either erythrocytes or leukocytes suggests noninvasive bacterial or viral causes (Northrup and Flanigan, 1994). Stool cultures, looking for common bacterial etiologies, and rotaviral antigen analysis may be warranted in epidemic situations where public health intervention may be required (Richards et al., 1993). Rotavirus group A and enteric adenoviruses may be detected by enzyme-linked immunosorbant assay techniques (Laney and Cohen, 1993). Stool cultures may be helpful in children who have an inflammatory clinical pattern of acute diarrhea with bloody stools and fever (DeWitt, 1989; Finkelstein et al., 1989; Richards et al., 1993), especially when diarrhea persists more than three days (Northrup and Flanigan, 1994). Finkelstein et al. (1989) found that, for infants less than 12 months old: (1) a history of fever and blood in the stool led to a likelihood ratio (LR) of 13.5 of a positive stool culture; (2) for blood in the stool and more than nine stools in 24 hours a LR of 11.8; and, (3) for fever and more than nine stools in 24 hours, a LR of 3.8. They found that the presence of only one of these factors led to a LR of 1.1. Northrup and Flanigan (1994) note that a simple laboratory evaluation consisting of stool culture, rotavirus determination, and analysis for ova and parasite may cost up to \$180 and analysis for *C. difficile* toxin \$50. The yield of stool cultures may be as low as two percent and have a cost of greater than \$900 per positive result (Richards et al., 1993). Those with persistent symptoms longer than 10 to 14 days may warrant stool examination for ova and parasites (DeWitt, 1989; Northrup and Flanigan, 1994). Diagnosis of *Giardia* may be made by direct microscopic examination of at least three stool specimens, duodenal fluid sample, or small bowel biopsies or by antigen detection using enzyme-linked immunosorbant assay (Northrup and Flanigan, 1994) or counterimmunoelectrophoresis (Laney and Cohen, 1993). The *C. difficile* toxin may be identified in a stool sample (Northrup and

Flanigan, 1994). It must be noted that the *C. difficile* toxin may be present in children without clinical disease (Northrup and Flanigan, 1994).

The 3 to 5 percent (Santosham and Greenough, 1991) of children whose diarrhea persists for more than ten to fourteen days warrant further evaluation to determine specific etiology.

Treatment

The treatment of acute diarrhea is first directed toward the prevention or correction of fluid and electrolyte imbalance and the prevention or treatment of possible sepsis and then toward pharmacologic or public health intervention for specific etiologic diagnoses. The WHO case management strategy for acute diarrhea includes (Richards et al., 1993):

1. early administration of appropriate fluids at home;
2. treatment of dehydration with WHO oral rehydration solution;
3. treatment of severe dehydration with intravenous electrolyte solution;
4. continued feeding throughout the diarrheal episode;
5. selective use of antibiotics;
6. non-use of antidiarrheal drugs

The WHO approach was associated with a 71 percent decrease in the median diarrhea case-fatality rate in fourteen sites in developing countries and a drop of 28 to 4.6 percent among low birth weight neonates in an Egyptian intensive care unit (Richards et al., 1993), and a decrease in the diarrhea-specific mortality rate during a two-year study in a village in Bangladesh (Santosham and Greenough, 1991). In general, most episodes of acute diarrhea will respond to fluid and electrolyte stabilization and feeding therapy without other intervention (DeWitt, 1989; Northrup and Flanigan, 1994).

Since dehydration is initially the greatest threat to the patient, treatment is directed toward restoration and stabilization of fluid and electrolyte balance. If the child is not yet dehydrated, the health care provider should promote the maintenance of the regular diet and

prescribe the early initiation of oral hydration therapy at home with the appropriate carbohydrate-electrolyte solution (20 to 50 milliequivalents of sodium per liter), as well as maintenance of the regular diet (Fitzgerald, 1989; Santosham and Greenough, 1991; Northrup and Flanigan, 1994). Conflicting somewhat with the previous recommendation in terms of the sodium concentration of extra fluids, Richards et al. (1993) state that appropriate home solutions would include WHO oral rehydration solution, soups, unsweetened fruit juices, yogurt-based drinks, and plain water given with starchy foods containing some salt, emphasizing the need to continue the regular diet to the extent possible. According to the 1990 WHO protocol, the child without dehydration should be reevaluated within three days for continuing diarrhea, vomiting, thirst, poor oral intake, fever, or bloody stools.

Northrup and Flanigan (1994) state that the child with mild-to-moderate dehydration should receive oral hydration therapy with an isotonic or hypotonic carbohydrate solution containing electrolytes and that intravenous therapy should be reserved for children with severe dehydration defined by impending cardiovascular collapse or those unable to take oral feedings because of coma, intractable vomiting, or other reasons. Other contraindications to oral rehydration include shock, purging greater than ten milliliters per kilogram per hour, or ileus (Laney and Cohen, 1993) and glucose intolerance causing severe purging with administration of oral rehydration (Santosham and Greenough, 1991). Oral rehydration is effective in both enterotoxigenic or secretory and inflammatory diarrhea (AAP, 1985). Northrup and Flanigan (1994) state that less than 2 percent of cases of acute diarrhea in the community and less than 20 percent of cases presenting for medical care should require intravenous therapy. Bhan et al. (1994) cite two studies with higher oral rehydration treatment failure rates of 7 percent and 24 to 27 percent.

