THE TREATMENT OF DIARRHOEA

A manual for physicians and other senior health workers



World Health Organization

Department of Child and Adolescent Health and Development

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1. INTRODUCTION

Diarrhoeal diseases are a leading cause of childhood morbidity and mortality in developing countries, and an important cause of malnutrition. In 2003 an estimated 1.87 million children below 5 years died from diarrhoea. Eight out of 10 of these deaths occur in the first two years of life. On average, children below 3 years of age in developing countries experience three episodes of diarrhoea each year. In many countries diarrhoea, including cholera, is also an important cause of morbidity among older children and adults.

Many new microbial causes of diarrhoea have been discovered during the past three decades. Research laboratories can now identify a microbial cause in over three quarters of children presenting at health facilities with diarrhoea. Information about the most important diarrhoea-causing pathogens is given in Annex 1.

Many diarrhoeal deaths are caused by dehydration. An important development has been the discovery that dehydration from acute diarrhoea of any aetiology and at any age, except when it is severe, can be safely and effectively treated in over 90% of cases by the simple method of oral rehydration using a single fluid. Glucose and several salts in a mixture known as Oral Rehydration Salts (ORS) are dissolved in water to form ORS solution (Annex 2). ORS solution is absorbed in the small intestine even during copious diarrhoea, thus replacing the water and electrolytes lost in the faeces. ORS solution and other fluids may also be used as home treatment to prevent dehydration. After 20 years of research, an improved ORS solution has been developed. Called reduced (low) osmolarity ORS solution, this new ORS solution reduces by 33% the need for supplemental IV fluid therapy after initial rehydration when compared to the previous standard WHO ORS solution. The new ORS solution also reduces the incidence of vomiting by 30% and stool volume by 20%. This new reduced (low) osmolarity ORS solution, containing 75 mEq/l of sodium and 75 mmol/l of glucose, is now the ORS formulation officially recommended by WHO and UNICEF. In this revised document, when ORS/ORT is mentioned, it refers to this new reduced (low) osmolarity ORS solution.

Bloody diarrhoea (dysentery) and persistent diarrhoea with malnutrition are also important causes of death. Repeated attacks of diarrhoea contribute to malnutrition, and diarrhoeal diseases are more likely to cause death in children who are malnourished. Research has shown, however, that the adverse effects of diarrhoea on a child's nutritional status can be lessened or prevented by continuing feeding during the illness.

Diarrhoea morbidity is increased in HIV positive children. However, the treatment of diarrhoea for HIV positive children is generally the same as for HIV uninfected children, although lactose and monosaccharide intolerances are more frequently present in these children.

Essential elements in management of the child with diarrhoea are the provision of oral rehydration therapy and continued feeding to all, and the use of antimicrobials only for those with bloody diarrhoea, severe cholera cases, or serious non-intestinal infections. The caretakers of young children should also be taught about feeding and hygiene practices that reduce diarrhoea morbidity.

This manual describes the principles and practices of treating infectious diarrhoea, especially in young children. It is intended for physicians and other senior level health workers. Other publications are available to assist in the training of other health staff, including community health workers¹.

This fourth revision of the manual reflects recent clinical experience and research findings in diarrhoea case management. Compared to earlier versions, it includes revised guidelines on the management of children with acute diarrhoea using the new reduced (low) osmolarity ORS formulation and using zinc supplements, which have been shown to reduce duration and severity of diarrhoeal episodes, and revised guidelines for the management of bloody diarrhoea. Guidelines in the manual are based on the revised WHO chart that are included at the end of this document.

¹ Diarrhoea Treatment Guidelines (including new recommendations for the use of ORS and zinc supplementation) for Clinic-Based Healthcare Workers. MOST, WHO, UNICEF, IZiNCG. 2005 (http://www.who.int/child-adolescent-health/Emergencies/Diarrhoea_guidelines.pdf)

2. ESSENTIAL CONCEPTS CONCERNING DIARRHOEA

2.1 Definition of diarrhoea

Diarrhoea is the passage of unusually loose or watery stools, usually at least three times in a 24 hour period. However, it is the consistency of the stools rather than the number that is most important. Frequent passing of formed stools is not diarrhoea. Babies fed only breastmilk often pass loose, "pasty" stools; this also is not diarrhoea. Mothers usually know when their children have diarrhoea and may provide useful working definitions in local situations.

2.2 Clinical types of diarrhoeal diseases

It is most practical to base treatment of diarrhoea on the *clinical type* of the illness, which can easily be determined when a child is first examined. Laboratory studies are not needed. Four clinical types of diarrhoea can be recognized, each reflecting the basic underlying pathology and altered physiology:

 \cdot acute watery diarrhoea (including cholera), which lasts several hours or days: the main danger is dehydration; weight loss also occurs if feeding is not continued;

 \cdot *acute bloody diarrhoea*, which is also called *dysentery*: the main dangers are damage of the intestinal mucosa, sepsis and malnutrition; other complications, including dehydration, may also occur;

 \cdot persistent diarrhoea, which lasts 14 days or longer: the main danger is malnutrition and serious non-intestinal infection; dehydration may also occur;

 \cdot diarrhoea with severe malnutrition (marasmus or kwashiorkor): the main dangers are severe systemic infection, dehydration, heart failure and vitamin and mineral deficiency.

The management of each type of diarrhoea should prevent or treat the main danger(s) that each presents.

2.3 Dehydration

During diarrhoea there is an increased loss of water and electrolytes (sodium, chloride, potassium, and bicarbonate) in the liquid stool. Water and electrolytes are also lost through vomit, sweat, urine and breathing. Dehydration occurs when these losses are not replaced adequately and a deficit of water and electrolytes develops.

The volume of fluid lost through the stools in 24 hours can vary from 5 ml/kg (near normal) to 200 ml/kg, or more. The concentrations and amounts of electrolytes lost also vary. The total body sodium deficit in young children with severe dehydration due to diarrhoea is usually about 70-110 millimoles per litre of water deficit. Potassium and chloride losses are in a similar range. Deficits of this magnitude can occur with acute diarrhoea of any aetiology. The most common causes of dehydration are rotavirus, enterotoxigenic *Escherichia coli* (ETEC) and, during epidemics, *Vibrio cholerae* O1 or O139.

The degree of dehydration is graded according to signs and symptoms that reflect the amount of fluid lost:

· In the early stages of dehydration, there are no signs or symptoms.

· As dehydration increases, signs and symptoms develop. Initially these include: thirst, restless or irritable behaviour, decreased skin turgor, sunken eyes, and sunken fontanelle (in infants).

• *In severe dehydration*, these effects become more pronounced and the patient may develop evidence of hypovolaemic shock, including: diminished consciousness, lack of urine output, cool moist extremities, a rapid and feeble pulse (the radial pulse may be undetectable), low or undetectable blood pressure, and peripheral cyanosis. Death follows soon if rehydration is not started quickly.

2.4 Malnutrition²

Diarrhoea is, in reality, as much a nutritional disease as one of fluid and electrolyte loss. Children who die from diarrhoea, despite good management of dehydration, are usually malnourished and often severely so.

During diarrhoea, decreased food intake, decreased nutrient absorption, and increased nutrient requirements often combine to cause weight loss and failure to grow: the child's nutritional status declines and any pre-existing malnutrition is made worse. In turn, malnutrition contributes to diarrhoea which is more severe, prolonged, and possibly more frequent in malnourished children. This vicious circle can be broken by:

· continuing to give nutrient rich foods *during and after diarrhoea*;

• giving a nutritious diet, appropriate for the child's age, when the child is well.

When these steps are followed, malnutrition can be prevented and the risk of death from a future episode of diarrhoea is much reduced.

2.5 Zinc

Zinc deficiency is widespread among children in developing countries and occurs in most part of Latin America, Africa, the Middle East, and South Asia. Zinc has been shown to play critical roles in metallo-enzymes, polyribosomes, the cell membrane, and cellular function, leading to the belief that it also plays a central role in cellular growth and in function of the immune system. Although the theoretical basis for a potential role of zinc has been postulated for some time, convincing evidence of its importance in child health has only come recently from randomized controlled trials of zinc supplementation.

Numerous studies have now shown that zinc supplementation (10-20 mg per day until cessation of diarrhoea) significantly reduces the severity and duration of diarrhoea in children less than 5 years of age. Additional studies have shown that short course supplementation with zinc (10-20 mg per day for 10 to 14 days) reduces the incidence of diarrhoea for 2 to 3 months.

Based on these studies, it is now recommended that zinc (10-20 mg/day) be given for 10 to 14 days to all children with diarrhoea.

2.6 Use of antimicrobials and "antidiarrhoeal" drugs

Antimicrobials should not be used routinely. This is because, except as noted below, it is not possible to distinguish clinically episodes that *might* respond, such as diarrhoea caused by enterotoxigenic *E. coli*, from those caused by agents unresponsive to antimicrobials, such as rotavirus or *Cryptosporidium*. Moreover, even for potentially responsive infections, selecting an effective antimicrobial requires knowledge of the likely sensitivity of the causative agent, information that is usually unavailable. In addition, use of antimicrobials adds to the cost of treatment, risks adverse reactions and enhances the development of resistant bacteria.

Antimicrobials are reliably helpful *only* for children with bloody diarrhoea (probable shigellosis), suspected cholera with severe dehydration, and serious non-intestinal infections such as pneumonia. Anti-protozoal drugs are *rarely* indicated.

"Antidiarrhoeal" drugs and anti-emetics have *no practical benefits* for children with acute or persistent diarrhoea. They do not prevent dehydration or improve nutritional status, which should be the main objectives of treatment.

Some have dangerous, and sometimes fatal, side-effects. These drugs should *never* be given to children below 5 years³.

² Management of severe malnutrition: a manual for physicians and other senior health workers, World Health Organization, Geneva, 1999.

³ See also: *The Rational Use of Drugs in the Management of Acute Diarrhoea in Children*. Geneva, World Health Organization, 1990.

3. ASSESSMENT OF THE CHILD WITH DIARRHOEA

A child with diarrhoea should be assessed for dehydration, bloody diarrhoea, persistent diarrhoea, malnutrition and serious non-intestinal infections, so that an appropriate treatment plan can be developed and implemented without delay. The information obtained when assessing the child should be recorded on a suitable form.

3.1 History

Ø Ask the mother or other caretaker about:

- presence of blood in the stool;
- duration of diarrhoea;
- number of watery stools per day;
- number of episodes of vomiting;
- presence of fever, cough, or other important problems (e.g. convulsions, recent measles);
- pre-illness feeding practices;
- type and amount of fluids (including breastmilk) and food taken during the illness;
- drugs or other remedies taken;
- immunization history.

3.2 Physical examination

First, check for signs and symptoms of dehydration.

Ø Look for these signs:

- General condition: is the child alert; restless or irritable; lethargic or unconscious?
- Are the eyes normal or sunken?
- When water or ORS solution is offered to drink, is it taken normally or refused, taken eagerly, or is the child unable to drink owing to lethargy or coma?

Ø Feel the child to assess:

• Skin turgor. When the skin over the abdomen is pinched and released, does it flatten immediately, slowly, or very slowly (more than 2 seconds)?

Then, check for signs of other important problems.

Ø Look for these signs:

- Does the child's stool contain red blood?
- Is the child malnourished? Remove all upper body clothing to observe the shoulders, arms, buttocks and thighs, for evidence of marked muscle wasting (marasmus). Look also for oedema of the feet; if this is present with muscle wasting, the child is severely malnourished. If possible, assess the child's weight-for-age, using a growth chart (Annex 3), or weight-for-length. Alternatively, measure the mid-arm circumference (Annex 4). Also see the footnote⁴.
- Is the child coughing? If so, count the respiratory rate to determine whether breathing is abnormally rapid and look for chest indrawing.

Ø *Take* the child's temperature:

• Fever may be caused by severe dehydration, or by a non-intestinal infection such as malaria or pneumonia.

Diagnosis er moderate	Diagnosis of moderate of severe maintainton						
Assessment	Weight-for-age ^a	Weight-for-height ^a	Mid-arm circumference ^b	Other			
Moderate malnutrition	60-75%	70-80%	Yellow band 11.0 - 12.5 cm				
Severe malnutrition	<60%	<70%	Red band Less than 11.0 cm	Obvious marasmus or oedema with muscle wasting			

⁴ Diagnosis of moderate or severe malnutri

^a As percent of U.S. National Center for Health Statistics median values (see Annex 3).

