Training-of-Trainees on Cholera Epidemic - Short Course

November 8-9, 2010
Port-au-Prince, Haiti
The Microbe that Causes Cholera
Vibrio cholerae O1
Cholera – The Epidemic Microorganism

Vibrio cholerae

01/0139

Epidemic Strains

Toxigenic
Microbiologic Characterization of *Vibrio cholerae*

- **Vibrio species**
  - **V. cholerae**
    - Biotype: El Tor, Classical
    - Serotype: Inaba, Ogawa
    - Toxin: Toxigenic, Non-toxigenic
  - **V. cholerae** non O1/O139
  - **V. cholerae** O1/O139
    - Toxin: Toxigenic, Non-toxigenic

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*All eight combinations exist*
Pathophysiology of Cholera
Secretory Diarrhea

Watery stool with sodium, potassium, chloride & bicarbonate

Bowel wall → Produces toxin → Attaches → Activates → cAMP → More secretion of chloride → Less absorption of sodium → Water, potassium, & bicarbonate flow into the bowels
The B subunit of the cholera toxin.
Electrolyte Composition of Cholera Stools and of Fluids Recommended for Treatment of Cholera, in mmol/L

<table>
<thead>
<tr>
<th></th>
<th>NA⁺</th>
<th>K⁺</th>
<th>Cl⁻</th>
<th>Base*</th>
<th>Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera stools</td>
<td>135</td>
<td>15</td>
<td>105</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>WHO ORS</td>
<td>90</td>
<td>20</td>
<td>80</td>
<td>10</td>
<td>111</td>
</tr>
<tr>
<td>Ringers lactate</td>
<td>130</td>
<td>4</td>
<td>109</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Normal saline</td>
<td>154</td>
<td>0</td>
<td>154</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Clinical Presentation and Case Management
Clinical Presentation

- Dehydrating diarrheal illness with loss of fluid and electrolytes

- Severe or moderate case
  - Profuse watery diarrhea
  - Vomiting
  - Leg cramps (hypokalemia)

- Symptoms range from asymptomatic infection through mild diarrhea, to severe hypovolemic shock
Spectrum of Illness in Persons Infected with *Vibrio cholerae* O1, Biotype El Tor

- **75%** Asymptomatic infection
- **18%** Moderate illness (outpatient)
- **5%** Severe illness (hospitalized)
- **2%** Mild illness
### Infectious Dose of Toxigenic V. cholerae O1, Biotype El Tor

<table>
<thead>
<tr>
<th>Inoculum</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10^3$, if gastric acid is neutralized</td>
<td>Mild diarrhea</td>
</tr>
<tr>
<td>$10^6$ with food</td>
<td>Severe diarrhea</td>
</tr>
<tr>
<td>&gt; $10^6$ with water</td>
<td>Severe diarrhea</td>
</tr>
</tbody>
</table>
Assessment of Hydration Status
Moderate Dehydration

- Loss of 5-10% of body weight
- Normal blood pressure
- Normal or rapid pulse
- Restless, irritable
- Sunken eyes
- Dry mouth and tongue
- Increased thirst, drinks eagerly
- Skin goes back slowly after skin pinch
- An infant: decreased tears, depressed fontanel
Severe Dehydration

- Loss of $\geq 10\%$ of body weight
- Hypovolemic shock
  - Low blood pressure
  - Rapid, weak or undetectable peripheral pulse
  - Minimal or no urine
- Skin has lost normal turgor ("tenting")
- Mouth and tongue are very dry
- Sunken eyes
- Mental status is dulled
Assessment of Dehydration

- Check pulse
- Examine condition, eyes, thirst, and skin turgor
- Determine status
- Treat
Dehydration Status - Pulse

- Not necessary to count pulse

- Check presence of pulse

- Check strength
  - Strong (beats easily felt)
  - Thready (beats weakly felt)

- Rapid, thready or absent pulse indicates hypovolemic shock
# Treatment According to Dehydration Status

