

Recommendations for clinical management of cholera

Washington, D.C., 4 November 2010

These guidelines will be reviewed and may be modified if new evidence comes to light or there are changes in the sensitivity profile of the pathogen.

Description of suspected cases of diarrhea caused by *Vibrio cholerae* O:1

These cases are characterized by the abrupt onset of painless watery diarrhea, usually without fever, that can rapidly become voluminous and is often followed by vomiting. If diarrhea continues, generalized cramps and oliguria can appear. This is the most severe manifestation and if untreated, can cause death. Approximately, 5% of the infected patients will develop this severe clinical form. Twenty percent of the patients attending health care centers will present watery diarrhea and signs of dehydration.

The majority of *V. cholerae* O:1 infections are asymptomatic, and moderate diarrhea from *V. cholerae* infection may be indistinguishable from other causes of gastroenteritis.

The “dry” form of the disease is infrequent and difficult to diagnose, because there is little stool output, since the fluids have accumulated in the intestinal lumen.

Cholera is not transmitted from person to person; its transmission is fecal-oral, and it is acquired by ingestion of contaminated water or food. In addition to the standard precautions, contact precautions must be observed when treating children in diapers or people who are incontinent.

Table 1- Summary of main clinical manifestations

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| <ul style="list-style-type: none">▪ Incubation period: 24-48 hours, but can vary from 5 hours to 5 days.▪ Diarrhea and vomiting may be accompanied by colic (or abdominal cramps).▪ Fever is typically absent.▪ Diarrhea is characteristically watery.▪ 5% of cases present severe symptoms, with dehydration and manifestations of hypovolemia. These cases can prove fatal within hours if they do not receive timely and appropriate treatment. |
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Recommendations

1. Recommendations for triage
2. Clinical assessment: hydration status
3. Rehydration
4. Antibiotic treatment

1. Recommendations for triage

The main objective of triage is to prioritize care for seriously ill patients and prevent suspected cases from coming into contact with non-infected patients as quickly as possible. It is therefore recommended that a different entrance to the health facility be set aside for patients with diarrhea.

If this is not feasible, the triage point should be as close as possible to the entrance and suspected patients should be directed to separate wards.

The triage wards should have sanitary facilities and safe water in order to guarantee proper excreta disposal, hand hygiene, and the cleanliness of the environment.

The treatment of cholera patients should be done urgently, mild and moderate cases can be treated in local rehydration points where the clinical assessment and full triage are performed. Therefore, patient transportation to other centers should be prevented as possible. Conditioning beds or chairs locally to ensure efficient hygiene should be considered.

2. Clinical assessment: hydration status

Assessment of patients' hydration status is based on the presence of the symptoms and signs outlined in Table 2. The presence of **one** of these signs or symptoms immediately classifies the patient as a more severe case.

All the moderate and severe patients require close monitoring, but patients at the extreme ages of life, especially children under 18 months, require meticulous observation and immediate measures if their condition worsens. These patients must be prioritized in triage.

Table 2. Classification of dehydration

<p>Severe dehydration</p> <ul style="list-style-type: none">○ Lethargic, unconscious○ Incapable of drinking or nursing (infants)○ Weak radial pulse○ Skin pinch goes back very slowly○ Decrease of the urine (oliguria) <p>Moderate dehydration</p> <ul style="list-style-type: none">- Sunken eyes with ocular hypotony- Absence of tears (only in children)- Dryness of the oral mucosa, tongue, and mucous membrane- Intense thirst; drinks eagerly- Skin pinch goes back slowly <p>No signs of dehydration</p> <ul style="list-style-type: none">- None of the above.
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3. Rehydration

This is the essential component of treatment, whose object is to replenish the water and electrolytes lost through diarrhea and vomiting.

Oral replenishment is preferred, with intravenous replenishment reserved for the rehydration of patients with severe dehydration or who eliminate more than 10-20 mL/kg/h. Refer to table 3 for guiding the rehydration.

For treatment at home, patients or caregivers should be told how to prepare the oral solution and the necessary hygiene measures. Clear explanations must be provided on the warning signs or symptoms that would require a return to the health facility. See Annex for details about home care.

Table 3– Rehydration

In the case of breastfeeding infants, this should always be maintained.