^b For children aged 1-5 years (see Annex 4)

3.3 Determine the degree of dehydration and select a treatment plan

3.3.1 Determine the degree of dehydration

Use the chart in Table 1 to determine the degree of dehydration and select the appropriate plan to treat or prevent dehydration. The signs typical of children with *no signs of dehydration* are in column A, the signs of *some dehydration* are in column B, and those of *severe dehydration* are in column C.

If two or more of the signs in column C are present, the child has "severe dehydration". If this is not the case, but two or more signs from column B (and C) are present, the child has "some dehydration". If this also is not the case, the child is classified as having "no signs of dehydration". Signs that may require special interpretation are accompanied by footnotes in Table 1. Annex 5 explains how these categories are related to the terms "no, mild, moderate or severe" dehydration used in some textbooks.

3.3.2 Select a plan to prevent or treat dehydration

Choose the *Treatment Plan* that corresponds with the child's degree of dehydration:

- No signs of dehydration follow Treatment Plan A at home to prevent dehydration and malnutrition
- *Some dehydration* follow *Treatment Plan B* to treat dehydration⁵
- Severe dehydration follow Treatment Plan C to treat severe dehydration urgently

3.3.3 Estimate the fluid deficit

Children with some dehydration or severe dehydration should be weighed without clothing, as an aid in estimating their fluid requirements. If weighing is not possible, a child's age may be used to estimate the weight (see Table 2). *Treatment should never be delayed because a scale is not readily available.*

A child's fluid deficit can be estimated as follows:

Assessment	Fluid deficit as % of body weight	Fluid deficit in ml/kg body weight
No signs of dehydration	<5%	<50 ml/kg
Some dehydration	5-10%	50-100 ml/kg
Severe dehydration	>10%	>100 ml/kg

For example, a child weighing 5 kg and showing signs of "some dehydration" has a fluid deficit of 250-500 ml.

3.4 Diagnose other important problems

- Diagnose *dysentery*: if the stool contains red blood or the mother says she saw blood.
- Diagnose *persistent diarrhoea*: if diarrhoea began at least 14 days ago (and any period without diarrhoea has not exceeded two days).
- Diagnose *malnutrition*: if weight-for-length or weight-for-age, using the child's weight after rehydration, indicate moderate or severe malnutrition; or there is oedema with muscle wasting; or the child has obvious marasmus.
- Diagnose a *serious non-intestinal infection*: based, for example, on signs of pneumonia or sepsis; in areas with falciparum malaria, fever or a history of recent fever is sufficient to suspect and treat malaria. If sepsis or meningitis are suspected, the child should be referred to the hospital.

⁵ After dehydration has been treated following Plan B or C, the patient should continue treatment at home with Plan A.

Table 1: Assessment of diarrhoea patients for dehydration					
A B C			С		
LOOK AT:	: CONDITION ^a	Well, alert	Restless, irritable	Lethargic or unconscious	
	EYES ^b	Normal	Sunken	Sunken	
	THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink	
FEEL:	SKIN PINCH ^c	Goes back quickly	Goes back slowly	Goes back very slowly	
DECIDE		The patient has NO SIGNS OF DEHYDRATION	If the patient has two or more signs in B, there is SOME DEHYDRATION	If the patients has two or more signs in C, there is SEVERE DEHYDRATION	
TREAT		Use Treatment Pan A	Weigh the patient, if possible, and use Treatment Plan B	Weigh the patient and use Treatment Plan C URGENTLY	

^a 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.

^b 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.

^c 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.

4. MANAGEMENT OF ACUTE DIARRHOEA (WITHOUT BLOOD)

4.1 Objectives

The objectives of treatment are to:

- *prevent dehydration*, if there are no signs of dehydration;
- *treat dehydration*, when it is present;
- prevent nutritional damage, by feeding during and after diarrhoea; and
- *reduce the duration and severity of diarrhoea, and the occurrence of future episodes,* by giving supplemental zinc.

These objectives can be achieved by following the selected treatment plan, as described below. The management of suspected cholera is described in section 5.

4.2 Treatment Plan A: home therapy to prevent dehydration and malnutrition

Children with no signs of dehydration need extra fluids and salt to replace their losses of water and electrolytes due to diarrhoea. If these are not given, signs of dehydration may develop.

Mothers should be taught how to prevent dehydration at home by giving the child more fluid than usual, how to prevent malnutrition by continuing to feed the child, and why these actions are important. They should also know what signs indicate that the child should be taken to a health worker. These steps are summarized in the *four rules of Treatment Plan A*:

4.2.1 Rule 1: Give the child more fluids than usual, to prevent dehydration

What fluids to give

Many countries have designated recommended home fluids. *Wherever possible, these should include at least one fluid that normally contains salt* (see below). Plain clean water should also be given. Other fluids should be recommended that are frequently given to children in the area, that mothers consider acceptable for children with diarrhoea, and that mothers would be likely to give in increased amounts when advised to do so.

Suitable fluids⁶

Most fluids that a child normally takes can be used. It is helpful to divide suitable fluids into two groups:

Fluids that normally contain salt, such as:

- ORS solution
- salted drinks (e.g. salted rice water or a salted yoghurt drink)
- vegetable or chicken soup with salt.

Teaching mothers to add salt (about 3g/l) to an unsalted drink or soup during diarrhoea is also possible, but requires a sustained educational effort.

A home-made solution containing 3g/l of table salt (one level teaspoonful) and 18g/l of common sugar (sucrose) is effective but is not generally recommended because the recipe is often forgotten, the ingredients may not be available or too little may be given.

Fluids that do <u>not</u> contain salt, such as:

- plain water
- water in which a cereal has been cooked (e.g. unsalted rice water)
- unsalted soup
- yoghurt drinks without salt
- green coconut water
- weak tea (unsweetened)
- unsweetened fresh fruit juice.

Unsuitable fluids

A few fluids are potentially dangerous and should be avoided during diarrhoea. Especially important are drinks sweetened with sugar, which can cause osmotic diarrhoea and hypernatraemia. Some examples are:

- commercial carbonated beverages
- commercial fruit juices
- sweetened tea.

Other fluids to avoid are those with stimulant, diuretic or purgative effects, for example:

- coffee
- some medicinal teas or infusions.

How much fluid to give

The general rule is: give as much fluid as the child or adult wants until diarrhoea stops. As a guide, after each loose stool, give:

⁶ See also: *The Selection of Fluids and Food for Home Therapy to Prevent Dehydration from Diarrhoea: Guidelines for Developing a National Policy.* WHO document WHO/CDD/93.44.

- children under 2 years of age: 50-100 ml (a quarter to half a large cup) of fluid;
- children aged 2 up to 10 years: 100-200 ml (a half to one large cup);
- older children and adults: as much fluid as they want.

4.2.2 Rule 2: Give supplemental zinc (10 - 20 mg) to the child, every day for 10 to 14 days

Zinc can be given as a syrup or as dispersible tablets, whichever formulation is available and affordable. By giving zinc as soon as diarrhoea starts, the duration and severity of the episode as well as the risk of dehydration will be reduced. By continuing zinc supplementation for 10 to 14 days, the zinc lost during diarrhoea is fully replaced and the risk of the child having new episodes of diarrhoea in the following 2 to 3 months is reduced.

4.2.3 Rule 3: Continue to feed the child, to prevent malnutrition

The infant usual diet should be continued during diarrhoea and increased afterwards. Food should *never* be withheld and the child's usual foods should *not* be diluted. Breastfeeding should *always* be continued. The aim is to give as much nutrient rich food as the child will accept. Most children with watery diarrhoea regain their appetite after dehydration is corrected, whereas those with bloody diarrhoea often eat poorly until the illness resolves. These children should be encouraged to resume normal feeding as soon as possible.

When food is given, sufficient nutrients are usually absorbed to support continued growth and weight gain. Continued feeding also speeds the recovery of normal intestinal function, including the ability to digest and absorb various nutrients. In contrast, children whose food is restricted or diluted lose weight, have diarrhoea of longer duration, and recover intestinal function more slowly.

What foods to give

This depends on the child's age, food preferences and pre-illness feeding pattern; cultural practices are also important. *In general, foods suitable for a child with diarrhoea are the same as those required by healthy children*. Specific recommendations are given below.

Milk

- *Infants of any age who are breastfed* should be allowed to breastfeed as often and as long as they want. Infants will often breastfeed more than usual; this should be encouraged.
- *Infants who are not breastfed* should be given their usual milk feed (or formula) at least every three hours, if possible by cup. Special commercial formulas advertised for use in diarrhoea are expensive and unnecessary; they should *not* be given routinely. Clinically significant milk intolerance is rarely a problem.
- *Infants below 6 months of age who take breastmilk and other foods* should receive increased breastfeeding. As the child recovers and the supply of breastmilk increases, other foods should be decreased. (If fluids other than breastmilk are given, use a cup, not a bottle.) This usually takes about one week. If possible, the infant should become exclusively breastfed (see Annex 6).

There is no value in routinely testing the stools of infants for pH or reducing substances. Such tests are oversensitive, often indicating impaired absorption of lactose when it is not clinically important. It is more important to monitor the child's clinical response (e.g. weight gain, general improvement). Milk intolerance is only clinically important when milk feeding causes a prompt increase in stool volume and a return or worsening of the signs of dehydration, often with loss of weight.

Other foods

If the child is at least 6 months old or is already taking soft foods, he or she should be given cereals, vegetables and other foods, in addition to milk. If the child is over 6 months and such foods are not yet being given, they should be started during the diarrhoea episode or soon after it stops.

Recommended foods should be culturally acceptable, readily available, have a high content of energy and provide adequate amounts of essential micronutrients. They should be well cooked, and mashed or ground to make them easy to digest; fermented foods are also easy to digest. Milk should be mixed with a cereal. If possible, 5-10 ml of

vegetable oil should be added to each serving of cereal⁷. Meat, fish or egg should be given, if available. Foods rich in potassium, such as bananas, green coconut water and fresh fruit juice are beneficial.

How much food and how often

Offer the child food every three or four hours (six times a day). Frequent, small feedings are tolerated better than less frequent, large ones.

After the diarrhoea stops, continue giving the same energy-rich foods and provide one more meal than usual each day for at least two weeks. If the child is malnourished, extra meals should be given until the child has regained normal weight-for-height.

4.2.4 Rule 4: Take the child to a health worker if there are signs of dehydration or other problems

The mother should take her child to a health worker if the child:

- starts to pass many watery stools;
- has repeated vomiting;
- becomes very thirsty;
- is eating or drinking poorly;
- develops a fever;
- has blood in the stool; or
- the child does not get better in three days.

4.3 Treatment Plan B: oral rehydration therapy for children with some dehydration

Children with some dehydration should receive oral rehydration therapy (ORT) with ORS solution in a health facility following Treatment Plan B, as described below. Children with some dehydration should also receive zinc supplementation as described above.

4.3.1 How much ORS solution is needed?

Use Table 2 to estimate the amount of ORS solution needed for rehydration. If the child's weight is known, this should be used to determine the *approximate* amount of solution needed. The amount may also be estimated by multiplying the child's weight in kg times 75 ml. If the child's weight is not known, select the approximate amount according to the child's age.

The *exact* amount of solution required will depend on the child's dehydration status. Children with more marked signs of dehydration, or who continue to pass frequent watery stools, will require more solution than those with less marked signs or who are not passing frequent stools. *If a child wants more than the estimated amount of ORS solution, and there are no signs of over-hydration, give more.*

Oedematous (puffy) eyelids are a sign of *over-hydration*. If this occurs, stop giving ORS solution, but give breastmilk or plain water, and food. Do not give a diuretic. When the oedema has gone, resume giving ORS solution or home fluids according to Treatment Plan A.

⁷ Most staple foods do not provide enough calories per unit weight for infants and young children. This is improved by adding some vegetable oil.