Oral rehydration therapy in the child with mild-to-moderate dehydration consists of replacement of the child's fluid deficit and ongoing losses and provision of maintenance fluid, electrolyte, and nutritional needs. Though the use of the WHO oral rehydration solution, with a glucose-to-sodium molar ratio of 1.2:1 and with supplemental

potassium chloride and trisodium citrate dihydrate or sodium bicarbonate, has been shown effective throughout the developing world in treatment of cholera and noncholera diarrheas and in hospital-based and clinic-based studies in the developed countries (Santosham and Greenough, 1991; Richards et al., 1993), solutions varying from the WHO oral rehydration solution have been suggested (Santosham et al., 1985; Walker-Smith, 1990; Northrup and Flanigan, 1994). One major difference in these solutions is their sodium chloride concentration, ranging from 45 milliequivalents per liter in Pedialyte (Ross) to 90 mEq/L in the WHO oral rehydration solution (Santosham and Greenough, 1991). Other modifications to the WHO oral rehydration solution are being tested including the substitution of complex carbohydrates such as rice or other cereals in place of glucose (Greenough and Khin-Maung-U, 1991; Khin-Maung-U and Greenough, 1991; Lebenthal and Lu, 1991) and the addition of amino acids (Ribeiro and Lifshitz, 1991) to facilitate fluid absorption, particularly in patients with excessive purging (Laney and Cohen, 1993; Bhan et al., 1994; Northrup and Flanigan, 1994). These cereal-based and amino acid supplemented oral rehydration solutions may reduce vomiting and diarrheal volume loss and shorten duration of the diarrheal episode (Greenough and Khin-Maung-U, 1991; Khin-Maung-U and Greenough, 1991; Lebenthal and Lu, 1991; Santosham and Greenough, 1991; Bhan et al., 1994). Bhan et al. (1994) in their exhaustive review of this literature come to the following conclusions:

1. Rice-based oral rehydration solutions were superior to the WHO oral rehydration solution for treatment of patients with cholera.
2. Rice-based oral rehydration solutions were as effective as the WHO oral rehydration solution for treatment of children with acute non-cholera diarrhea if feeding was resumed promptly after rehydration. This was also true for young infants, severely malnourished children, and children with increased risk of glucose malabsorption.
3. Maltodextrin-based oral rehydration solutions were as effective as the WHO oral rehydration solution for treatment of children with non-cholera diarrhea.

4. Amino-acid-containing oral rehydration formulas have no clinical advantage over the WHO oral rehydration solution for treatment of children with cholera or non-cholera diarrhea.

In 1985 the AAP endorsed the use of the WHO oral rehydration solution for the rehydration of dehydrated infants, whatever the presenting serum osmolality, and for the maintenance of hydration when given in equal amounts with water, breast milk, or low carbohydrate juices. The AAP recommended that the oral rehydration solution contain 75 to 90 millimoles per liter of sodium, 20 mmol/L potassium, 20 to 30 percent of anions as base and the remainder as chloride, and 2 to 2.5 percent glucose (Santosham and Greenough, 1991). The AAP (1993) also endorsed the basic treatment approach to dehydration due to acute diarrhea advocated by the WHO. Physicians in the developed countries, including Great Britain (Walker-Smith, 1990) and the United States, (Avery and Snyder, 1990; Richards et al., 1993) have been slow to adopt the use of oral rehydration solution despite these recommendations (Santosham and Greenough, 1991). The high cost of oral rehydration solutions in the United States, five-to-six dollars per liter, compared to the ten cents per liter cost borne by the United Nations, may contribute to the lack of adherence by U.S. physicians who fear parental noncompliance due to financial reasons (Richards et al., 1993).

In mild-to-moderate dehydration in the child of any age, oral fluid deficit replacement should occur over the initial 4 to 6 hours of therapy in a health care setting (Fitzgerald, 1989; Santosham and Greenough, 1991; Laney and Cohen, 1993; WHO, 1993; Northrup and Flanigan, 1994). Initially small, frequent feedings may be more appropriate, especially when vomiting is a problem. Vomiting is not an absolute contraindication to oral rehydration (AAP, 1985; Fitzgerald, 1989; Santosham and Greenough, 1991; Laney and Cohen, 1993; Richards et al., 1993). The volume of feedings is increased as tolerated. In certain cases nasogastric feeding may be considered (Fitzgerald, 1989). Ongoing stool losses should be estimated by the health care provider and replaced on a one to one-and-a-half by volume basis with oral carbohydrate-electrolyte solution; maintenance needs must also be met

(Santosham and Greenough, 1991; Northrup and Flanigan, 1994). Richards et al. (1993) believe that the child may continue the WHO oral rehydration solution during the maintenance phase with as much free water allowed as tolerated by the child and resumption of regular feedings as described below. The AAP (1985) also feels the WHO oral rehydration solution is adequate as a maintenance solution as long as it is diluted with equal amounts of low solute fluid. A recent study done in the United States of male infants less than two years of age in mild-to-moderate dehydration seemed to indicate that the a 45-50 mmol/L solution of sodium might be suitable for use in both the rehydration and maintenance phases of intervention; however, these low sodium solutions were not compared to the WHO oral rehydration solution, and the sample size was too small to adequately monitor for adverse effects (Cohen et al., 1995). Once the child has been rehydrated and the maintenance phase established, the child may be discharged home. The AAP (1985) recommends that the daily volume of maintenance solution not be greater than 150 milliliters per kilogram per day and that the excess needs be provided with a low-solute fluid. The child's hydration status must be monitored by the health care provider (Richards et al., 1993; Northrup and Flanigan, 1994), perhaps the day following discharge from the health care setting. Richards et al. (1993) note that the non-breast-fed infant less than six months of age should be given 100 to 200 milliliters of additional water during the rehydration phase while the breast-fed infant should continue breast-feeding as noted below. The use of oral rehydration solution in an urban American hospital resulted in a decrease in treatment time, eleven hours compared to 103 hours for intravenous therapy, and a decrease in cost, \$273 versus \$2300 (Richards et al., 1993).