## EXAMINE

<table>
<thead>
<tr>
<th>Status</th>
<th>Symptoms</th>
<th>Skin Pinch Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well, alert</td>
<td>Sunken eyes: No</td>
<td>Skin pinch goes back quickly</td>
</tr>
<tr>
<td>Restless, irritable</td>
<td>Sunken eyes: Yes</td>
<td>Skin pinch goes back slowly</td>
</tr>
<tr>
<td>Lethargic or unconscious</td>
<td>Sunken eyes: Yes</td>
<td>Skin pinch goes back very slowly</td>
</tr>
</tbody>
</table>

## ASSESS

<table>
<thead>
<tr>
<th>Dehydration Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dehydration</td>
</tr>
<tr>
<td>Moderate dehydration</td>
</tr>
<tr>
<td>Severe dehydration</td>
</tr>
</tbody>
</table>

## TREAT

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain hydration</td>
</tr>
<tr>
<td>Oral rehydration</td>
</tr>
<tr>
<td>IV and oral rehydration</td>
</tr>
</tbody>
</table>
Treatment
Rehydration Therapy

- Can reduce mortality to less than 1%

- **Oral therapy:**
  - Oral rehydration salts (ORS) are recommended
  - 80-90% of patients can be treated with ORS
  - Patients requiring IV can soon switch to ORS

- **Intravenous therapy:**
  - Ringers lactate is the recommended IV fluid
  - Normal or ½ normal saline are less effective, but can be used
  - D5W is ineffective, and should not be used
Oral Rehydration Therapy

- Replace estimated losses for older children and adults at 100ml/5 min
- Replace ongoing losses plus 1 liter water daily
- Reassess every 1-2 hours
- May need > 5 liters: Give it!
## Treatment When There is No Dehydration

<table>
<thead>
<tr>
<th>Age</th>
<th>Amount of ORS after each loose stool</th>
<th>ORS quantity needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24 months</td>
<td>100 ml</td>
<td>~ 500 ml/day (1 sachet)*</td>
</tr>
<tr>
<td>2 to 9 years</td>
<td>200 ml</td>
<td>~ 1000 ml/day (1 sachet)*</td>
</tr>
<tr>
<td>≥ 10 years</td>
<td>As much as wanted</td>
<td>~ 2000 ml/day (2 sachets)*</td>
</tr>
</tbody>
</table>
Treatment of Moderate Dehydration

- Provide ORS immediately, according to weight and age (see handout)
- Monitor every hour for first 2 hours
  - Fluid input:
    - Ensure adequate intake of ORS
    - Count number of cups drunk
    - Re-administer 10 minutes after patient vomits
  - Fluid output:
    - Number and nature of stools
    - Vomitus
- Reassess hydration status after 4 hours and treat accordingly (no, moderate, severe)
- Can administer ORS by nasogastric tube
Treatment of Severe Dehydration

- Give intravenous (IV) fluid rapidly until blood pressure normal (3-6 hours)
  - Hang infusion bag high
  - Use 2 intravenous lines if necessary
  - For adults, give a liter in the first 15 minutes
  - Remember, Ringers lactate solution is the best option
  - Use a new IV set for every patient

- Give ORS if patient can drink
  - Only if conscious
  - Do not use oral or nasogastric route if severely hypovolemic or unconscious
Intravenous (IV) Rehydration Therapy of Severe Dehydration

Give IV fluid rapidly until blood pressure normal

> 1 year old

First 30 mins:
30 ml/kg

Every 2.5 hours:
70 ml/kg

≤ 1 year old

First 60 mins:
30 ml/kg

Every 5 hours:
70 ml/kg

200 ml/kg or more may be needed in first 24 hours
Intravenous Rehydration Therapy

- Monitor pulse and stay with patient until strong radial pulse
- Reassess hydration status at 30 minutes, then every 1-2 hours until rehydration is complete
- Check for rapid respiratory rate, a sign of possible overhydration
- Add oral solution as soon as possible
- Discontinue and remove IV when patient is stable and drinking ORS
IV Rehydration: Fluid Management

- **Input**
  - Record liters of IV fluids and cups of ORS administered
  - Mark quantity per hour on each bag
  - Ensure cup and ORS are within reach
  - ORS consumption is easier sitting up, if able

- **Output**
  - Record volume and nature of stool
  - Record presence of urine
Watch for Complications

- **In young children: hypoglycemia**
  - Lethargy and convulsions
  - Early ORS and feeding will prevent
  - Treat with glucose, if available

- **In elderly and young children: pulmonary edema**
  - Cough, rapid breathing while on IV fluids
  - Slow down IV fluids and sit patient up

- **In patients not receiving ORS: hypokalemia**
  - Painful leg cramps
  - Provide ORS
Watch for Complications, cont.