Table 2: Guidelines for treating children and adults with some dehydration **APPROXIMATE AMOUNT OF ORS SOLUTION TO GIVE IN THE FIRST 4 HOURS** Age^a Less than 4 4 – 11 12 - 232 - 4 years 5 – 14 years 15 years or months older months months Weight Less than 5 5-7.9 kg 8-10.9 kg 11-15.9kg 16-29.9kg 30 kg or kg more 200-400 400-600 600-800 800-1200 1200-2200 2200-4000 In ml in local measure

^a Use the patient's age only when you do not know the weight. The approximate amount of ORS required (in ml) can also be calculated by multiplying the patient's weight in kg by 75.

• If the patient wants more ORS than shown, give more.

- Encourage the mother to continue breastfeeding her child.
- For infants under 6 months who are not breastfed, if using the old WHO ORS solution containing 90 mmol/L of sodium, also give 100-200ml clean water during this period. However, if using the new reduced (low) osmolarity ORS solution containing 75mmol/L of sodium, this is not necessary.

NOTE: During the initial stages of therapy, while still dehydrated, adults can consume up to 750 ml per hour, if necessary, and children up to 20 ml per kg body weight per hour.

4.3.2 How to give ORS solution

A family member should be taught to prepare and give ORS solution. The solution should be given to infants and young children using a clean spoon or cup. Feeding bottles should *not* be used. For babies, a dropper or syringe (without the needle) can be used to put small amounts of solution into the mouth. Children under 2 years of age should be offered a teaspoonful every 1-2 minutes; older children (and adults) may take frequent sips directly from the cup.

Vomiting often occurs during the first hour or two of treatment, especially when children drink the solution too quickly, but this rarely prevents successful oral rehydration since most of the fluid is absorbed. After this time vomiting usually stops. If the child vomits, wait 5-10 minutes and then start giving ORS solution again, but more slowly (e.g. a spoonful every 2-3 minutes).

4.3.3 Monitoring the progress of oral rehydration therapy

Check the child from time to time during rehydration to ensure that ORS solution is being taken satisfactorily and that signs of dehydration are not worsening. If at any time the child develops signs of severe dehydration, shift to Treatment Plan C.

After four hours, reassess the child fully, following the guidelines in Table 1. Then decide what treatment to give next:

- If signs of *severe dehydration* have appeared, intravenous (IV) therapy should be started following Treatment Plan C. This is very unusual, however, occurring only in children who drink ORS solution poorly and pass large watery stools frequently during the rehydration period.
- If the child still has signs indicating *some dehydration*, continue oral rehydration therapy by repeating Treatment Plan B. At the same time start to offer food, milk and other fluids, as described in Treatment Plan A, and continue to reassess the child frequently.
- If there are *no signs of dehydration*, the child should be considered fully rehydrated. When rehydration is complete:
 - the skin pinch is normal;
 - thirst has subsided;
 - urine is passed;
 - the child becomes quiet, is no longer irritable and often falls asleep.

Teach the mother how to treat her child at home with ORS solution and food following Treatment Plan A. Give her enough ORS packets for two days. Also teach her the signs that mean she should bring her child back (see section 4.2.4).

4.3.4 Meeting normal fluid needs

While treatment to replace the existing water and electrolyte deficit is in progress the child's *normal daily fluid requirements* must also be met. This can be done as follows:

- Breastfed infants: Continue to breastfeed as often and as long as the infant wants, even during oral rehydration.
- Non breastfed infants under 6 months of age: If using the old WHO ORS solution containing 90 mmol/L of sodium, also give 100-200ml clean water during this period. However, if using the new reduced (low) osmolarity ORS solution containing 75mmol/L of sodium, this is not necessary. After completing rehydration, resume full strength milk (or formula) feeds. Give water and other fluids usually taken by the infant.
- *Older children and adults*: Throughout rehydration and maintenance therapy, offer as much plain water to drink as they wish, *in addition* to ORS solution.

4.3.5 If oral rehydration therapy must be interrupted

If the mother and child must leave before rehydration with ORS solution is completed:

- show the mother how much ORS solution to give to finish the four-hour treatment at home;
- give her enough ORS packets to complete the four hour treatment and to continue oral rehydration for two more days, as shown in Treatment Plan A;
- show her how to prepare ORS solution;
- teach her the four rules in Treatment Plan A for treating her child at home.

4.3.6 When oral rehydration fails

With the previous ORS, signs of dehydration would persist or reappear during ORT in about 5% of children. With the new reduced (low) osmolarity ORS, it is estimated that such treatment "failures" will be reduced to 3%, or less. The usual causes for these "failures" are:

- continuing rapid stool loss (more than 15-20 ml/kg/hour), as occurs in some children with cholera;
- insufficient intake of ORS solution owing to fatigue or lethargy;
- frequent, severe vomiting.

Such children should be given ORS solution by nasogastric (NG) tube or Ringer's Lactate Solution intravenously (IV) (75 ml/kg in four hours), usually in hospital. After confirming that the signs of dehydration have improved, it is usually possible to resume ORT successfully.

Rarely, ORT should not be given. This is true for children with:

- abdominal distension with paralytic ileus, which may be caused by opiate drugs (e.g. codeine, loperamide) and hypokalaemia;
- glucose malabsorption, indicated by a marked increase in stool output when ORS solution is given, failure of the signs of dehydration to improve and a large amount of glucose in the stool when ORS solution is given.

In these situations, rehydration should be given IV until diarrhoea subsides; NG therapy should not be used.

4.3.7 Giving Zinc

Begin to give supplemental zinc, as in Treatment Plan A, as soon the child is able to eat following the initial fourhour rehydration period.

4.3.8 Giving food

Except for breastmilk, food should not be given during the initial four-hour rehydration period. However, children continued on Treatment Plan B longer than four hours should be given some food every 3-4 hours as described in Treatment Plan A. *All children* older than 6 months should be given some food before being sent home. This helps to emphasize to mothers the importance of continued feeding during diarrhoea.

4.4 Treatment Plan C: for patients with severe dehydration

4.4.1 Guidelines for intravenous rehydration

The preferred treatment for children with severe dehydration is rapid intravenous rehydration, following Treatment Plan C. If possible, the child should be admitted to hospital. Guidelines for intravenous rehydration are given in Table 3.

Children who can drink, even poorly, should be given ORS solution by mouth until the IV drip is running. In addition, *all* children should start to receive some ORS solution (about 5 ml/kg/h) when they can drink without difficulty, which is usually within 3-4 hours (for infants) or 1-2 hours (for older patients). This provides additional base and potassium, which may not be adequately supplied by the IV fluid.

Table 3: Guidelines for intravenous treatment of children and adults with severe dehydration

Start IV fluids immediately. If the patient can drink, give ORS by mouth until the drip is set up. Give 100 ml/kg Ringer's Lactate Solution^a divided as follows:

Age	First give 30 ml/kg in:	Then give 70 ml/kg in:
Infants (under 12 months)	1 hour ^b	5 hours
Older	30 minutes ^b	2½ hours

• Reassess the patient every 1-2 hours. If hydration is not improving, give the IV drip more rapidly.

• After six hours (infants) or three hours (older patients), evaluate the patient using the assessment chart. Then choose the appropriate Treatment Plan (A, B or C) to continue treatment.

^a If Ringer's Lactate Solution is not available, normal saline may be used (See Annex 2).

^b Repeat once if radial pulse is still very weak or not detectable.

4.4.2 Monitoring the progress of intravenous rehydration

Patients should be reassessed every 15-30 minutes until a strong radial pulse is present. Thereafter, they should be reassessed at least every hour to confirm that hydration is improving. If it is not, the IV drip should be given more rapidly.

When the planned amount of IV fluid has been given (after three hours for older patients, or six hours for infants), the child's hydration status should be reassessed fully, as shown in Table 1.

Ø Look and feel for all the signs of dehydration:

- If signs of *severe dehydration* are still present, repeat the IV fluid infusion as outlined in Treatment Plan C. This is very unusual, however, occurring only in children who pass large watery stools frequently during the rehydration period.
- If the child is improving (able to drink) but still shows signs of *some dehydration*, discontinue the IV infusion and give ORS solution for four hours, as specified in Treatment Plan B.
- If there are *no signs of dehydration*, follow Treatment Plan A. If possible, observe the child for at least six hours before discharge while the mother gives the child ORS solution, to confirm that she is able to maintain the child's hydration. Remember that the child will require therapy with ORS solution until diarrhoea stops.

If the child cannot remain at the treatment centre, teach the mother how to give treatment at home following Treatment Plan A, give her enough ORS packets for two days and teach her the signs that mean she should bring her child back (see section 4.2.4).

4.4.3 What to do if intravenous therapy is not available

If IV therapy is not available at the facility, but can be given nearby (i.e. within 30 minutes), send the child *immediately* for IV treatment. If the child can drink, give the mother some ORS solution and show her how to give it to her child during the journey.

If IV therapy is not available nearby, health workers who have been trained can give ORS solution by NG tube, at a rate of 20 ml/kg body weight per hour for six hours (total of 120 ml/kg body weight). If the abdomen becomes swollen, ORS solution should be given more slowly until it becomes less distended.

If NG treatment is not possible but the child can drink, ORS solution should be given by mouth at a rate of 20 ml/kg body weight per hour for six hours (total of 120 ml/kg body weight). If this rate is too fast, the child may vomit repeatedly. In that case, give ORS solution more slowly until vomiting subsides.

Children receiving NG or oral therapy should be reassessed at least every hour. If the signs of dehydration do not improve after three hours, the child must be taken immediately to the nearest facility where IV therapy is available. Otherwise, if rehydration is progressing satisfactorily, the child should be reassessed after six hours and a decision on further treatment made as described above for those given IV therapy.

If neither NG nor oral therapy is possible, the child should be taken *immediately* to the nearest facility where IV or NG therapy is available.

4.5 Electrolyte disturbances

Knowing the levels of serum electrolytes rarely changes the management of children with diarrhoea. Indeed, these values are often misinterpreted, leading to inappropriate treatment. It is usually *not helpful* to measure serum electrolytes. The disorders described below are *all* adequately treated by ORT with ORS solution.

4.5.1 Hypernatraemia

Some children with diarrhoea develop *hypernatraemic dehydration*, especially when given drinks that are hypertonic owing to their excessive content of sugar (e.g. soft drinks, commercial fruit drinks, too concentrated infant formula) or salt. These draw water from the child's tissues and blood into the bowel, causing the concentration

of sodium in extra-cellular fluid to rise. If the solute in the drink is not fully absorbed, the water remains in the bowel, causing osmotic diarrhoea.

Children with hypernatraemic dehydration (serum Na >150 mmol/l) have thirst that is out of proportion to other signs of dehydration. Their most serious problem is convulsions, which usually occur when the serum sodium concentration exceeds 165 mmol/l, and especially when IV therapy is given. Seizures are much less likely when hypernatraemia is treated with ORS solution, which usually causes the serum sodium concentration to become normal within 24 hours.

4.5.2 Hyponatraemia

Children with diarrhoea who drink mostly water, or watery drinks that contain little salt, may develop hyponatraemia (serum Na <130 mmol/l). Hyponatraemia is especially common in children with shigellosis and in severely malnourished children with oedema. Severe hyponatraemia can be associated with lethargy and, less often, seizures. ORS solution is safe and effective therapy for nearly all children with hyponatraemia. An exception is children with oedema (see section 8), for whom ORS solution provides too much sodium.

4.5.3 Hypokalaemia

Inadequate replacement of potassium losses during diarrhoea can lead to potassium depletion and hypokalaemia (serum K+ <3 mmol/l), especially in children with malnutrition. This can cause muscle weakness, paralytic ileus, impaired kidney function and cardiac arrhythmia. Hypokalaemia is worsened when base (bicarbonate or lactate) is given to treat acidosis without simultaneously providing potassium. Hypokalaemia can be prevented, and the potassium deficit corrected, by using ORS solution for rehydration therapy and by giving foods rich in potassium during diarrhoea and after it has stopped (see Section 4.2).

5. MANAGEMENT OF SUSPECTED CHOLERA

Cholera differs from acute diarrhoea of other causes in three ways:

- it occurs in large epidemics that involve both children and adults;
- voluminous watery diarrhoea may occur, leading rapidly to severe dehydration with hypovolaemic shock;
- for cases with severe dehydration appropriate antibiotics may shorten the duration of the illness.