In severe dehydration or where oral replacement is not possible, intravenous fluids administered in the health care setting may be needed. In contrast to intravenous infusion rates typical in the United States in which rehydration occurs over the initial 24-48 hours of treatment (DeWitt, 1989; Kallen, 1990), Richards et al. (1993) and Northrup and Flanigan (1994), echoing the WHO recommendations, stress the need for much more rapid rates of intravenous resuscitation.

Northrup and Flanigan (1994) advocate replacing the initial fluid deficit in addition to ongoing losses in no more than six hours with 30 milliliters per kilogram in infants and 40 milliliters per kilogram in older children being infused in the first 30 minutes and the remainder in the next five hours for infants and two-and-a-half hours for the older child. Isotonic solutions such as Ringer lactate or normal saline are required for resuscitation in these cases (Santosham and Greenough, 1991; Northrup and Flanigan, 1994). Though such rapid rates might be a problem in cases of hypernatremic dehydration if a hypotonic solution was infused (Kallen, 1990), with isotonic solutions this might not be a problem. According to the 1990 WHO guidelines, the child's hydration status should be reassessed every one to two hours by the health care provider. Oral hydration is begun as soon as the child is stable, as assessed by the pulse, blood pressure, and state of consciousness (Santosham and Greenough, 1991), or as soon as tolerated (Richards et al., 1993; Northrup and Flanigan, 1994). Once intravenous resuscitation has been successful, the child may be treated as for mild-to-moderate dehydration with complete rehydration being accomplished within four to six hours (Santosham and Greenough, 1991).

In addition to fluid and electrolyte resuscitation, the issue of refeeding in children of all ages, particularly infants, has been a controversial one (Brown, 1991). In Great Britain and the United States it has been the practice to cease breast milk, formula or milk, and solids until after at least the initial twenty-four hours of glucose-electrolyte solution therapy and then to slowly reintroduce regular feeds (Darrow et al., 1949; Hamilton, 1985; Walker-Smith, 1990). Northrup and Flanigan (1994) advocate "the basic principle of giving more food and giving it earlier than previously recommended." The AAP (1995) has recommended that feeding resume within twenty-four hours of the onset of diarrhea. The majority of U.S. pediatricians do not follow the WHO or AAP recommendations regarding refeeding much less for oral rehydration (Snyder, 1991; Bezerra, 1992; Richards et al., 1993). Benefits of refeeding include an increase in intestinal disaccharidases and pancreatic secretion leading to induction of mucosal cell growth and proliferation, preventing natriuria and decreasing the incidence of

malnutrition (Laney and Cohen, 1993). Fitzgerald (1989) mentions increased protein production in intestinal epithelial cells. Some studies have shown improved weight gain and shorter duration of diarrhea when full nutrition is restored soon after rehydration (Brown, 1991; Northrup and Flanigan, 1994). Other studies show improved nutritional status and no increase in duration of diarrhea (Richards et al., 1993). On balance, many studies show no difference in the duration of diarrhea with early refeeding (Ransome and Roode, 1984; Isolauri et al., 1986; Brown et al., 1988; Gazala et al., 1988; Margolis et al., 1990; Santosham et al., 1990; Chew et al., 1993) though a few show a slight decrease (Isolauri and Vesikari, 1985; Santosham et al., 1985; Santosham et al., 1991). Breastfeeding should continue through the diarrheal episode (Hamilton, 1985; Walker-Smith, 1990; Santosham and Greenough, 1991; Laney and Cohen, 1993; Richards et al., 1993; Northrup and Flanigan, 1994). Those continued on breast milk had lower stool output in one study (Khin-Maung-U et al., 1985) and shorter illness duration in rotaviral diarrhea (Brown, 1991).

Differences of opinion exist with regard to the use of nonhuman milk formulas in refeeding of children with acute diarrhea (Brown et al., 1994). Northrup and Flanigan (1994) state that children on milk-based formulas may continue these formulas in smaller, more frequent feedings or diluted with cereals and other foods. The AAP (1985), Hamilton (1985), Fitzgerald (1989), Walker-Smith (1990), Richards et al. (1993), and Northrup and Flanigan (1994) acknowledge that some clinicians advocate lactose-free formulas for children with acute diarrhea, though they feel it is not routinely required. DeWitt (1989) and Laney and Cohen (1993) still advocate lactose-free formula for the first 48 hours of refeeding. Brown et al. (1994) in a meta-analytic review of studies addressing this question concluded that the routine use of lactose-free milk formula was not warranted since the increased duration of diarrhea with lactose-containing formula was not clinically significant. Brown et al. (1994) felt that lactose-free formula might be justified in children with severe dehydration on presentation, previous treatment failure, underlying severe malnutrition, or worsening diarrhea upon consumption of lactose-containing formula.

Another point of contention has been the need for dilution of formula during the period of refeeding (Brown et al., 1994). Santosham and Greenough (1991) state that lactose-free formula may be given without dilution while other formulas should be diluted one-to-one. Richards et al. (1993) assert that dilution is not necessary though they find dilution acceptable if diarrhea worsens when milk is given. The AAP (1985) and Hamilton (1985), in contrast, recommend the reintroduction of formula or milk in dilute mixtures. Brown et al. (1994) in their meta-analytic review concluded that routine dilution of formula was not necessary as a small increased risk of treatment failure with undiluted formula was balanced by a poorer weight gain with diluted formula.

Richards et al. (1993) state that children normally on a semisolid or solid diet should continue on a "balanced, energy-rich and easily digestible diet" such as "lentils, meat or fish, eggs and dairy products, mashed cooked vegetables and bananas" and "starches such as cooked cereals" rather than sugar. Brown (1991) summarizes the studies with regard to refeeding of mixed diets as indicating "that mixtures of accessible staple foods are safe to use during diarrheal illness and yield purging rates during early therapy that are generally similar to, or in some cases possibly less than, those observed with milk- or soy-based formula diets. Of particular interest was the consistent finding that the duration of diarrhea was markedly reduced among the groups that received the staple foods." Brown (1991) also goes on to warn that "it is somewhat worrisome that the children tended to consume more dietary energy and to gain slightly more weight when they received the formula diets." Laney and Cohen (1993) and Northrup and Flanigan (1994) agree in general with these recommendations regarding reintroduction of solids.