Dehydration status	Treatment	
Mild ¹	<p>Oral rehydration salts, at home.</p> <p><i>Practical advice</i></p> <ul style="list-style-type: none"> - Liquids should be administered in small amounts frequently (each 15-30 minutes) - For children over 14 years old and adults: ensure at least 2 liters per day and add one glass (200 ml) per each bowel movement <p><i>Refer to Annex for further information</i></p>	<p>Children less than 2 years old: 50-100 ml of oral rehydration solution (ORS), after each evacuation, providing a volume similar to the assessed fluid loss (gastrointestinal and urinary).</p> <p>Children between 1 and 14 years old: 100-200 ml of oral rehydration solution (ORS), after each evacuation, providing a volume similar to the assessed fluid loss (gastrointestinal and urinary).</p> <p>Children over 14 years old and adults: drink the amount of ORS needed, ingesting a volume similar to the assessed fluid loss (gastrointestinal and urinary); up to two liters daily.</p>
Moderate ¹	<p>Oral rehydration salts and close clinical monitoring, especially in children under 18 months of age.</p> <p><i>Practical advice</i></p> <ul style="list-style-type: none"> - It is recommended that the patient be sitting up during treatment. - If the taste of the solution causes nausea: oral rehydration via nasogastric tube. 	<p>Administer within first 4 hours:</p> <p>Children less than 4 months (less than 5 kg): 200-400 ml</p> <p>Children 4 to 11 months (5 to 7.9 kg): 400-600 ml</p> <p>Children 13 to 23 months (8 to 10.9 kg): 600-800 ml</p> <p>Children 2 to 4 years (11 to 15.9kg): 800-1200 ml</p> <p>Children 5 to 14 years (16 to 29.9 kg): 1200-2200 ml</p> <p>Children over 15 years and adults (30 kg or more): 2200-4000 ml</p>

¹ Based on WHO, First steps for managing an outbreak of acute diarrhea, leaflet. OMS, Geneva, 2004. http://www.who.int/topics/cholera/publications/en/first_steps.pdf

<p>Severe²</p>	<p>Rehydrate in two phases:</p> <p>1. Intravenous rehydration</p> <p><i>Practical advice</i></p> <ul style="list-style-type: none"> - Absence of or weak radial pulse indicates a life-threatening emergency. Two or more lines should be installed in order to reach the necessary perfusion speed. Solutions may be pumped into the patient. As soon as radial pulse is palpable, the perfusion can be adjusted to the guideline. - Lactated Ringer's solution is the first option. In an emergency situation, if it is not available, isotonic saline solution (CINa 0.9%) can be used. <p><u>NEVER USE GLUCOSE SOLUTION</u></p> <p>2. Oral rehydration</p> <p><i>Practical advice</i></p> <ul style="list-style-type: none"> - Sit the patient, supporting the arms on a table, at the beginning of the oral rehydration. This keeps the patient alert and improves the oral tolerance. <p style="text-align: center;">Closely monitor fluid balance during this phase in order to guarantee sufficient replenishment of volume. If this is not done, the patient is at risk of developing renal failure.</p>	<p>1. Intravenous rehydration (2-4 h):</p> <p>Intravenous lactated Ringer's solution is recommended at the following perfusion rate:</p> <p>1st hour: 50 ml/ kg 2nd hour: 25 ml/ kg 3rd hour: 25 ml/ kg</p> <p>Clinical assessment should be used to determine whether to continue intravenous rehydration.</p> <p>Closely monitor radial pulse or capillary nail refill³ time to assess the dehydration. If the pulse is weak or the capillary perfusion is greater than 2 seconds, increase the speed of perfusion</p> <p>2. Oral rehydration:</p> <p>Start oral rehydration as soon as the patient is able to drink. Follow the guidelines for moderate dehydration, always adapting to the volume of fluid loss.</p>
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It is extremely important to keep a written record of fluid loss and intake in order to adjust the administration of fluids to patients.

² Based on: Luis Suárez Ognio. *Protocolo de Vigilancia Epidemiológica de Cólera*. Oficina General de Epidemiología, Ministerio de Salud de Peru.

³ **Capillary Nail Refill Test:** A pressure is applied on the nail bed until this becomes white. Once the tissue has paled, pressure is removed. While the patient sustains the hand above of the heart, the health professional measures the time that it leads him to the blood to return to the tissue, indicated by the return of the pink color to the nail. This time has to be less than 2 seconds. If it is longer, indicates severe dehydration or shock.

Zinc Supplements

The use of zinc supplements reduces the duration and severity of diarrhea in children, whatever the infectious etiology. Supplement should be started at the beginning of the symptoms.

Recommended doses and duration⁴

For children below 6 months of age: 10 mg daily zinc supplement for 10 days.

For children 6 months to 5 years of age: 20mg daily zinc supplement for 10 days.

Criteria for hospital discharge

After receiving therapy of adequate hydration, patients that fulfill these three criteria can be discharged of the hospital:

1. Adequate oral intake
2. Normal urinary flow (40-50 cc by hour)
3. Maximum diarrhea flow of 400 cc per hour

4. Antibiotic treatment

In addition to rehydration, antibiotic treatment is recommended. Antimicrobial therapy is useful for (a) prompt eradication of the vibrio, (b) diminish the duration of diarrhea, and (c) decrease the fluid loss. Antibiotics should be administered to moderate or severe cases.