5.1 When to suspect cholera⁸

Cholera should be suspected when a child older than 5 years or an adult develops severe dehydration from acute watery diarrhoea (usually with vomiting), or any patient older than 2 years has acute watery diarrhoea when cholera is known to be occurring in the area. Younger children also develop cholera, but the illness may be difficult to distinguish from other causes of acute watery diarrhoea, especially rotavirus.

5.2 Treatment of dehydration

Initial treatment of dehydration from cholera follows the guidelines given above for patients with some or severe dehydration. For patients with severe dehydration and shock, the initial intravenous infusion should be given *very rapidly* to restore an adequate blood volume, as evidenced by normal blood pressure and a strong radial pulse. Typically, an adult weighing 50 kg and with severe dehydration would have an estimated fluid deficit of five litres. Of this, two litres should be given within 30 minutes, and the remainder within three hours.

With cholera, unusually large amounts of ORS solution may be required to replace large continuing losses of watery stool after dehydration is corrected⁹. The amount of stool lost is greatest in the first 24 hours of illness, being largest in patients who present with severe dehydration. During this period, the *average* fluid requirement of such patients

⁸ See also: Cholera outbreak: assessing the outbreak response and improving preparadness. WHO/CDS/CPE/ZFK/2004.4

⁹ Rice-based ORS is superior to standard ORS for adults and children with cholera, and may be used to treat such patients wherever its preparation is convenient; R-ORS may be available in packets containing pre-cooked rice powder. Alternatively, uncooked rice powder may be added to water, boiled for 5 minutes and allowed to cool before adding salts in the same concentration as for ORS. It does not have this benefit, however, for children with acute non-cholera diarrhoea.

is 200 ml/kg of body weight, but some need 350 ml/kg or more. Patients whose ongoing stool losses are in this range, or higher, usually require intravenous maintenance therapy using Ringer's Lactate Solution with added potassium chloride. Additional potassium can also be provided by ORS solution as soon as the patient can drink.

After being rehydrated, patients should be reassessed for signs of dehydration at least every 1-2 hours, and more often if there is profuse ongoing diarrhoea. If signs of dehydration reappear, ORS solution should be given more rapidly. If patients become tired, vomit frequently or develop abdominal distension, ORS solution should be stopped and rehydration should be given IV with Ringer's Lactate Solution (50 ml/kg in three hours), with added potassium chloride. After this it is usually possible to resume treatment with ORS solution.

If possible, suspected cholera patients should be treated under observation until diarrhoea stops, or is infrequent and of small volume. This is especially important for those who present with severe dehydration.

5.3 Antimicrobial therapy

All cases of suspected cholera with severe dehydration should receive an oral antimicrobial known to be effective against strains of *Vibrio cholerae* in the area (Annex 7). This reduces the total volume of stool passed, causes diarrhoea to stop within 48 hours, and shortens the period of faecal excretion of *V. cholerae*. The first dose should be given as soon as vomiting stops, which is usually 4-6 hours after starting rehydration therapy.

6. MANAGEMENT OF ACUTE BLOODY DIARRHOEA (DYSENTERY)¹⁰

6.1 Initial treatment and follow-up

The outpatient management of bloody diarrhoea in children is summarized in Figure 1.

Any child with bloody diarrhoea and severe malnutrition should be referred immediately to hospital. All other children with bloody diarrhoea should be assessed, given appropriate fluids to prevent or treat dehydration, and given food, as described in sections 3 and 4.

In addition, they should be treated for three days with ciprofloxacin, or for five days with another oral antimicrobial to which most *Shigella* in the area are sensitive (Annex 7). This is because *Shigella* cause most episodes of bloody diarrhoea in children, and nearly all episodes that are severe. Determining the sensitivity of local strains of *Shigella* is essential, as antimicrobial resistance is frequent and the pattern of resistance is unpredictable. Antimicrobials that are ineffective for treatment of shigellosis, irrespective of the sensitivity of local strains are listed in Table 4. They should *never* be given to treat presumed shigellosis. Recently it was recommended that nalidixic acid should no longer be recommended for the management of *Shigella* infection.¹¹

	Table 4: Antimicrobials that are <i>ineffective</i> for treatment of Shigellosis				
٠	metronidazole	٠	nitrofurans (e.g. nitrofurantoin, furazolidone)		
•	streptomycin ·	٠	aminoglycosides (e.g. gentamicin, kanamycin)		
٠	tetracyclines ·	•	first and second generation cephalosporins (e.g.		
٠	chloramphenicol ·		cephalexin, cefamandole)		
•	sulfonamides				
٠	amoxycillin				

The child should be seen again after two days if he or she:

- was initially dehydrated
- is less than 1 year old
- had measles during the past six weeks
- is not getting better.

¹⁰ This topic is discussed more fully in: *The Management of Bloody Diarrhoea in Young Children*. WHO document WHO/CDD/94.49 and in Guidelines for the control of shigellosis including epidemics due to *Shigella dysenteriae* type 1 WHO/FCH/CAH/05.3

¹¹ Antibiotics in the management of shigellosis. Weekly Epidemiological Record, 2004; 79:355-356.

Signs of improvement include the disappearance of fever, less blood in the stool, passage of fewer stools, improved appetite and a return to normal activity. If there is little or no improvement after two days, children in the first three categories above should be referred to hospital because they are at increased risk of serious complications or death. For other children, the antimicrobial should be changed to another recommended for *Shigella* in the area. Children whose condition has not improved after giving the second antimicrobial for two days should also be referred to hospital. If the child is improving, the antimicrobial should be continued for five days.



Figure 1: Outpatient management of bloody diarrhoea in children below 5 years of age^a

^a Treatment should also include (i) oral rehydration therapy to treat or prevent dehydration, and (ii) continued frequent feeding, including breastfeeding.

^b Use of oral antimicrobial effective for *Shigella* in the area (see Annex 7). Give enough of the antimicrobial to last 3 to 5 days. ^c If trophozoites of *E. histolytica* are seen in the stool at any time by a reliable technician, treatment for amoebiasis should be given.

6.2 When to consider amoebiasis

Amoebiasis is an *unusual* cause of bloody diarrhoea in young children, usually causing less than 3% of episodes. *Young children with bloody diarrhoea should not be treated routinely for amoebiasis.* Such treatment should be considered only when microscopic examination of fresh faeces done in a reliable laboratory reveals trophozoites of *E. histolytica* containing red blood cells, or two different antimicrobials usually effective for *Shigella* in the area have been given without clinical improvement, as summarized in Figure 1.

7. MANAGEMENT OF PERSISTENT DIARRHOEA

This is diarrhoea, with or without blood, that begins acutely and *lasts at least 14 days*. It is usually associated with weight loss and, often, with serious non-intestinal infections. Many children who develop persistent diarrhoea are malnourished before the diarrhoea starts. Persistent diarrhoea almost never occurs in infants who are exclusively breastfed. The child's history should be carefully reviewed to be certain there is diarrhoea, rather than several soft or pasty stools each day, which is normal for breastfed infants.

The objective of treatment is to restore weight gain and normal intestinal function. Treatment of persistent diarrhoea consists of giving:

- appropriate fluids to prevent or treat dehydration
- a nutritious diet that does not cause diarrhoea to worsen
- supplementary vitamins and minerals, including zinc for 10 14 days.
- antimicrobial(s) to treat *diagnosed* infections.

Children who have persistent diarrhoea and severe malnutrition should be treated in hospital as described in section 8 (see footnote 3, page 10).

The treatment of children with persistent diarrhoea who are not severely malnourished is described below.

7.1 Where to give treatment

Most children with persistent diarrhoea can be treated at home with careful follow-up to ensure they are improving. Some, however, require treatment in hospital, at least until their condition is stable, their diarrhoea has lessened and they are gaining weight. These include:

- children with a serious systemic infection, such as pneumonia or sepsis
- children with signs of dehydration
- infants below 4 months of age.

As the risk of nutritional decline and death in such children is high, every effort should be made to persuade parents that treatment in hospital is necessary.

7.2 Prevent or treat dehydration

Assess the child for signs of dehydration and give fluids according to Treatment Plan A, B or C, as appropriate.

ORS solution is effective for most children with persistent diarrhoea. In a few, however, glucose absorption is impaired and ORS solution is not as effective as usual. When such children take ORS solution, stool volume increases markedly, thirst increases, signs of dehydration develop or worsen, and the stool contains a large amount of unabsorbed glucose. These children require IV rehydration until ORS solution can be taken without causing diarrhoea to worsen.

7.3 Identify and treat specific infections

Routine treatment of persistent diarrhoea with antimicrobials is not effective and should not be given. Some children, however, have non-intestinal (or intestinal) infections that require specific antimicrobial therapy. The persistent diarrhoea of such children will not improve until these infections are diagnosed and treated correctly.

7.3.1 Non-intestinal infections

Every child with persistent diarrhoea should be examined for non-intestinal infections, such as: pneumonia, sepsis, urinary tract infection and otitis media. Treatment of these infections with antimicrobials should follow standard guidelines.

7.3.2 Intestinal infections

Persistent diarrhoea with blood in the stool should be treated with an oral antimicrobial effective for *Shigella* as described in section 6 (and Annex 7).

Treatment for amoebiasis (Annex 7) should be given *only* if the diagnostic criteria in section 6.2 are met.

Treatment for giardiasis (Annex 7) should be given *only* if cysts or trophozoites of G. *duodenalis* are seen in the faeces.

7.3.3 Hospital-acquired infections

Serious infections are often acquired in hospital. These may include pneumonia, rotavirus diarrhoea and cholera, among others. Hospital-acquired infection should be considered in any child who is lethargic and eats or drinks poorly (but is not dehydrated), or who develops fever, cough, worsening diarrhoea or other signs of serious illness at least two days after being admitted. Treatment should follow standard guidelines.

7.4 Give a nutritious diet

This is essential treatment for all children with persistent diarrhoea. As the normal diet of such children is often inadequate, their treatment provides an important opportunity to teach their mothers how to feed them correctly. Outpatients should be given a diet appropriate for their age, but with a limited content of lactose. Children treated in hospital require special diets until their diarrhoea lessens and they are gaining weight. In either situation, the goal is a daily intake of *at least 110 calories/kg*.

7.4.1 Feeding of outpatients

The following feeding recommendations should be given:

- Continue breastfeeding.
- If yoghurt is available, give it in place of any animal milk usually taken by the child; yoghurt contains less lactose and is better tolerated. Otherwise, limit animal milk to 50 ml/kg/day; greater amounts may aggravate the diarrhoea. *Mix the milk with the child's cereal*. Do not dilute the milk.
- Give other foods that are appropriate for the child's age, as described in section 4.2.3. Give enough of these to ensure an adequate energy intake. Infants older than 6 months whose only food has been animal milk should begin to take solid foods.
- Give frequent small meals, at least six times a day.

7.4.2 Feeding in hospital

Continue breastfeeding as often and as long as the child wants. Other food should be withheld for 4-6 hours for children being rehydrated following Treatment Plan B or C.

Infants below age 6 months

- Encourage *exclusive* breastfeeding. Help mothers who are not breastfeeding exclusively to re-establish lactation (see Annex 6).
- If animal milk *must* be given, replace it with yoghurt (given with a spoon). If this is not possible, give a lactose-free milk formula (given from a cup).

Older infants and young children

Use standard diets prepared from local ingredients. Two diets are described below. The first contains reduced lactose. The second, for children who do not improve with the first, contains no lactose and reduced starch.

The first diet: reduced lactose

This should be started as soon as the child can eat and should be given six times a day. Many children will eat poorly, however, until any serious infection is treated for 24-48 hours. Such children may require nasogastric feeding initially. The diet should contain at least 70 Kcal/100g, provide milk or yoghurt as a source of animal protein, but no more than 3.7 g lactose/kg body weight/day, and provide at least 10% of calories as protein. A mixture of cow's milk, cooked cereal, vegetable oil and cane sugar is satisfactory. Diets can also be prepared from local ingredients following the above guidelines. The following example provides 83 Kcal/100g, 3.7g lactose/kg body weight/day and 11% of calories as protein:

- full-fat dried milk 11 g (or whole liquid milk: 85 ml)
- rice 15 g (uncooked rice)
- vegetable oil 3.5 g
- cane sugar 3.0 g, and
- water to make 200 ml

With this diet, 130 ml/kg provides 110 Kcal/kg.