Concomitant to fluid and electrolyte stabilization, concerns about possible sepsis must be addressed during the initial phase of treatment. (See review of Chapter 12 for the general approach to the child with possible bacteremia or sepsis.)

Though treatment of acute diarrhea is primarily concerned with issues of hydration, in a few cases knowledge of specific etiology may

aid to eradicate infection, shorten the duration of disease, reduce shedding of infectious material through the use of antimicrobial agents, and promote necessary public health intervention. In viral diarrheas, hydration is the mainstay of treatment whether it be oral or parenteral, and specific pharmacologic therapy is not available.

Of the bacterial diarrheas, very few are aided by pharmacologic therapy. Fitzgerald (1989) states that "(E)mpirical antibiotic treatment is unwarranted in the management of the nontoxic infant with acute diarrhea." In Salmonella diarrhea, though amoxicillin, trimethoprim-sulfamethoxazole, or the new quinolones are thought to be effective, treatment guided by susceptibility testing is usually considered only for patients with sickle cell anemia, lymphoma, leukemia, and immunocompromise to prevent or treat possible bacteremia (Northrup and Flanigan 1994) or metastatic pyogenic infection (Pickering, 1991). Laney and Cohen (1993) also recommend that any child less than one year of age with a positive blood culture with Salmonella or any infant less than three months of age with a positive stool culture with Salmonella be treated with parenteral antibiotics. Antibiotic treatment of salmonella diarrhea, however, may prolong the period of fecal shedding of the organism (Richards et al., 1993) and increase the risk of the asymptomatic carrier state (Laney and Cohen, 1993). Northrup and Flanigan (1994) recommend amoxicillin, trimethoprim-sulfamethoxazole, or the new quinolones for treatment of Salmonella; and, Pickering (1991) also recommends consideration of ampicillin, chloramphenicol, ceftriaxone, and cefotaxime. Treatment of shigellosis is generally felt to be effective in decreasing the duration of symptoms and decreasing the length of excretion (Laney and Cohen, 1993). Treatment of Shigella should be directed by susceptibility testing, though trimethoprim-sulfamethoxazole is the initial antibiotic of choice (Pickering, 1991; Northrup and Flanigan, 1994) and nalidixic acid or pivmecillinam may be alternatives (Richards et al., 1993). Pickering (1991) and Laney and Cohen (1993) mention ampicillin as a choice in treating Shigella; however, ampicillin resistance has become a problem. Tetracycline (Laney and Cohen, 1993) and ciprofloxacin and norfloxacin (Pickering, 1991; Laney and Cohen, 1993) are other

alternatives for treating *Shigella* in the older patient. Antibiotic therapy, specifically erythromycin, for campylobacter diarrhea may only be effective when given early in the course of the illness (Richards et al., 1993), within four days of onset of symptoms (Pickering, 1991) or in epidemic situations, such as in child care centers, or for illness associated with severe fever or bloody diarrhea (Northrup and Flanigan, 1994). Campylobacter is also susceptible to furazolidone, the quinolones, aminoglycosides, tetracycline, chloramphenicol, and clindamycin (Pickering, 1991). Antibiotic therapy is not useful for the treatment of *Y. enterocolitica* diarrhea though it may be used in those with severe diarrhea or underlying illness (Pickering, 1991; Laney and Cohen, 1993). In cases of suspected cholera with severe dehydration, trimethoprim-sulfamethoxazole or the alternatives of tetracycline, furazolidone, erythromycin, or chloramphenicol may be helpful in shortening the duration of illness and the period of excretion (Pickering, 1991; Richards et al., 1993). Ampicillin may also be an alternative treatment for cholera (Pickering, 1991). Cessation of antibiotic usage is the primary treatment of *C. difficile* pseudomembranous colitis, though in some cases metronidazole or vancomycin may be necessary (Pickering, 1991; Northrup and Flanigan, 1994). Treatment of hemolytic uremic syndrome associated with *E. coli* enteritis, requires mainly supportive treatment.

Giardia may be treated with furazolidone, which has fewer side effects, or with metronidazole or quinacrine hydrochloride (Northrup and Flanigan, 1994). Richards et al. (1993) note that giardiasis should only be treated if symptoms persist for at least fourteen days and if cysts or trophozoites are found in stool or small bowel fluid samples and lists tinidazole and ornidazole as alternative antimicrobials. Paromomycin, a nonadsorbable aminoglycoside, may be an effective agent against cryptosporidium (Northrup and Flanigan, 1994). Pickering (1991) states that antimicrobial therapy is usually not needed in cryptosporidial diarrhea. Richards et al. (1993) state that amoebiasis may be treated with metronidazole though only if fresh stool samples reveal trophozoites with ingested erythrocytes. Pickering (1991) recommends iodoquinol, paromomycin, or diloxanide furoate for the

asymptomatic cyst excretor and reserves metronidazole for mild-to-moderate or severe intestinal disease or liver abscess or other extraintestinal amebic disease. When metronidazole is ineffective, Pickering (1991) mentions various alternatives for the antimicrobial treatment of recalcitrant amebiasis.