- **In patients with prolonged shock: renal failure (anuria)**
  - Urine output should resume within 6 to 8 hours
  - May require dialysis

- **In pregnant women: miscarriage**
  - Stillbirth and miscarriage common in third trimester with severe cholera
  - Treatment remains the same

- **In persons receiving IV for more than 3 days: infection at site of IV line**
  - Redness, swelling, and pain at IV site
  - Remove IV line and continue with ORS
Signs of Adequate Rehydration

- Skin goes back normally when pinched
- Thirst has subsided
- Urine has been passed
- Pulse is strong
Antimicrobial Therapy

- Antimicrobial therapy reduces
  - Fluid losses
  - Duration of illness
  - Duration of carriage

- Recommended for moderately and severely ill patients, particularly those passing large volumes of stools and all hospitalized patients

- Resistance pattern can change over time

- Not recommended for prophylaxis
Effect of Tetracycline Treatment on Duration of Diarrhea

Mean Duration

Treated: 0.8 days
Control: 1.8 days

Percentage with Continuing Diarrhea

Days After Start of Treatment

Bull WHO (1968) 38: 787-792
## Antimicrobials Recommended by WHO for Treatment of Cholera for Haitian Adults

<table>
<thead>
<tr>
<th>Patient classification</th>
<th>First Choice</th>
<th>Second Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (non-pregnant)</td>
<td>Doxycycline: 300 mg by mouth in 1 dose</td>
<td>Azithromycin: 1 gram in 1 dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tetracycline: 500 mg 4 x/day for 3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erythromycin: 500 mg 4 x/day for 3 days</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Azithromycin: 1 gram in 1 dose</td>
<td>Erythromycin: 500 mg 4 x/day for 3 days</td>
</tr>
</tbody>
</table>
Antimicrobials Recommended by WHO for Treatment of Cholera for Haitian Children

<table>
<thead>
<tr>
<th>Patient classification</th>
<th>First choice</th>
<th>Second choice</th>
</tr>
</thead>
</table>
| Children ≥12 months old and capable of swallowing pills and/or tablets | Azithromycin: 20 mg/kg in one dose  
Erythromycin: 12.5 mg/kg 4 times a day for 3 days  
Doxycycline: 2-4 mg/kg in one dose* | Tetracycline: 12.5 mg/kg 4 times a day for 3 days |
| Children <12 months old and others unable to swallow pills and/or tablets | Azithromycin oral suspension: 20 mg/kg in one dose  
Erythromycin oral suspension: 12.5 mg/kg 4 times a day for 3 days  
Doxycycline oral suspension: 2-4 mg/kg in one dose* | Tetracycline oral suspension: 12.5mg/kg 4 times a day for 3 days |

* Doxycycline is safe for treatment of cholera in children at the recommended dose. The Pan American Health Organization recommends doxycycline as a second-line choice because of limited regional availability and to avoid future overuse in children.
Zinc Supplementation in Children

- Reduces the severity and duration of most childhood diarrhea caused by infection
- Reduces severity and duration of cholera in children by ~10%
- Zinc supplementation (10-20 mg zinc by mouth per day) should be started immediately, if available
Summary of Treatment

- **No dehydration**
  - ORS to maintain hydration

- **Moderate dehydration**
  - ORS to replace losses
  - Consider antibiotics (if hospitalized or still passing large volumes of stool)

- **Severe dehydration**
  - IV Fluids (Ringers lactate)
  - Switch to ORS when tolerated
  - Antibiotics