The second diet: lactose-free with reduced starch

About 65% of children will improve on the first diet. Of those who do not, more than half will improve when given a second diet prepared from egg, cooked cereal, vegetable oil and glucose, and providing at least 10% of calories as protein. The following example provides 75 Kcal/100g:

•	whole egg	64 g
•	rice	3 g

- vegetable oil 4 g
- glucose 3 g, and
- water to make 200 ml

With this diet, 145 ml/kg provides 110 calories/kg. If finely ground, cooked chicken meat (12 g) is used in place of whole egg, the diet provides 70 Kcal per 100 g.

7.5 Give supplementary multivitamins and minerals

All children with persistent diarrhoea should receive supplementary multivitamins and minerals each day for two 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. As a guide, one RDA for a child aged one year is:

- folate 50 ug
- zinc 10 mg
- vitamin A 400 ug
- copper 1 mg
- magnesium 80 mg

7.6 Monitor the response to treatment

7.6.1 Children treated as outpatients

Children should be re-evaluated after seven days, or earlier if diarrhoea worsens or other problems develop. Those who have gained weight and who have less than three loose stools per day, may resume a normal diet for age. Those who have not gained weight or whose diarrhoea has not improved should be referred to hospital.

7.6.2 Children treated in hospital

The following should be measured and recorded in a standard manner, at least daily:

(i) body weight, (ii) temperature, (iii) food taken, and (iv) number of diarrhoea stools.

Successful treatment with either diet is characterized by:

- adequate food intake
- weight gain
- fewer diarrhoeal stools
- lack of fever.

Many children will lose weight for 1-2 days, and then show steady weight gain as infections come under control and diarrhoea subsides. There should be at least three successive days of increasing weight to conclude that weight gain is occurring; for most children, weight on day 7 will be greater than on admission.

Dietary failure is manifest by:

- an increase in stool frequency (usually to more than 10 watery stools/day), often with a return of signs of dehydration; this usually occurs shortly after a new diet is begun; or
- a failure to establish daily weight gain within seven days, as described above.

The first diet should be given for seven days, unless signs of dietary failure occur earlier, in which case the first diet should be stopped and the second diet given, also for seven days.

Children responding satisfactorily to either diet should be given additional fresh fruit and well cooked vegetables as soon as improvement is confirmed; after seven days' treatment with the effective diet, they should resume an appropriate diet for age, including milk, that provides at least 110 Kcal/kg/day. Occasionally it is necessary to restrict milk intake for more than seven days. Children may return home, but should be followed up regularly to ensure continued weight gain and compliance with feeding advice.

8. MANAGEMENT OF DIARRHOEA WITH SEVERE MALNUTRITION

Diarrhoea is a serious and often fatal event in children with severe malnutrition. Although treatment and prevention of dehydration are essential, care of these children must also focus on careful management of their malnutrition and treatment of other infections¹² (see footnote 3, page 10, for diagnosis of severe malnutrition).

8.1 Assessment for dehydration

Assessment of hydration status is difficult because many of the normally-used signs are unreliable. Skin turgor appears poor in children with marasmus owing to the absence of subcutaneous fat; their eyes may also appear sunken. Diminished skin turgor may be masked by oedema in children with kwashiorkor. In both types of malnutrition the child's irritability or apathy make assessment of the mental state difficult. Signs that remain useful for assessing hydration status include: eagerness to drink (a sign of some dehydration), and lethargy, cool and moist extremities, weak or absent radial pulse, and reduced or absent urine flow (signs of severe dehydration). In children with severe malnutrition it is often impossible to distinguish reliably between some dehydration and severe dehydration.

¹² See also: Management of the Child with a Serious Infection or Severe Malnutrition. WHO/FCH/CAH/00.1

Of equal importance, it is also difficult to distinguish severe dehydration from septic shock, as both conditions reflect hypovolaemia and reduced blood flow to vital organs. An important distinguishing feature is that severe dehydration requires a history of watery diarrhoea. A severely malnourished child with signs suggesting severe dehydration but without a history of watery diarrhoea should be treated for septic shock.

8.2 Management of dehydration

This should take place in hospital. Rehydration should usually be by mouth; an NG tube may be used for children who drink poorly. IV infusion easily causes over-hydration and heart failure; it should be used *only* for the treatment of shock.

Oral rehydration should be done *slowly*, giving 70-100 ml/kg over 12 hours. Start by giving about 10 ml/kg/hour during the first two hours. Continue at this rate or a lower rate based on the child's thirst and ongoing stool losses. Increasing oedema is evidence of over-hydration. Fluids given to maintain hydration after dehydration has been corrected should be based on the amount of ongoing stool losses, as described in Treatment Plan A.

Full-strength ORS solution should not be used for oral or NG rehydration. It provides too much sodium and too little potassium. Two approaches to develop a suitable oral solution are possible.

When using the new ORS solution containing 75 mEq/l of sodium:

- dissolve one ORS packet into two litres of clean water (to make two litres instead of one litre);
- add 45 ml of potassium chloride solution (from stock solution containing 100g KCl/l); and
- add and dissolve 50g sucrose.

These modified solutions provide less sodium (37.5 mmol/l), more potassium (40 mmol/l) and added sugar (25g/l), each of which is appropriate for severely malnourished children with diarrhoea.

8.3 Feeding

Mothers should remain with their children to breastfeed them and to help with other feeding, which should begin as soon as possible, usually within 2-3 hours of starting rehydration. Food should be given every 2-3 hours, day and night.

8.3.1 Initial diet

The initial diet should be given from admission until the child's appetite returns to normal.

Some children will eat normally at admission, but many will recover their appetite only after 3-4 days, when infections have been treated. The diet contains 75 Kcal/100 ml and is composed as follows:

•	skimmed milk powder	25 g
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- vegetable oil 20 g
- sugar 60 g
- rice powder (or other cereal powder) 60 g, and
- water to make 1000 ml

Combine the ingredients and boil gently for five minutes to cook the cereal powder.

Children should receive 130 ml/kg/day of the diet. Those who will not drink the minimum amount should be given the diet by NG tube in six divided feedings.

8.3.2 Subsequent diet

After appetite returns, children should be given the following diet, which contains 100 Kcal/100ml:

•	skimmed milk powder	80 g
•	vegetable oil	60 g
•	sugar	50 g, and
•	water to make	1000 ml

Fresh skimmed milk, briefly boiled, may be used in place of skimmed milk powder and water.

Children should be given as much of the diet as they will take, aiming for a minimum daily intake of 120 ml/kg/day, and reaching 200 ml/kg/day, or more, as appetite improves.

8.3.3 Vitamins, minerals and salts

The following mixture of salts should be added to every two litres of both liquid diets described above.

KCl	3.6 g
K ₃ citrate	1.3 g
MgCl ₂ .6H ₂ O	1.2 g
Zn acetate.2H ₂ 0	130 mg
CuSO ₄ .7H ₂ O	22 mg
NaSeO ₄ .10H ₂ O	0.44 mg
KI	0.20 mg

Vitamin A should be given as described in section 9.3. Multivitamin mixtures that provide at least two RDAs of all vitamins should be added to the diet or given separately. Supplementary iron should be given when weight gain is established (see also section 7.5).

8.4 Use of antimicrobials

All severely malnourished children should receive broad spectrum antimicrobial treatment, e.g. gentamicin and ampicillin, for several days when admitted to hospital. This combination or another that provides broad spectrum coverage should also be given to any child with signs of septic shock. Children should be checked daily for other infections and treated when these are identified.

9. OTHER PROBLEMS ASSOCIATED WITH DIARRHOEA

9.1 Fever

Fever in a child with diarrhoea may be caused by another infection (e.g. pneumonia, bacteraemia, urinary tract infection or otitis media). Young children may also have fever on the basis of dehydration. The presence of fever should prompt a search for other infections. This is especially important when fever persists after a child is fully rehydrated.

Children with fever (38°C or above) or a history of fever in the past five days, and who live in a *Plasmodium falciparum* malarious area, should also be given an antimalarial or treated according to the policy of the national malaria programme.

Children with high fever (39°C or greater) should be treated promptly to bring the temperature down. This is best done with treating any infection with appropriate antibiotics as well as an antipyretic (e.g. paracetamol). Reducing fever also improves appetite and diminishes irritability.

9.2 Convulsions

In a child with diarrhoea and a history of convulsions during the illness, the following diagnoses and treatments should be considered:

- *Febrile convulsion*: This usually occurs in infants, especially when their temperature exceeds 40°C or rises very rapidly. Treat fever with paracetamol. Sponging with tepid water and fanning may also be used if the temperature exceeds 39°C. Evaluate for possible meningitis.
- *Hypoglycaemia*: This occasionally occurs in children with diarrhoea, owing to inadequate gluconeogenesis. If hypoglycaemia is suspected in a child with seizures or coma, give 5.0 ml/kg of 10% glucose solution intravenously over five minutes. If hypoglycaemia is the cause, recovery of consciousness is usually rapid. In such cases ORS solution should be given (or 5% glucose should be added to the IV solution) until feeding starts, to avoid recurrence of symptomatic hypoglycaemia.
- *Hypernatraemia or hyponatraemia*: Treat the dehydration with ORS solution, as described in sections 4.5.1. and 4.5.2.

9.3 Vitamin A deficiency

Diarrhoea reduces the absorption of, and increases the need for, vitamin A. In areas where bodily stores of vitamin A are often low, young children with acute or persistent diarrhoea can rapidly develop eye lesions of vitamin A deficiency (xerophthalmia) and even become blind. This is especially a problem when diarrhoea occurs during or shortly after measles, or in children who are already malnourished.

In such areas, children with diarrhoea should be examined routinely for corneal clouding and conjunctival lesions (Bitot's spots). If either is present, oral vitamin A should be given at once and again the next day: 200 000 units/dose for age 12 months to 5 years, 100 000 units for age 6 months to 12 months, and 50 000 units for age less than 6 months. Children without eye signs who have severe malnutrition or have had measles within the past month should receive the same treatment. Mothers should also be taught routinely to give their children foods rich in carotene; these include yellow or orange fruits or vegetables, and dark green leafy vegetables. If possible, eggs, liver, or full fat milk should also be given.

10. ANTIMICROBIALS AND DRUGS

10.1 Antimicrobials

Except as listed below, antimicrobial therapy should not be given routinely to children with diarrhoea. Such treatment is ineffective and may be dangerous.

The diseases for which antimicrobials should be given are listed below (the agents of choice for their treatment are presented in Annex 7):

- *Cases of bloody diarrhoea (dysentery).* These should all be treated with an antimicrobial effective for *Shigella* in the area (see section 6.1.). Children with dysentery should *not* be treated routinely for amoebiasis. Guidelines for when to treat for amoebiasis are given in section 6.2.
- Suspected cases of cholera with severe dehydration. These should be treated with an oral antimicrobial effective against *V. cholerae 01 and 0139* in the area (see section 5.3).
- Laboratory proven, symptomatic infection with Giardia duodenalis. Infection with G. duodenalis occurs very frequently and is usually asymptomatic. Treatment for giardiasis should be given only when the child has persistent diarrhoea and cysts or trophozoites of G. duodenalis are seen in the faeces or small bowel fluid. Children with acute diarrhoea should not be treated for giardiasis.

When diarrhoea is associated with another acute infection (e.g. pneumonia, urinary tract infection), that infection also requires specific antimicrobial therapy.

10.2 "Antidiarrhoeal" drugs

These agents, though commonly used, have no practical benefit and are never indicated for the treatment of acute diarrhoea in children. Some of them are dangerous. Products in this category include:

Adsorbents (e.g. kaolin, attapulgite, smectite, activated charcoal, cholestyramine). These drugs are promoted for the treatment of diarrhoea on the basis of their ability to bind and inactivate bacterial toxins or other substances that

cause diarrhoea, and their claim to "protect" the intestinal mucosa. None, however, has proven practical value in the routine treatment of acute diarrhoea in children.

Antimotility drugs (e.g. loperamide hydrochloride, diphenoxylate with atropine, tincture of opium, camphorated tincture of opium, paregoric, codeine). These opiate or opiate like drugs and other inhibitors of intestinal motility may reduce the frequency of stool passage in adults. However, they do not appreciably decrease the volume of stool in young children. Moreover, they can cause severe paralytic ileus, which can be fatal, and they may prolong infection by delaying elimination of the causative organisms. Sedation may occur at usual therapeutic doses and fatal central nervous system toxicity has been reported for some agents. None of these agents should be given to infants or children with diarrhoea.