All articles reviewed agreed that antimotility medications and nonabsorbable antibiotics or adsorbents should not be used in the treatment of acute diarrhea in children (Hamilton, 1985; DeWitt, 1989; Fitzgerald, 1989; Avery and Snyder, 1990; WHO, 1990; Richards et al., 1993; Northrup and Flanigan, 1994). Most of these so-called antidiarrheal compounds are not approved for use in children less than two or three years of age (Pickering, 1991). Apparently none have been shown effective in well-controlled studies in decreasing stool volume or duration of symptoms (Richards et al., 1993). In particular, adsorbents and lactobacillus compounds have not been shown effective in well-controlled studies (Pickering, 1991). Fitzgerald (1989) postulates that prolonging the transit time of the intestine increases the time "injurious agents" remain in contact with the intestinal epithelium. Pickering (1991) notes that side effects may occur due to salicylate or bismuth absorption from bismuth-salicylate preparations, impairment of absorption of needed medications or nutrients, and interference with identification of enteropathogens. Antimotility medications have been shown to worsen the clinical course in shigellosis and in antimicrobial-associated colitis and have the risks attendant with overdose (Pickering, 1991). Others mention the possibility of dangerous side effects (Richards et al., 1993), including toxic megacolon and colonic hemorrhage (Northrup and Flanigan, 1994) and ileus (Avery and Snyder, 1990) with the use of antimotility or antidiarrheal medications.

Follow-up

Follow-up may be necessary in certain cases. The health care provider should check the child with acute diarrhea without dehydration for continued diarrhea, vomiting, thirst, poor oral intake, fever, or bloody stools three days after initiation of therapy and the child with mild-to-moderate or severe diarrhea one week after discharge from

therapy in the health care setting. Persistent diarrhea may be more likely in younger children, malnourished children, or immunocompromised children, such as those with acquired immunodeficiency syndrome (Northrup and Flanigan, 1994). Young infants and those with severe diarrhea are more likely to be treatment failures (Brown and Lifshitz, 1991) Children who have parasitic diarrheas or those with more severe, invasive bouts of acute diarrhea leading to enterocyte brush border damage and decreased disaccharidase levels may also be more prone to persistent diarrhea (Northrup and Flanigan, 1994). Children with diarrheal illness of greater than 14 day duration should be evaluated for persistent or chronic diarrhea (Walker-Smith, 1990; Northrup and Flanigan, 1994).

RECOMMENDED QUALITY INDICATORS FOR ACUTE DIARRHEA

The following clinical indicators apply to children up to age 3-5 years.

Diagnosis

| Indicator | Quality of evidence | Literature | Benefits | Comments |
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| 1. In all children presenting with acute diarrhea, history should be obtained regarding: | III | DeWitt, 1989; Richards et al., 1993; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in assessing the hydration status. An accurate assessment of hydration status is essential for appropriate treatment. If the duration has been greater than 2 weeks the child should be evaluated for chronic diarrhea rather than acute diarrhea. |
| a. the date of onset or duration of diarrheal stools; | III | DeWitt, 1989; Richards et al., 1993; Northrup and Flanigan, 1994 | | |
| b. stool consistency, frequency (e.g., number per day), and volume; | III | DeWitt, 1989; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in establishing the presence of diarrhea. One must admit, however, that the definition of diarrhea is not well established and dependent on a relative departure from the child's normal bowel pattern in terms of increased frequency and decreased consistency. |
| c. presence or absence of blood in the stool; | III | DeWitt, 1989; Baraff et al., 1993; Richards et al., 1993; Northrup and Flanigan, 1994 | Decrease morbidity from untreated diarrhea.* Prevent sepsis and its complications.** | This information is useful in establishing the presence of inflammatory or bacterial diarrhea and the possibility of sepsis. The possibility of a bacterial etiology for diarrhea in a child will lead the health care provider to consider diagnostic procedures such as fecal leukocyte examination and stool culture, to consider an evaluation to rule-out sepsis or bacteremia, and to consider the possible need for antibiotic therapy. |
| d. presence or absence of fever, as reported by the parent; | III | DeWitt, 1989; Baraff et al., 1993; Northrup and Flanigan, 1994 | Decrease morbidity from untreated diarrhea.* Prevent sepsis and its complications.** | This information is useful in establishing the presence of inflammatory or bacterial diarrhea and the possibility of sepsis. The possibility of a bacterial etiology for diarrhea in a child will lead the health care provider to consider diagnostic procedures such as fecal leukocyte examination and stool culture, to consider an evaluation to rule-out sepsis or bacteremia, and to consider the possible need for antibiotic therapy. |

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| e. presence or absence of vomiting; | III | DeWitt, 1989; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in determining the hydration status and the possible course of treatment. If the child has intractable vomiting, oral rehydration therapy may fail. Intractable vomiting is a relative contraindication for oral rehydration therapy; but, it is felt that less than 2 percent of all children with diarrhea in the community will not respond well to oral rehydration therapy for any reason. |
| f. frequency and volume of fluid intake; | III | DeWitt, 1989; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in determining the hydration status and the possible course of treatment. The child who is comatose and unable to take fluids orally will require intravenous rehydration. |
| 2. History should be obtained regarding the frequency and volume of urinary output. | III | DeWitt, 1989; Fitzgerald, 1989; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in assessing the hydration status. |
| 3. The weight should be recorded and, if available, compared to a recent weight obtained prior to the onset of diarrhea. | III | DeWitt, 1989; AAP, 1993 | Prevent or correct dehydration. | This information is useful in assessing the hydration status and monitoring the progress of therapy. Weight measurement is the gold standard of hydration status. Progress in treatment of dehydration is most easily assessed by comparative weights from the start to the end of therapy. |
| 4. Documentation should also include: a. heart rate b. respiratory rate c. blood pressure d. temperature | III | DeWitt, 1989 | Prevent or correct dehydration. | This information is useful in assessing the hydration status and monitoring the progress of therapy. |
| 5. All of the following findings regarding hydration status should be recorded: | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | Prevent or correct dehydration. Decrease morbidity from untreated diarrhea.* Prevent sepsis and its complications.** | These factors represent the World Health Organization's criteria for assessing the degree of dehydration of the child with diarrhea. Also, if shock or fever is present, the health care provider should consider the possibility of sepsis. The possibility of a bacterial etiology for diarrhea in a child will lead the health care provider to consider diagnostic procedures such as fecal leukocyte examination and stool culture, to consider an evaluation to rule-out sepsis or bacteremia, and to consider the possible need for antibiotic therapy. |