- **Monitor for treatment complications**

- **Zinc supplementation**
  - All children with diarrhea
Cholera in a Severely Malnourished Child: 
Key Principles

- Typical signs of dehydration are often unreliable
- Children with severe malnutrition are at high risk of complications due heart, kidney, and electrolyte abnormalities
  - Oral rehydration is preferred method
  - IV hydration should be avoided unless shock is present because of a high risk of fluid overload
- Severely malnourished children should be sent to a specialized malnutrition center as soon as they have been stabilized
Assess for Malnutrition

- Is weight-for-height Z-score more than 3 standard deviations below expected?
- Is mid-upper arm circumference <115 mm?
- Is there bilateral edema of legs/feet?
- Are the ribs prominent?
- Is there visible wasting, particularly of gluteal muscles?
Assessment for Dehydration and Shock among Severely Malnourished Children

- **Dehydration is difficult to assess**
  - At baseline, children with marasmus may have poor skin turgor and sunken eyes
  - Children with kwashiorkor may have turgid skin due to edema

**Suspect dehydration if:**
- Current or recent diarrhea
- Thirst (restlessness in an infant)
- Recent appearance of sunken eyes
- Decreased urine output

**Suspect shock if:**
- Child is unresponsive
- Pulses are weak or thready
- Feet or hands are cold
- Urine production has stopped
Treatment of Shock in Severely Malnourished Children

- **IV fluid rate:** 10 mL/kg/h for 2 hours
- **Solution type:**
  - Preferred:
    - Lactated Ringer’s with 5% glucose
    - Half-normal saline with 5% glucose
  - Acceptable:
    - Lactated Ringer’s
- **Every 10 minutes, check for heavy or labored breathing and reassess hydration:**
  - If worse:
    - STOP IV infusion
    - Refer to physician immediately
  - No improvement:
    - Transfuse whole blood or packed red cells at 10mL/kg over 3 hours
    - Feed F-75
  - If improvement:
    - Continue IV at 5 mL/kg/h until rehydrated
    - And/or
    - Begin oral rehydration when child can drink
Oral Rehydration Solutions for Severely Malnourished Children

- ReSoMal (Rehydration Solution for Malnutrition) differs from low-osmolarity ORS. It has:
  - Less sodium
  - More glucose and potassium
  - Trace minerals like zinc and magnesium

- If ReSoMal is not available, low-osmolarity ORS is acceptable
Oral Rehydration Methods in Severely Malnourished Children

- **For children who can drink adequately**
  - Offer ORS/ReSoMal frequently in small sips or by spoon
  - Breastfed children should continue to breastfeed
  - Children may tire quickly and not take enough fluid

- **For children who are alert but cannot drink adequately**
  - Give ORS/ReSoMal by nasogastric tube

- **ORS / ReSoMal dosing:**
  - Goal: total of 70 – 100 mL/kg over 12 hours. Give as:
    - 5 mL/kg every 30 min for 2 hours, then
    - 5 – 10 mL/kg/hour for 4 - 10 hours as needed to complete rehydration
Assessments during Rehydration in Severely Malnourished Children

- Should be done at least hourly due to high risk for cardiac failure and pulmonary edema and to estimate on-going losses

- Stop oral rehydration if signs of cardiac failure develop (increased respiratory rate, engorged jugular veins, increasing edema)

- Rehydration is complete when child is no longer thirsty, urine production has normalized, and other signs of dehydration have resolved
Maintenance Treatment After Dehydration is Corrected in Severely Malnourished Children

- Administer ORS / ReSoMal to replace on-going losses
  - Children < 2 years old: 50 – 100 mL per loose stool
  - Children ≥2 years old: 100 – 200 mL per loose stool

- Administer F-75 formula per WHO recommendations to meet basal fluid and nutritional needs
  - If F-75 is unavailable, feed age-appropriate foods until child can be taken to a specialized center

- If child is breastfed, continue breastfeeding
Assess for and Treat Infection in Severely Malnourished Children

- Concomitant infections are common among severely malnourished children with diarrhea

- While starting rehydration therapies, assess for fever, respiratory compromise, hypothermia, hypoglycemia, and other signs of infection