Bismuth subsalicylate. Bismuth subsalicylate decreases the number of diarrhoea stools and subjective complaints in adults with travellers' diarrhoea. When given every four hours, it is reported to decrease stool output in children with acute diarrhoea by about 30%. This treatment schedule is, however, rarely practical.

Combinations of drugs. Many products combine adsorbents, antimicrobials, antimotility drugs or other agents. Manufacturers may claim that these formulations are appropriate for various diarrhoeal diseases; however, such combinations are irrational and their cost and side effects are substantially higher than for individual drugs. They have *no place* in the treatment of diarrhoea in children.

10.3 Other drugs

Antiemetics. These include drugs such as prochlorperazine and chlorpromazine, which cause sedation that can interfere with ORT. For this reason antiemetics should *never* be given to children with diarrhoea. Moreover, vomiting stops when a child is rehydrated.

Cardiac stimulants. Shock in acute diarrhoeal disease is caused by dehydration and hypovolaemia. Correct treatment is rapid IV infusion of a balanced electrolyte solution. The use of cardiac stimulants and vasoactive drugs (e.g. adrenaline, nicotinamide) is *never* indicated.

Blood or plasma. Blood, plasma or synthetic plasma expanders are *never* indicated for children with dehydration due to diarrhoea. These children require the replacement of lost water and electrolytes. These treatments are used, however, for patients with hypovolaemia due to septic shock.

Steroids. Steroids have no benefit and are never indicated.

Purgatives. These can make diarrhoea and dehydration worse; they should never be used.

11. PREVENTION OF DIARRHOEA

Proper treatment of diarrhoeal diseases is highly effective in preventing death, but has no impact on the incidence of diarrhoea. Health staff working in treatment facilities are well placed to teach family members and motivate them to adopt preventive measures. Mothers of children being treated for diarrhoea are likely to be particularly receptive to such messages. To avoid overloading mothers with information, it is best to emphasize only one or two of the following points, selecting those most appropriate for the particular mother and child.

11.1 Breastfeeding

During the first 6 months of life, infants should be *exclusively* breastfed. This means that the healthy baby should receive breastmilk and *no other foods or fluids*, such as water, teas, juice, cereal drinks, animal milk or formula. Exclusively breastfed babies are much less likely to get diarrhoea or to die from it than are babies who are not breastfed or are partially breastfed. Breastfeeding also protects against the risk of allergy early in life, aids in child spacing and provides protection against infections other than diarrhoea (e.g. pneumonia). Breastfeeding should continue until at least 2 years of age. The best way to establish the practice is to put the baby to the breast immediately after birth and not to give any other fluids.

The advantages of breastfeeding are listed in Table 5. Some or all of them may be explained to mothers using simple language.

If breastfeeding is not possible, cow's milk (modified if given to infants younger than 6 months) or milk formula should be given from a cup. This is possible even with very young infants. Feeding bottles and teats should *not* be used because they are very difficult to clean and easily carry the organisms that cause diarrhoea. Careful instructions should be given on the correct hygienic preparation of milk formula using water that has been boiled briefly before use.

Table 5: Advantages of breastfeeding

1. Breastmilk is a complete food: it provides *all* the nutrients and water needed by a healthy infant during the first 6 months of life and continues to provide about one half of nutrients in the second year of life.

2. The composition of breastmilk is always ideal for the infant; formula or cow's milk may be too dilute (which reduces its nutritional value) or too concentrated (so that it does not provide enough water), and the proportions of different nutrients are not ideal.

3. Breastmilk has immunological properties that protect the infant from infection, especially diarrhoea; these are not present in animal milk or formula.

4. Breastfeeding is clean: it does not require the use of bottles, nipples, water and formula which are easily contaminated with bacteria that can cause diarrhoea.

5. Breastfeeding immediately after delivery encourages the "bonding" of the mother to her infant, which has important emotional benefits for both and helps to secure the child's place within the family.

6. Milk intolerance is very rare in infants who take only breastmilk.

7. Breastfeeding helps with birth spacing: mothers who breastfeed usually have a longer period of infertility after giving birth than do mothers who do not breastfeed.

11.2 Improved feeding practices

Complementary foods should normally be started when a child is 6 months old. These may be started any time after 4 months of age, however, if the child is not growing satisfactorily. Good feeding practices involve selecting nutritious foods and using hygienic practices when preparing them. The choice of complementary foods will depend on local patterns of diet and agriculture, as well as on existing beliefs and practices. In addition to breastmilk (or animal milk), soft mashed foods (e.g. cereals) should be given.. When possible, eggs, meat, fish and fruit should be also given. Other foods, such as well cooked pulses and vegetables, to which some vegetable oil (5-10 ml/serving) has been added, should be given.(see section 4.2).

To encourage exclusive breastfeeding and proper feeding practices, health workers should be instructed in the regular use of growth charts to monitor the weight of children. Before a child with diarrhoea leaves a health facility, his or her weight should be taken and recorded on the child's growth chart (Annex 3).

11.3 Use of safe water

The risk of diarrhoea can be reduced by using the cleanest available water and protecting it from contamination. Families should:

- Collect water from the cleanest available source.
- Not allow bathing, washing, or defecation near the source. Latrines should be located more than 10 metres away and downhill.
- Keep animals away from protected water sources.
- Collect and store water in clean containers; empty and rinse out the containers every day; keep the storage container covered and not allow children or animals to drink from it; remove water with a long handled dipper that is kept especially for the purpose so that hands do not touch the water.

• If fuel is available, boil water used for making food or drinks for young children. Water needs only to be brought to a rolling boil (vigorous or prolonged boiling is unnecessary and wastes fuel).

The *amount* of water available to families has as much impact on the incidence of diarrhoeal diseases as the *quality* of water. This is because larger amounts of water facilitate improved hygiene. If two water sources are available, the highest quality water should be stored separately and used for drinking and preparing food.

11.4 Handwashing

All diarrhoeal disease agents can be spread by hands that have been contaminated by faecal material. The risk of diarrhoea is substantially reduced when family members practice regular handwashing. All family members should wash their hands thoroughly after defecation, after cleaning a child who has defecated, after disposing of a child's stool, before preparing food, and before eating. Good handwashing requires the use of soap or a local substitute, such as ashes or soil, and enough water to rinse the hands thoroughly.

11.5 Food safety

Food can be contaminated by diarrhoeal agents at all stages of production and preparation, including: during the growing period (by use of human fertilisers), in public places such as markets, during preparation at home or in restaurants, and when kept without refrigeration after being prepared.

Individual food safety practices should also be emphasized. Health education for the general population should stress the following key messages concerning the preparation and consumption of food :

- Do not eat raw food, except undamaged fruits and vegetables that are peeled and eaten immediately;
- Wash hands thoroughly with soap after defecation and before preparing or eating food;
- Cook food until it is hot throughout;
- Eat food while it is still hot, or reheat it thoroughly before eating;
- Wash and thoroughly dry all cooking and serving utensils after use;
- Keep cooked food and clean utensils separately from uncooked food and potentially contaminated utensils; and
- Protect food from flies by means of fly screens.

11.6 Use of latrines and safe disposal of stools

An unsanitary environment contributes to the spread of diarrhoeal agents. Because the pathogens that cause diarrhoea are excreted in the stools of an infected person or animal, proper disposal of faeces can help to interrupt the spread of infection. Faecal matter can contaminate water where children play, where mothers wash clothes, and where they collect water for home use. Every family needs access to a clean, functioning latrine. If one is not available, the family should defecate in a designated place and bury the faeces immediately. Stools of young children are especially likely to contain diarrhoeal pathogens; they should be collected soon after defecation and disposed of in a latrine or buried.

11.7 Measles immunization

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

ANNEX 1: IMPORTANT MICROBIAL CAUSES OF ACUTE DIARRHOEA IN INFANTS AND CHILDREN

AGENT	INCIDENCE	PATHOGENESIS	COMMENTS
Viruses			
1. Rotavirus	Rotavirus is responsible for 15-25% of diarrhoea episodes in children aged 6-24 months visiting treatment facilities but for only 5-10% of cases in the same age group in the community. Prevalence is worldwide and spread is by faecal/oral transmission or possibly by airborne droplets Peak incidence of diseases is in cold or dry seasons.	Rotavirus causes patchy damage to the epithelium of the small intestine, resulting in the blunting of the villi. There is some reduction in the activity of lactase and other dissacharidases, resulting in reduced absorption of carbohydrates, but this is usually of no clinical significance. The intestinal morphology and absorptive capacity return to normal within 2-3 weeks.	Rotavirus causes watery diarrhoea with vomiting and low grade fever (less than 101 °F). Illness ranges from asymptomatic infection to acute dehydrating diarrhoea that may lead to death. Five serotypes of rotavirus are epidemiologically important.
Bacteria			
1. Escherichia coli	<i>E. coli</i> cause up to one quarter of all diarrhoea in developing countries. Transmission usually occurs through contaminated food (especially weaning foods) and water. ETEC are the major cause	Two important virulent	Five groups of <i>E. coli</i> are recognised: enterotoxigenic, localised- adherent, diffuse-adherent, enteroinvasive and enterohaemorrhagic.
a.Enterotoxigenic <i>E. coli</i> (ETEC)	of acute watery diarrhoea in children and adults in developing countries, especially during the warm, wet season.	1 wo important virulent factors of ETEC are: (1) colonisation factors that allow ETEC to adhere to enterocytes of the small bowel, and (2) enterotoxins. ETEC produce heat-labile (LT) and/or heat stable (ST) enterotoxins that cause secretion of fluid and electrolytes, resulting in watery diarrhoea. ETEC do not destroy the brush border or invade the mucosa	ETEC are the most common cause of diarrhoea in travellers from developed to developing countries. The diarrhoea is self-limited.
b.,Localized-adherent <i>E. coli</i> (LA-EC)	In some urban areas, up to 30% of acute diarrhoea cases in young infants are attributed to LA-EC. Many infections are acquired in hospital nurseries.	LA-EC are detected by patchy adherence to the HeLA cells or by specific gene probes. Entero- adherence and production of a potent cytotoxin are important mechanisms for causing diarrhoea.	The disease is usually self- limited, but can be severe (LA-EC) or result in persistent diarrhoea, particularly in formula-fed infants under 6 months of age.

AGENT	INCIDENCE	PATHOGENESIS	COMMENTS
c. Diffuse-adherent <i>E. coli.</i> (DA-EC).	DA-EC are widespread and appear to cause a small percentage of episodes of acute diarrhoea in young children	DA-EC are detected by typical diffuse adherence to HeLa cells.	
d.Enteroinvasive E. coli (EIEC)	EIEC are uncommon in developing They cause sporadic food-borne outbreaks that affect children and adults. Symptoms of illness are similar to those of shigellosis.	EIEC are similar to Shigella both biochemically and serologically. Like Shigella, EIEC penetrate and multiply within the colonic epithelial cells.	Antimicrobials for Shigella are probably effective, provided countries. strains are susceptible, but efficacy has not been established in controlled studies.
e. Enterohaemorrhagic <i>E. coli</i> (EHEC)	EHEC are found in Europe and in parts of North and South America, where outbreaks may be caused by undercooked meat. Recent outbreaks in southern Africa were traced to river water contaminated by cattle carcasses.	EHEC produce a Shiga- like toxin that may be responsible for oedema and diffuse bleeding in the colon, as well as the haemolytic-uraemic syndrome that sometimes develops in children.	Illness is characterized by acute onset of cramps, absent or low-grade fever, and watery diarrhoea that may rapidly become bloody. Type O157:H7 is the most common serotype associated with haemolytic-uraemic syndrome.
2. Shigella	Shigella cause 10-15% of acute diarrhoeas in children under 5 years and are the most common cause of bloody diarrhoea in children. Spread occurs by person-to-person contact since the infectious dose is low (10 to100 organisms). Food borne and waterborne transmission also occurs. Peak incidence is in warmer seasons.	Shigella invade and multiply within colonic epithelial cells, causing cell death and mucosal ulcers. Shigella occasionally invade the bloodstream. The virulence factors include: a smooth lipopolysaccharide cell-wall antigen, antigens that promote cell invasion, and Shiga toxin which is cytotoxic, neurotoxic and perhaps also causes watery diarrhoea.	Shigella are subdivided into 4 serogroups: S. flexneri - the most common serogroup in developing countries; S. sonnei - the most common in developed countries; S. dysenteriae type 1 - which causes epidemics of severe disease with high mortality; S. boydii is less common. Shigella infection may cause fever and watery diarrhoea, or dysentery with fever, abdominal cramps, and tenesmus, and frequent small, bloody, mucoid stools with many leukocytes. Antibiotic resistance is frequent Shigellosis is particularly severe in malnourished and non-breastfed infants.