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| a. general condition; | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | General condition characterized by: well, alert; restless, irritable; or lethargic or unconscious, floppy. |
| b. appearance of eyes; | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | Appearance of eyes characterized by: normal; sunken; or very sunken and dry. |
| c. presence or absence of tears; | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | |
| d. degree of oral moisture; | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | Degree of oral moisture characterized by: moist; dry; or very dry. |
| e. degree of thirst; | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | Degree of thirst characterized by: drinks normally, not thirsty; thirsty, drinks eagerly; or drinks poorly or not able to drink. |
| f. degree of skin turgor; and | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | Degree of skin turgor characterized by: skin goes back quickly; skin goes back slowly; or skin goes back very slowly. |
| g. condition of anterior fontanelle. | III | DeWitt, 1989; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | | Condition of anterior fontanelle characterized by: normal/flat; slightly sunken; or severely sunken. |
| 6. The exam should note the presence or absence of blood in the stools, either by visual inspection or by chemical means. | III | DeWitt, 1989; Northrup and Flanigan, 1994 | Prevent or correct dehydration. Decrease morbidity from untreated diarrhea.* Prevent sepsis and its complications.** | This information is useful in establishing the presence of inflammatory or bacterial diarrhea and the possibility of sepsis. The possibility of a bacterial etiology for diarrhea in a child will lead the health care provider to consider diagnostic procedures such as fecal leukocyte examination and stool culture, to consider an evaluation to rule-out sepsis or bacteremia, and to consider the possible need for antibiotic therapy. |

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| <p>7. The assessment of hydration status should be recorded in terms of percent dehydration or fluid deficit in milliliters per kilogram or as:</p> <ul style="list-style-type: none"> • not dehydrated (less than 50 milliliters per kilogram fluid deficit), • mild-moderate dehydration (50-100 milliliters per kilogram fluid deficit), or • severe dehydration (greater than 100 milliliters per kilogram fluid deficit). | III | AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | This information is useful in determining the possible course of treatment. |
| <p>8. Serum electrolytes should have been obtained if the child's dehydration was severe or if the pulse rate was elevated and the blood pressure was low.</p> | III | DeWitt, 1989; Kallen, 1990; Northrup and Flanigan, 1994 | Avoid complications of cerebral edema and seizures. | A child in severe dehydration may have severe electrolyte imbalances requiring correction and requiring modification of intravenous therapy. For example, with severe hypernatremia, the health care provider may opt to correct the sodium concentration excess over a period of 48 hours rather than 24 hours or less. Blood pressure and pulse changes will be specified based on the age of the child. |
| <p>9. Urinalysis should have been obtained if the child's dehydration was severe or if the pulse rate was elevated and the blood pressure was low.</p> | III | DeWitt, 1989; Fitzgerald, 1989; Kallen, 1990; Northrup and Flanigan, 1994 | Prevent or correct dehydration. | Urine specific gravity, as part of the urinalysis, would provide a useful monitor as to the success or failure of hydration therapy and may be particularly useful in the case of severe dehydration. |
| <p>10. Fecal leukocytes should have been obtained if the child with diarrhea is less than 36 months of age and had fever or blood in the stool.</p> | II-2 | DeWitt et al., 1985; Finkelstein et al., 1989; | Prevent morbidity/mortality due to bacterial infection. | The reviews on acute diarrhea indicate fecal leukocyte determination might not be needed until diarrhea has persisted despite three days of hydration therapy. In their guideline on workup of fever, Baraff et al. (1993) indicate that fecal leukocytes should be obtained in the child less than 36 months of age with fever and diarrhea. Though not well documented, this recommendation seems to be based on the findings of DeWitt et al. (1985) and Finkelstein et al. (1989). The appropriate use of the fecal leukocyte determination would lead to appropriate treatment of bacterial diarrhea and reduced costs of evaluation since not all children would require fecal leukocyte determination. |

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| 11. Stool culture should be obtained if the child with diarrhea is less than 36 months of age and had fever or blood in the stool or > 5 fecal leukocytes per high power field. | II-2 | DeWitt et al., 1985; Finkelstein, 1989; | Prevent morbidity/mortality due to bacterial infection. | See above discussion of the use of fecal leukocyte examination. In their guideline on workup of fever, Baraff et al. (1993) indicate that a stool culture should be obtained in the child less than 36 months of age with fever and diarrhea with blood and mucous or with > 5 fecal leukocytes per high power field. The appropriate use of the stool culture would lead to appropriate treatment of bacterial diarrhea and reduced costs of evaluation since not all children would require stool culture determination. |
| 12. A stool examination for ova and parasites should be obtained if the child had a history of recent travel to a developing country, acquired or congenital immunocompromise, or exposure to a potential carrier of parasitic diarrhea. | III | DeWitt, 1989; Laney and Cohen, 1993; Northrup and Flanigan, 1994 | Decrease morbidity from untreated diarrhea.* | Parasites are the least common cause of diarrhea in children. Evaluation for possible parasitic causes of diarrhea should, therefore, be limited to children at high risk for parasitic infection. Such focused evaluation will reduce the overall costs of evaluation of diarrhea among children. Conversely, even with a history of recent travel, residence in a child care setting, immunocompromise or exposure to a potential carrier of parasitic diarrhea, stool examination for ova and parasite might not be needed unless diarrhea has persisted greater than 10-14 days or a public health concern existed. |
| 13. If stool was obtained for ova and parasite examination, three stool samples, obtained on three consecutive days, should have been ordered. | III | Northrup and Flanigan, 1994 | Decrease morbidity from untreated diarrhea.* | The false negative rate may be high with a single stool specimen. Though the incidence of parasitic diarrhea is low, when present appropriate treatment will be enhanced by identifying the parasite on stool examination. Although these should ideally be obtained on 3 consecutive days, extension of that period to 5-7 days may be appropriate. |