The drug sensitivity test of the strains isolated to date in Haiti confirmed the resistance to trimethoprim–sulfamethoxazole, furazolidone, nalidixic acid and streptomycin. Based upon this information, the recommended antibiotics are listed in Table 3.

These recommendations are subject to review as new evidence develops or the sensitivity of the pathogen changes.

The antibiotic selection should be made for each individual case according to clinical criterion and the available medications.

These recommendations should be adapted to local circumstances when national guidelines are developed.

⁴ WHO, Cholera outbreak: assessing the outbreak response and improving preparedness WHO/CDS/CPE/ZFK/2004.4
http://www.who.int/topics/cholera/publications/cholera_outbreak/en/index.html

Table 4–Antibiotic Treatment

	Option 1	Option 2
Adults	Doxycycline, 300 mg po single dose	Ciprofloxacin, 1g po single dose OR azithromycin, 1g po single dose.
Pregnant Women	Erythromycin 500 mg/ 6 hours for 3 days OR azithromycin ⁵ , 1g po single dose	---
Children over 3 year, who can swallow tablets	Erythromycin 12.5 mg/kg/ 6 hours for 3 days. OR azithromycin, 20 mg/kg, in a single dose, without exceeding 1 g	Ciprofloxacin, suspension or tablets, 20 mg/kg, in a single dose OR doxycycline, suspension or tablets, 2-4 mg/kg po in single ⁶ dose.
Children under 3 year, or infants who cannot swallow tablets	Erythromycin, suspension, 12.5 mg/kg/ 6 hours for 3 days OR azithromycin, suspension 20 mg/kg, in a single dose.	Ciprofloxacin, suspension, 20 mg/kg, in a single dose OR doxycycline, syrup, 2-4 mg/kg po in a single dose ² .

⁵ The FDA classifies azythromycin as a Category B drug, which means that there is no confirmed risk in studies with human subjects.

⁶ Although doxycycline has been associated with a low risk of yellowing of the teeth in children, its benefits outweigh its risks.

- ANNEX - RECOMMENDATIONS FOR HOME CARE

How to properly prepare the oral solution

To prepare the oral rehydration solution (ORS), follow the steps below:

- Wash your hands with soap and clean water.
- Pour one liter of clean water (water that has been boiled and cooled) into a clean container.
- Pour all of the ORS powder into the container with the water.
- Mix well, until the powder is completely dissolved.
- The ORS should be kept covered and administered at room temperature.

Warning signs:

Can the child drink or nurse?

Does the child vomit everything it ingests?

Has the child had convulsions?

Is the child lethargic or unconscious?

Source: *Manejo del Paciente con Diarrea, Curso sobre Habilidades de Supervisión, Programa Salud Materno Infantil, Control de las Enfermedades Diarreicas, OPS/OMS, December 1991*

MOTHERS AND CAREGIVERS SHOULD

- Prevent dehydration by administering more of the fluids available in the home, together with ORS solution, at the first sign of cholera
- Keep feeding the child (or increase the frequency of breast-feeding) during the episode and increase feeding afterwards
- Recognize the signs of dehydration and take the child to a health center so that ORS or intravenous electrolyte solution can be administered, and familiarize themselves with other symptoms that require medical treatment (for example, bloody diarrhea)
- Administer 20mg zinc supplements to children daily for 10 to 14 days (administer 10 mg daily to infants under 6 months).

HEALTH CARE PROVIDERS SHOULD

- Advise mothers to begin giving children appropriate fluids already in the home at the first sign of cholera
- Treat dehydration with ORS (or an intravenous electrolyte solution, in cases of severe dehydration)
- Stress the importance of continuing feeding or increasing breast-feeding during the episode and increasing it afterwards
- Administer antibiotics only when indicated (for example, when there is bloody diarrhea or shigellosis) and refrain from administering antidiarrheal drugs
- Administer 20 mg zinc supplements daily for 10 to 14 days (give infants under 6 months 10 mg daily)
- Warn mothers that when their children get cholera again they should give them more fluids than usual and continue to feed them

When treating cases of cholera, health care providers should give mothers or other caregivers two 1-liter packets of ORS for each patient below 10 years and four packets for older patients, to use at home, as well as zinc supplements for 10 to 14 days of treatment. They should also hand out printed materials (with text and illustrations) containing advice for preventing and treating cholera at home.

Source: *Clinical Treatment of Acute Diarrhea, WHO/UNICEF, 2004*