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AGENT	INCIDENCE	PATHOGENESIS	COMMENTS
3. Campylobacter jejuni	<i>C. jejuni</i> cause 5-15% of diarrhoea in infants worldwide, but because it is also found in many without diarrhoea, the true proportion of cases due to <i>C. jejuni</i> is not known In developing countries most children acquire immunity during the first year of life; the pathogen is frequently found in stools of healthy older children. Spread is by chickens and other animals.	<i>C. jejuni</i> probably produce diarrhoea by invasion of the ileum and the large intestine. Two types of toxin are produced: a cytotoxin and a heat-labile enterotoxin.	Diarrhoea may be watery but in one-third of cases dysenteric stools appear after a day or two. Vomiting is not common and fever is usually low.
4. <i>Vibrio cholerae</i> O1 and O139	Cholera is endemic in many countries of Africa, Asia and Latin America, where epidemics often occur annually, usually during the hot, wet season. In such areas cholera occurs most often in children 2-9 years of age, and many cases are severe. In newly-affected areas, adults are also affected. Both contaminated water and food can transmit cholera; person-to-person spread is much less common.	<i>V. cholerae</i> adhere to and multiply on the mucosa of the small intestine where they produce an enterotoxin which causes the diarrhoea. Cholera toxin is closely related to the heat-labile toxin (LT) of ETEC.	Cholera is caused by <i>V.</i> <i>cholerae</i> O1 and O139. <i>V.</i> <i>cholerae</i> O1 has two biotypes (El Tor and classical) and two serotypes (Ogawa, Inaba). Biotyping and serotyping are not important for treatment and control. Tetracycline-resistant strains of <i>V. cholerae</i> O1 have occurred in many countries;
5. Salmonella (non-typhoid)	Salmonella cause 1-5% of gastroenteritis cases in most developing countries. Infection usually results from ingestion of contaminated animal products.	Salmonella invade the ileal epithelium. An enterotoxin causes watery diarrhoea. When mucosal damage occurs, diarrhoea may be bloody. Bacteraemia may occur and can lead to localized infection in other tissues, such as bone and meninges.	There are over 2000 serotypes, about 6-10 of which account for most episodes of salmonella gastroenteritis in man. <i>Salmonella</i> usually cause acute watery diarrhoea with nausea, cramps and fever. Antimicrobial therapy may prolong shedding of the pathogen in the stool. Strains resistant to ampicillin, chloramphenicol and cotrimoxazole are now found worldwide.

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ACENT	INCIDENCE	DATHOGENESIS	COMMENTS
Protozog	INCIDENCE	FAIIOOENESIS	COMMENTS
1. Giardia duodenalis	<i>G. duodenalis</i> has a worldwide distribution, the prevalence of infection in young children approaching 100% in some areas. Children aged 1-5 years are most commonly infected.	<i>G. duodenalis</i> infects the small bowel; the pathogenic mechanism is unclear. Flattening of the intestinal epithelium is seen in severe cases. <i>Giardia</i> infections are foodborne, waterborne, or spread by faecal-oral route; the latter occurs particularly in children living in crowded circumstances or attending day-care centres.	<i>Giardia</i> can cause acute or persistent diarrhoea, sometimes malabsorption, with fatty stools, abdominal pain and bloating. However, the vast majority of infections are asymptomatic. This makes it very difficult to determine when <i>Giardia</i> is actually the cause of a diarrhoeal episode.
2. Entamoeba histolytica	Prevalence rates of <i>E.</i> <i>histolytica</i> infection vary widely but its distribution is worldwide. The incidence of disease increases with age, being highest in adult males.	<i>E. histolytica</i> invades the mucosa of the large intestine, where it is thought to elaborate neurohumoral substances that cause intestinal secretion and damage, resulting in an inflammatory type of diarrhoea.	At least 90% of infections are asymptomatic, being caused by strains of <i>E</i> . <i>histolytica</i> that are non- pathogenic; they should not be treated. The diagnosis of invasive disease requires identification of haematophageous trophozoites in faeces or colonic ulcers. Symptomatic amoebiasis ranges from persistent mild diarrhoea to fulminant dysentery to liver abscess.
3. Cryptosporidium	In developing countries, cryptosporidia may account for5-15% of childhood diarrhoea. Cryptosporidia are transmitted by the faecal- oral route.	Cryptosporidia attach to the microvillous surface of enterocytes and produce mucosal damage, which causes malabsorption and fluid secretion.	Illness is characterized by acute watery diarrhoea. Persistent diarrhoea occurs in severely malnourished or immuno-suppressed children and adults, particularly those with acquired immuno- deficiency syndrome (AIDS). However, diarrhoea due to <i>Cryptosporidium</i> is self- limited in persons who are not immuno-deficients

ANNEX 2: ORAL AND INTRAVENOUS REHYDRATION SOLUTIONS

1. ORS solution

For more than 25 years WHO and UNICEF have recommended a single formulation of glucose-based ORS to prevent or treat dehydration from diarrhoea irrespective of the cause or age group affected. This product has contributed substantially to the dramatic global reduction in mortality from diarrhoeal disease during this period. Despite this success, research to develop an "improved" ORS has continued. This would be an ORS that would be at least as safe and effective as standard ORS for preventing or treating dehydration from all types of diarrhoea, but would, in addition, reduce stool output or have other important clinical benefits. One approach has been to reduce the osmolarity of ORS solution to avoid possible adverse effects of hypertonicity on net fluid absorption. This was done by reducing the solution's glucose and salt (NaCl) concentrations.

The studies¹³ that evaluated this approach showed that the efficacy of ORS solution for treatment of children with acute non-cholera diarrhoea was improved by reducing the sodium concentration to 75 mEq/l, the glucose concentration to 75 mmol/l, and the total osmolarity to 245 mOsm/l. The need for unscheduled supplemental IV therapy in children given this solution was reduced by 33% when compared with standard ORS (311 mOsm/l). In a combined analysis of this study and studies with other reduced osmolarity ORS solutions (osmolarity 210-268 mOsm/l, sodium 50-75 mEq/l) stool output was also reduced by about 20% and the incidence of vomiting by about 30%. The 245 mOsm/l solution also appeared to be as safe and at least as effective as standard ORS for use in children with cholera.

Based on the greater efficacy of reduced osmolarity ORS solution, especially for children with acute, non-cholera diarrhoea, WHO and UNICEF now recommend that countries use and manufacture the following formulation in place of the previously recommended standard ORS solution.

Reduced osmolarity ORS	grams/litre	Reduced osmolarity ORS	mmol/litre
Sodium chloride	2.6	Sodium	75
Glucose, anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Glucose, anhydrous	75
Trisodium citrate, dihydrate	2.9	Potassium	20
		Citrate	10
		Total Osmolarity	245

Table A: Composition by weight and molar concentrations of reduced (low) osmolarity ORS solution.

When prepared and given correctly, ORS solution provides sufficient water and electrolytes to correct the deficits associated with acute diarrhoea. Potassium is provided to replace the large potassium losses associated with acute diarrhoea, especially in infants, thus preventing serious hypokalaemia. Citrate is provided to prevent or correct base deficit acidosis. Glucose is essential because, when it is absorbed, it promotes the absorption of sodium and water in the small intestine. This is true irrespective of the cause of the diarrhoea. Without glucose, ORS solution would be ineffective.

2. Solutions for intravenous infusion

A number of solutions are available for IV infusion. Most, however, do not contain appropriate amounts of the electrolytes required to correct the deficits associated with acute diarrhoea. Early provision of ORS solution and early resumption of feeding help to ensure adequate electrolyte replacement. Table C shows the composition of IV fluids that can be used.

¹³ Reduced osmolarity oral rehydration salts (ORS) formulation - A report from a meeting of experts jointly organised by UNICEF and WHO - UNICEF House, New York, USA, 18 July 2001 (WHO/FCH/CAH/01.22).

Solution	Cation	s – mmol/l	Anions – mmol/l		
	Na+	K+	Cl-	Lactate ^a	Glucose
Preferred:					
Ringer's lactate	130	4	109	28	0
Ringer's lactate With 5% dextrose	130	4	109	28	278
Dhaka solution	133	13	98	48	140
Half strengthDarrow With 5% glucose	61	17	51	27	278
Acceptable: Normal saline (0.9% NaCl)	154	0	154	0	0
Not acceptable: Glucose (dextrose) solutions	0	0	0	0	278
a Lactate is converted by the liver to dicardonate, which is required for correction of base-deficit acidosis.					

Table B: Ionic composition of intravenous infusion solutions

The relative suitability of each IV solution is discussed below:

Preferred solutions

- Ringer's Lactate Solution (also called Hartmann's Solution for Injection) is the best commercially available solution¹⁴. It supplies an adequate concentration of sodium and sufficient lactate (which is metabolized to bicarbonate) for the correction of acidosis. The concentration of potassium is low and there is no glucose to prevent hypoglycaemia. It can be used in all age groups for the initial treatment of severe dehydration caused by acute diarrhoea of any etiology.
- Ringer's Lactate Solution with 5% dextrose has the added advantage of providing glucose to help prevent hypoglycaemia. If available, it is preferred to Ringer's Lactate Solution without dextrose.

Acceptable solution

• Normal saline (0.9% NaCl; also called isotonic or physiological saline) is often available. It does not contain a base to correct acidosis and does not replace potassium losses.

Unsuitable solution

• Plain glucose (dextrose) solution should *not* be used since it does not contain electrolytes and thus does not correct the electrolyte losses or the acidosis. It does not effectively correct hypovolaemia.

3. IV infusion technique

IV therapy should be given only by trained persons. Several important points are:

• The needles, tubing, bottles and fluid used *must be sterile*. Needles should not be reused unless specifically designed for this purpose, and then *only* after thorough cleaning and re-sterilization.

¹⁴ In some countries special IV solutions are produced for treatment of dehydration caused by diarrhoea. These are preferred, provided they contain at least 90 mmol/L of sodium and provide base and potassium in amounts similar to those in ORS solution. The solution should also contain glucose, which helps to prevent severe hypoglycaemia.

- IV therapy can be given into any convenient vein. The most accessible veins are those in front of the elbow or, in infants, on the side of the scalp. Incision to locate a vein is not necessary and should be avoided. In some cases of very severe dehydration, particularly in adults, simultaneous infusion into two veins may be necessary; one infusion can be stopped when rehydration is well under way.
- It is useful to put a mark on the IV fluid bottle showing the times when the fluid should have fallen to specified levels. This allows easy monitoring of the rate of infusion.

4. Rice-based ORS

a) Clinical evaluation

Studies to evaluate cooked rice as a replacement for glucose in ORS solution began in 1980. Initially, solutions were prepared by cooking rice powder (50-80g/l) for at least 10 minutes and then adding salts in concentrations identical to those of the ORS recommended by WHO. Some studies used "popped" rice in place of cooked rice. An instant, pre-cooked ORS was used in later studies. This was specially developed in close collaboration with a private company in Switzerland.

Other cooked cereal powders have also been evaluated in ORS formulations, including wheat, maize, sorghum and millet. Although fewer studies have been done, results have been similar to those obtained with rice-base ORS. Conclusions for rice-based ORS can, therefore, be applied to these other cereal-base ORS solutions.