Treatment

| Indicator | Quality of evidence | Literature | Benefits | Comments |
|--|---------------------|---|----------------------|--|
| 14. If the child had diarrhea but was not dehydrated, the practitioner should recommend additional fluid intake beyond what is normal for the child. | III | AAP, 1993; Richards et al., 1993; Northrup and Flanigan, 1994 | Prevent dehydration. | The extra fluid should have a sodium concentration of about 20-50 milliequivalents per liter of fluid. |

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| <p>15. If the child had mild-moderate dehydration, is not comatose, and is without intractable vomiting, has evidence of ileus, and moderate or severe purging upon administration of oral electrolyte-sugar solution, oral rehydration therapy should be prescribed and consist of:</p> <ol style="list-style-type: none"> electrolyte, sugar solution as specified by the American Academy of Pediatrics (1993) or the World Health Organization (Richards et al., 1993); correction of the initial fluid deficit in the first 6 hours of treatment; and be monitored in the office or emergency room setting during entire period of rehydration. | I | Santosham et al., 1982; Santosham et al., 1985; Tamer et al., 1985; Listernick et al., 1986; Herzog et al., 1987; AAP, 1993; WHO, 1993 | Prevent or correct dehydration. | Oral rehydration therapy has been shown to be an effective treatment for the child with mild-moderate dehydration and avoids the need for intravenous therapy and its possible morbidity. It is felt that less than 2 percent of all children with diarrhea in the community will not respond well to oral rehydration therapy. In some cases, nasogastric feedings may be an alternative rather than intravenous intervention. References AAP (1993) and Richards et al. (1993) review the American Academy of Pediatrics and World Health Organization guidelines. |
| <p>16. If the child had severe dehydration, intravenous rehydration should be prescribed and consist of:</p> <ol style="list-style-type: none"> replacement of the fluid deficit with either isotonic fluid, such as normal-saline or Ringer's Lactate solution as specified by the World Health Organization, or electrolyte solution based on serum electrolyte deficits; the pulse and blood pressure should be stabilized within normal limits for age within 6 hours of initiation of treatment; replacement of the fluid deficit within 48 hours of initiation of treatment; monitoring of input and output; and completion of all rehydration in the inpatient setting or observation unit. | III | DeWitt, 1989; Kallen, 1990; AAP, 1993; WHO, 1993; Northrup and Flanigan, 1994 | Reverse the complications of severe dehydration and prevent end-organ damage and death. | Complications of severe dehydration include death, cardiovascular collapse, seizure, and coma. |
| <p>17. If while healthy the child was being breast fed, the health care provider should advise the parent to continue breast feeding if the child is able to feed orally.</p> | I | Khin-Maung-U et al., 1985; AAP, 1993; WHO, 1993 | Prevent or correct dehydration. | In children 6 to 24 months of age with moderate or severe dehydration due to diarrhea, the continued provision of breast feeding in addition to oral rehydration solution resulted in decreased number of bowel movements, while in the hospital 12.1 versus 17.4, and stool output, 89.2 milliliters/kilogram/patient versus 115.8 ml/kg/patient, while requiring less total volume of oral rehydration solution. AAP (1993) and Richards et al. (1993) review the American Academy of Pediatrics and World Health Organization guidelines. |

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| <p>18. If while healthy the child was formula fed or weaned, the health care provider should have instituted refeeding within twenty-four hours of the onset of hydration therapy.</p> | <p>I</p> | <p>Rees and Brook, 1979; Placzek and Walker-Smith, 1984; Ransome et al., 1984; Isolauri and Vesikari, 1985; Santosham et al., 1985; Isolauri et al., 1986; Brown et al., 1988; Gazala et al., 1988; Conway and Ireson, 1989; Fox et al., 1990; Margolis et al., 1990; Santosham et al., 1990; Lifshitz et al., 1991; Santosham et al., 1991; AAP, 1993; Chew et al., 1993</p> | <p>Prevent malnutrition and associated complications of poor nutrition.</p> | <p>On balance the randomized controlled studies show at best a small decrease in duration of diarrhea; but, the theoretical positive effect on nutritional status would warrant early refeeding, especially in the young infant or child with underlying malnutrition.</p> |
| <p>19. Antimicrobial agents should be used in a child with:</p> <ul style="list-style-type: none"> a. suspected or culture-proven cholera with severe dehydration; or b. salmonella in patients with sickle cell anemia, lymphoma, leukemia, other immune compromise (acquired or congenital), positive stool culture for bacterial pathogen and less than 3 months of age, or bacteremia with salmonella and less than 6 months of age; or c. giardia with symptoms of greater than 10-14 days duration and with positive stool ova and parasite examination; or d. amoeba with positive stool ova and parasite examination. | <p>III</p> | <p>WHO, 1990; Pickering, 1991; Laney and Cohen, 1993; Northrup and Flanigan, 1994</p> | <p>Decrease morbidity from untreated diarrhea.* Prevent sepsis and its complications.**</p> | <p>If antimicrobials are to be used, in order to enhance the probability of eradicating the intended target, the choice of antimicrobial agent should be based on the most likely organism. Conversely, even when a bacterial or parasitic etiology of diarrhea is identified, the health care provider need not automatically treat with an antimicrobial. Antibiotics may be useful in diarrhea caused by shigella as well as the listed indications.</p> |