Treat quickly!
Other Treatments to Begin Within the First 1-2 Days of Care in Severely Malnourished Children

- **Vitamin A, if not given in the previous month:**
  - Children 6 – 12 months old: 100,000 IU by mouth
  - Children ≥12 months old: 200,000 IU by mouth

- **Zinc:**
  - Children < 6 months old: 10 mg by mouth for 10 – 14 days
  - Children ≥ 6 months old: 20 mg by mouth for 10 – 14 days
Disposition of Severely Malnourished Children

- As soon as possible after child is stable, transfer to center specializing in management of malnutrition
Modes of Transmission
Transmission

- By water or food contaminated with *V. cholerae* O1 from:
  - Human feces
  - Environmental reservoir (estuarine environment)

- **NOT** by person-to-person contact
## Documented Vehicles of Cholera Transmission

<table>
<thead>
<tr>
<th><strong>Water:</strong></th>
<th><strong>Seafood:</strong></th>
<th><strong>Others:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Municipal</td>
<td>Raw mussels</td>
<td>Millet gruel</td>
</tr>
<tr>
<td>Shallow wells</td>
<td>Raw oysters</td>
<td>Leftover rice, corn</td>
</tr>
<tr>
<td></td>
<td></td>
<td>porridge, peas</td>
</tr>
<tr>
<td>River water</td>
<td>Raw &quot;concha&quot;</td>
<td>Rice with peanut sauce</td>
</tr>
<tr>
<td>Bottled water</td>
<td>Raw clams</td>
<td>Airline hors d’oeuvres</td>
</tr>
<tr>
<td>Ice</td>
<td>Raw fish</td>
<td>Frozen coconut milk</td>
</tr>
<tr>
<td></td>
<td>Partly dried fish</td>
<td>Raw vegetables</td>
</tr>
<tr>
<td></td>
<td>Undercooked crab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Street-vended squid</td>
<td></td>
</tr>
</tbody>
</table>
Cholera Transmission

“I am not a supporter of the exclusive drinking-water theory. I think that the ways in which cholera can spread in a place are extremely diverse, and that, as almost every place has its own peculiar conditions, which must be thoroughly searched out, the measures which are of use for protecting the particular place from the pestilence must correspond to these conditions.”

Robert Koch

Br Med J (1884) 2:403-407, 453-459
Foodborne Transmission of Cholera: Microbiologic Factors

- Grows rapidly: Moist, alkaline foods held at ambient temperatures are good media

- Fragile organism: Does not tolerate drying, acidity, sunlight or competition

- Produces chitinase: Environmental niche related to copepods, mollusks and crustacea
Growth of *V. cholerae* O1 El Tor in Cooked Rice

Fig. 2. Growth of *V. cholerae* in cooked rice. F4290 (classical) at 22 °C (-----) and 30 °C (○○○); F4292 (eltor) at 22 °C (-----) and 30 °C (□□□).
Growth of *V. cholerae* O1 El Tor in Cooked Mussels

Fig. 1. Growth of *V. cholerae* in cooked mussels. F2618 (classical) at 22 °C (-----), at 30 °C (○—○) and 37 °C (-----); F4292 (eltor) at 22 °C (-----), at 30 °C (□—□) and 37 °C (-----).
Prevention of Cholera
Prevention in the Patient’s Household

- **Education**
  - Drink and use safe water
  - Wash hands with soap and safe water
  - Use latrines or bury your feces; do not defecate in any body of water
  - Cook food thoroughly
  - Clean up safely in kitchen and bathing areas
  - If diarrhea develops, drink ORS and go to clinic quickly

- **Chemoprophylaxis**
  - Not recommended
Advice for Travelers to Areas Affected by Epidemic Cholera

- Do not drink unboiled or untreated water
- Carbonated drinks without ice are safe
- Avoid food and beverages from street vendors
- Avoid raw and undercooked seafood
- Eat foods that are cooked and hot, and fruits you peel yourself