A total of 22 randomized clinical trials comparing the safety and efficacy of rice-based ORS solution with that of standard ORS solution have been conducted in adults and children with cholera (seven trials) or in children with acute non-cholera diarrhoea (15 trials). A joint WHO/ICDDR, B Consultative Meeting on ORS Formulation, held in Dhaka from 10 to 12 December 1994, reviewed the results of these trials. On the basis of that review, it was concluded that:

- rice-based ORS is superior to standard ORS for adults and children with cholera, and may 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 non-cholera diarrhoea, especially when food is given shortly, after rehydration, as is recommended to prevent malnutrition.

b) The development of a pre-packaged rice-based ORS

Solutions of rice-based ORS evaluated in Bangladesh and India were made with local rice flour. This entails cooking of the solution, which must be used promptly after it is prepared. For clinical trials, however, a product was needed that did not require cooking and could be produced industrially in sachets, similar to standard ORS. As rice-based products are traditionally produced by baby-food manufacturers, contacts were established with a number of such companies. In 1989, a Swiss company working closely with the CDD Programme of WHO, developed a product that dissolved readily in cold water and remained in suspension over 24 hours without sedimentation of rice particles.

c) The manufacturing process

Manufacture of this product consists of three steps, i) dissolving the salts and rice powder in water, ii) heating of the solution, and iii) drying of the product. Drying can be done in a fluid bed drier or on a rotating cylinder. The test product was produced with the latter system, a technology commonly used for cereals that provides good homogeneity, gelatinisation (and hence good digestibility), and chemically and bacteriological stability. Other technologies exist and it remains with the manufacturer to select the most appropriate one.

d) The production facility

The various technologies suitable for manufacture of rice-based ORS are all commonly used by the food processing industries. Therefore, pharmaceutical companies that currently produce ORS and wish to manufacture rice-based

ORS, will most likely need to adapt their production facility and install the required equipment. As this will involve substantial investment, it may be justified only where regular production is guaranteed.

e) The manufacturing conditions

Pharmaceutical products, such as ORS, should be manufactured only by licensed manufacturers. The production facility and manufacturing process should meet *Good manufacturing practices for pharmaceutical products" (GMP), established by WHO. If rice-based ORS is classified as a drug, its production would be limited to manufacturers who follow such standards.

Manufacturing conditions in the food industry, including quality assurance and control, do not normally meet GMP standards. Even if rice-based ORS were not classified as a drug, it would be important to set minimal production standards, based on GMP; for example, the allocation of a separate room for at least the filling/dosing/sealing process. Moreover, the individual and total substance concentrations of rice-based ORS should be strictly within the limits given in the monograph for ORS (B.P., USP, IP, etc.), regardless of whether a wider range is commonly applied in this sector of industry. In addition, it would be important to ensure strict controls for microbial contamination of the rice and the water used in the manufacturing process.

Specific guidelines for the manufacture of rice-based ORS are not yet available, but most of the necessary information can be found in the document "Oral Rehydraiton Salts, Planning, establishment and operation of production facilities" (WHO/CDD/SER/85.8).

f) The classification of rice-based ORS

The ORS formulation recommended by UNICEF and WHO is classified as a drug and considered as such by local drug administrations worldwide, except in the USA, where it is classified as a "medical-food". Given that the formulation of rice-based ORS contains the same individual and total substance concentrations for the various salts (in mmol/l), it would seem appropriate to accept it as an alternative formulation. So far, however, neither UNICEF nor WHO has taken a formal decision on this point. Some of the reasons are given below.

As rice is a natural organic product, it is normal to find varying compositions, the presence of impurities, and infestations with insect larvae. It is likely that microbial growth may develop if the rice or the rice flour is stored, particularly in hot and humid ambient conditions. It is also possible that the rice has been exposed to pollutants in air or chemicals and therefore contains undesired heavy metals, pesticides, etc. (the maximum pesticide residue limits are given in the CODEX ALIMENTARIUS, Supplement 1 of Volume 2). Moreover, rice often is chemically treated against oxidation after harvest in order to prevent its becoming rancid. The undesired residues are neither removed nor eliminated during the process of milling, except in cases where rice or rice flour is specially treated or purified (by heat, gas, radiation, etc.)

Rice of rice flower in its natural form is not normally used in pharmaceutical preparations and relevant quality standards therefore not available. It is used, however, in the form of starch, for which applicable quality criteria are established. The quality of rice used in food specialities must comply with specifications or standards established by the national Food and Drug Administration /(FDA). These are normally based on guidelines prepared by the Food and Agriculture Organization of the United Nations (FAO). A draft codex standard for rice is included in ALIFORM 95/29, Appendix III.

g) The stability of rice-based ORS

After some time and under certain conditions, rice with a high content of fat can become rancid. For this reason, the theoretical shelf life of rice-based ORS is estimated at around one year, similar to infant/baby food products containing rice. A crucial condition, however, is hermetic packing. In order to ensure absolute protection against humidity and contamination, an appropriate quality of aluminium laminate must be selected. Polyethylene bags should be considered only when the product is prepared for immediate use.

h) The packing of rice-based ORS

Rice-based ORS has a rather low density (high voluminosity) and therefore requires a much larger sachet than standard ORS. The size of sachet to pack a dose for one litre cannot normally be handled on automatic packing machines in food industries. For this reason rice-based ORS used by WHO in clinical trials was packed in doses for

500 ml only. This quantity still required a pouch size of 125x165 mm, or four times more packaging material than for standard ORS. The need for more packaging material is an important factor in the increased cost of the final product.

An adaptation/change of a national dose of ORS (e.g. from a one-litre dose to a dose for 500 ml) has major operational and programmatic implications. Prior to any change in package size, it is therefore important to discuss such a step carefully with the local authorities or the national CDD Programme manager.

i) The cost of rice-based ORS

The price of rice-based ORS, supplied in 30 kg lots for the WHO's clinical trials, was US\$2.10 per kg, or approximately US\$0.13 for a dose of 57.9 g, sufficient for a one-litre solution. Produced on a larger scale, a packet for 500 ml would cost around US\$ 0.10, or about US\$ 0.20 for one litre of solution. This is three times the price of standard ORS (US\$ 0.07 for one litre).

ANNEX 3: GROWTH CHART

An example of a growth chart that can be used for plotting the changes in body weight of an infant or young child is shown below. As maintenance of good nutrition is important in the prevention of diarrhoea, an episode of diarrhoea is an excellent time to start using a growth chart, if one is not already being used.

The value of a growth chart is not to determine the nutritional status of a child at a particular time. Rather, its principal use should be to monitor *growth over time* by measuring changes in weight (an example of a child's growth curve is shown). The infant or young child should be weighed at regular intervals and each weight entered on the chart in the vertical column corresponding to the child's age. If the direction of the line joining successive weights is upwards and parallel to the solid lines (arrows A and C on the chart), the child is growing satisfactorily. A horizontal or downwards direction of the line (arrow B) is a sign of poor growth resulting from inadequate nutrition and/or illness. These patterns are especially helpful in the first year of life; in older children slight fluctuations in growth normally occur without signalling danger.

The two curved lines that run across the chart show the *shape* of normal growth curves. The growth curves of most healthy children will lie between these lines or above the upper line. If a child's weight is much below the lower reference line there is reason for concern. However, even in this case it is the direction of the child's growth curve that is most important.



ANNEX 4: USING MIDARM CIRCUMFERENCE TO DETECT MALNUTRITION

When a child is about 1 year old, there should be quite a lot of fat under the skin of the arms. When the child is 5 years old, there is much less fat and more muscle. For this reason, the distance around the upper arm of a well-nourished child remains almost the same between the ages of 1 and 5 years. If a child is malnourished, however, this distance is reduced and the arm becomes thin. This is due to a reduction in muscle and fat. By placing a special measuring tape around the middle of the upper arm one can determine whether a child between the ages of 1 and 5 is malnourished or not.

The measuring strip has three colours and looks like this:



The strip must be made from material that *does not stretch* and the markings on the strip must be placed accurately. To use the strip:

Put the strip around the mid-point of the upper arm of the child with the elbow extended, pull the two ends firmly, and see which colour is touched by the 0 cm mark on the strip.

- if the green part is touched, the child is *well nourished*.
- If the yellow part is touched, the child is *moderately malnourished*.
- If the red part is touched, the child is *severely malnourished*.

This method is useful for *detecting* malnutrition and does not require a scale or knowledge of a child's age. However, it is *not* suitable for monitoring to determine whether a child's nutrition is improving or becoming worse. This is because it detects only large changes in a child's nutritional condition. The method also is *not* suitable for evaluating infants below 6 months of age.



ANNEX 5: COMPARAISON OF PREVIOUS AND CURRENT CLASSIFICATIONS OF DEHYDRATION CAUSED BY DIARRHOEA



ANNEX 6: HOW TO HELP A MOTHER TO RELACTATE¹⁵.

Explain why it would help her baby to breastfeed exclusively, and what she needs to do to increase her breastmilk supply. Explain that it takes patience and perseverance.

- Build her confidence. Help her to feel that she can produce enough breastmilk for her baby. Try to see her and talk to her often *at least twice a day*.
- Make sure that she has enough to eat and drink.
- Encourage her to rest more, and to try to relax when she breastfeeds.
- Explain that she should *keep her baby near her*, give him plenty of skin-to-skin contact, and do as much as possible for him herself. Grandmothers can help if they take over other responsibilities but they should not care for the baby at this time. Later they can do so again.
- Explain that the most important thing is to *let her baby suckle more*, at least 10 times in 24 hours, more if he is willing:
 - she can offer her breast every two hours;
 - she should let him suckle whenever he seems interested;
 - she should let him suckle longer than before at each breast;
 - she should keep him with her and breastfeed at night;
 - sometimes it is easiest to get a baby to suckle when he is sleepy.
- Discuss how to give other milk feeds, while she waits for her breastmilk to flow, and how to reduce the other milk as her milk increases.
- Show her how to give the other feeds from a cup, not from a bottle. She should not use a pacifier.
- If her baby refuses to suckle on an `empty' breast, help her to find a way to give the baby milk while he is suckling. For example, with a dropper or a syringe.
- For the first day or two, she should give the full amount of artificial feed for a baby of his weight or the same amount that he has been having before. As soon as her breastmilk begins to flow, she can start to reduce the daily total by 30-60 ml each day.
- Check the baby's weight gain and urine output, to make sure that he is getting enough milk.
 if he is not getting enough, do not reduce the artificial feed for a few days;
 if necessary, increase the amount of artificial milk for a day or two. Some women can decrease the amount by more than 30-60 ml each day.
- If a baby has been breastfeeding sometimes, the breastmilk supply increases in a few days. If a baby has stopped breastfeeding, it may take 1-2 weeks or more before much breastmilk comes.

¹⁵ Reference: *Helping mothers to breastfeed* by F. Savage King. Revised edition 1992. African Medical and Research Foundation (AMREF), Box 30125, Nairobi, Kenya. Indian adaptation by R.K. Anand, ACASH, P.O. Box 2498, Bombay 400002)

ANNEX 7: ANTIMICROBIALS USED TO TREAT SPECIFIC CAUSES OF DIARRHOEA

Cause	Antibiotic(s) of choice ^(a)		Alternative(s)		
Cholera ^{b,c}	Doxycycline		Erythromycin		
	Adults:	300 mg once	Children:	12.5 mg/kg 4 times a day x 3 days	
	Tetracycline	or	Adults:	250 mg 4 times a day x 3 days	
	Children:	12.5 mg/kg 4 times a day x 3 days			
	Adults:	500 mg 4 times a day x 3 days			
Shigella dysentery ^b	Ciprofloxaci	Ciprofloxacin			
	Children:	15 mg/kg 2 times a day x 3 days	Children:	20 mg/kg 4 times a day x 5 days	
	Adults:	500 mg 2 times a day x 3 days	Adults:	400 mg 4 times a day x 5 days	
			Ceftriaxone Children:	50-100 mg/kg once a day IM x 2 to 5 day	
Amoebiasis	Metronidazo	le		· · ·	
	Children:	10 mg/kg 3 times a day x 5 days (10 days for severe disease)			
	Adults:	750 mg 3 times a day x 5 days (10 days for severe disease)			
Giardiasis	Metronidazo	le ^d			
	Children:	5 mg/kg 3 times a day x 5 days			
	Adults:	250 mg 3 times a day x 5 days			

^a 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.

^b Selection of an antimicrobial should be based on sensitivity patterns of strains of *Vibrio cholerae* O1 or O139, or *Shigella* recently isolated in the area.

^c An antimicrobial is recommended for patients older than 2 years with suspected cholera and severe dehydration.

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

ANNEX 8: DIARRHOEA TREATMENT CHART





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