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| 20. Antidiarrheal or antimotility medications should never be used in treatment of diarrhea in a child. | III | Hamilton, 1985; DeWitt, 1989; Fitzgerald, 1989; Avery and Snyder, 1990; WHO, 1990; Pickering, 1991; Northrup and Flanigan, 1994 | Prevent side effects of antidiarrheal and antimotility medications. | No evidence is cited by any of the reviews that antidiarrheal or antimotility medications are effective in the treatment of diarrhea in children. The reviews cited on the contrary all indicate that the use of these medications have been associated with serious side effects, such as toxic megacolon, colonic hemorrhage, and ileus. |
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Follow-up

| Indicator | Quality of evidence | Literature | Benefits | Comments |
|--|---------------------|--|----------------------|--|
| 21. The young infant less than three months of age with acute diarrhea should have follow-up by the health care provider within: a. three days of intervention for diarrhea without dehydration; b. one week after rehydration (either inpatient or outpatient) of mild-moderate or severe diarrhea. | III | Brown and Lifshitz, 1991; AAP, 1993; Northrup and Flanigan, 1994 | Prevent dehydration. | The cited reviews do not define young infant. The choice of three months is based on clinical opinion. The young infant is at greater risk of failing therapy. Since diarrhea may continue for several days as noted in the text, the health care provider needs to monitor the hydration status of the child over the natural course of the disease process. Maintenance of normal hydration status depends on the continuation of appropriate treatment outside of the medical setting by the child's guardians. Through close followup, the health care provider can increase the likelihood that the child will maintain normal hydration status until the end of the diarrhea process. Children whose hydration status has been corrected through medical intervention are more likely to be close to the end of their illness. The choice of three days and one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes. |

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| <p>22. The child with growth delay or malnutrition should have follow-up by the health care provider within:</p> <ul style="list-style-type: none"> a. three days of intervention for diarrhea without dehydration; b. one week after rehydration (either inpatient or outpatient) of mild-moderate or severe diarrhea. | <p>III</p> | <p>Northrup and Flanigan, 1994</p> | <p>Prevent dehydration.</p> | <p>The child with growth delay or malnutrition is at greater risk than the child without these conditions to fail therapy. Since diarrhea may continue for several days as noted in the text, the health care provider needs to monitor the hydration status of the child over the natural course of the disease process. Maintenance of normal hydration status depends on the continuation of appropriate treatment outside of the medical setting by the child's guardians. Through close followup, the health care provider can increase the likelihood that the child will maintain normal hydration status until the end of the diarrhea process. The choice of three days and one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes.</p> |
| <p>23. The child with immunocompromise should have follow-up by the health care provider within:</p> <ul style="list-style-type: none"> a. three days of intervention for diarrhea without dehydration; b. one week after rehydration (either inpatient or outpatient) of mild-moderate or severe diarrhea. | <p>III</p> | <p>Northrup and Flanigan, 1994</p> | <p>Prevent dehydration.</p> | <p>The child with immunocompromise is at greater risk than the child without these conditions to fail therapy. The choice of three days and one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes.</p> |
| <p>24. Any child with severe dehydration should have follow-up by the health care provider within one week after discharge for intervention.</p> | <p>III</p> | <p>Brown and Lifshitz, 1991</p> | <p>Prevent dehydration.</p> | <p>Maintenance of normal hydration status depends on the continuation of appropriate treatment outside of the medical setting by the child's guardians. The choice of one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes.</p> |
| <p>25. Any child with inflammatory or invasive diarrhea should have follow-up by the health care provider within:</p> <ul style="list-style-type: none"> a. three days of intervention for diarrhea without dehydration; b. one week after discharge for intervention of mild-moderate or severe diarrhea. | <p>III</p> | <p>Northrup and Flanigan, 1994</p> | <p>Prevent dehydration.</p> | <p>Through close follow-up, the health care provider can increase the likelihood that the child will maintain normal hydration status until the end of the diarrhea process. The choice of three days and one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes.</p> |

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| <p>26. Any child with diarrhea and culture positive for parasites should have follow-up by the health care provider within:</p> <ul style="list-style-type: none"> a. three days of intervention for diarrhea without dehydration; b. one week after discharge for intervention of mild-moderate or severe diarrhea. | <p>III</p> | <p>Northrup and Flanigan, 1994</p> | <p>Prevent dehydration.</p> | <p>Parasitic diarrhea may be quite persistent and may require follow-up stool examinations to document its eradication. The choice of three days and one week for follow-up is partly based on clinical opinion and partly on the natural course of the majority of acute diarrheal episodes.</p> |
| <p>27. If there is no improvement in diarrhea after 3 days of hydration therapy, the following work-up should be performed:</p> <ul style="list-style-type: none"> a. serum electrolytes b. urinalysis c. fecal leukocyte examination d. stool culture | <p>III</p> | <p>DeWitt et al., 1985; DeWitt, 1989; Fitzgerald, 1989; Kallen, 1990; Richards et al., 1993; Northrup and Flanigan, 1994</p> | <p>Prevent dehydration.</p> | <p>The child with diarrhea persisting greater than three days while on treatment is at risk of advancing degrees of dehydration.</p> |

*Morbidity may include severe hydration, abdominal and rectal pain, weight loss, lost school days, and lost work days for the parent.

**Complications of sepsis include multi-organ failure and death.

Quality of Evidence Codes:

- I: RCT
- II-1: Nonrandomized controlled trials
- II-2: Cohort or case analysis
- II-3: Multiple time series
- III: Opinions or descriptive studies

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