-- Boil it, cook it, peel it, or forget it. --
Cholera Vaccine

- One oral vaccine is commercially available and prequalified by WHO
- Not licensed in the U.S. or Haiti
- Requires a cold chain and two doses 7–14 days apart
- Protective effectiveness 85% for first 6 months, lasts at least two years

Dukoral
  - Manufactured in Sweden
  - Requires 150 ml water and buffer

- Not recommended by WHO for epidemic control
Cholera Vaccine

- **Not recommended for epidemic control**
  - Delay in achieving immunity
    - Immunity begins 1 week after second dose
    - 14-21 days after first dose
  - Major logistical challenges, as it requires
    - Dosing the same people twice
    - Cold chain
    - Clean water
    - Personnel and support

- **Does not prevent carriage**

- **Not recommended for travelers or health care workers**
History and Global Burden of Cholera
Distribution of Cholera, 1817-1950

Adapted from American Geographical Society of New York
Global Spread of Cholera, 1961-1991
Figure 2. Number of countries that reported cholera cases to WHO by region (Africa, Asia, Latin America) and year, 1968–2005. *Includes countries reporting both indigenous and imported cases of cholera. Does not depict countries in Europe or Oceania that reported cases of cholera.
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2010. All rights reserved.
New Epidemic of Cholera in 1992: *Vibrio cholerae* O139

- Immune population got cholera again
- Genetically resembles V. *cholerae* O1, El tor
- New O antigen= mutation in Rfb genes that make O antigen
- Shellfish, foods, water
- No further spread since then

Reference: Tauxe, Chapter 6, Emerging Infections 2, ASM Press, 1998
Cholera in the Americas
Cholera in the Americas, 1973-1995
Cholera in the Western Hemisphere Related to the Latin American Epidemic: Reported Cases 1991-1994

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentine</td>
<td>3522</td>
<td>64</td>
</tr>
<tr>
<td>Bolivie</td>
<td>35310</td>
<td>695</td>
</tr>
<tr>
<td>Brésil</td>
<td>137896</td>
<td>1444</td>
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<tr>
<td>Chili</td>
<td>147</td>
<td>3</td>
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<tr>
<td>Brésil</td>
<td>137896</td>
<td>1444</td>
</tr>
<tr>
<td>Colombie</td>
<td>28334</td>
<td>383</td>
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<tr>
<td>Équateur</td>
<td>86808</td>
<td>993</td>
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<tr>
<td>Guyane française</td>
<td>19</td>
<td>0</td>
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<tr>
<td>Guyane</td>
<td>622</td>
<td>10</td>
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<tr>
<td>Paraguay</td>
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<tr>
<td>Pérou</td>
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<td>Surinam</td>
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<tr>
<td>Vénézuela</td>
<td>3264</td>
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<tr>
<td>Bélize</td>
<td>300</td>
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<tr>
<td>Costa Rica</td>
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<td>Salvador</td>
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<td>Guatémala</td>
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<tr>
<td>Honduras</td>
<td>7660</td>
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<tr>
<td>Mexique</td>
<td>25623</td>
<td>382</td>
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<tr>
<td>Nicaragua</td>
<td>17520</td>
<td>400</td>
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<tr>
<td>Panama</td>
<td>3636</td>
<td>82</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td><strong>1,061,008</strong></td>
<td><strong>9,988</strong></td>
</tr>
</tbody>
</table>
Cholera in Latin America: Risk Factors for Transmission

- **Drinking unboiled water**
  - Large municipal water systems
  - Deficient peripheral distribution
  - Home water storage
  - Water contamination in the home
  - Ice made from untreated water

- **Eating raw and undercooked shellfish**
  - Shrimp, concha, oysters, crabs

- **Eating foods and drinking beverages from street vendors**

- **Eating rice left out for > 3 hours**
Cholera in the Americas: Control Measures

- **Short term: Emergency Interventions**
  - Improve diagnosis, treatment, and surveillance
  - Chlorinate water supplies
  - Educate public
  - Boil water, avoid raw shellfish
  - Identify other control measures by epidemiologic investigations

- **Mid term: Sustainable, cheap control measures**
  - Home water storage vessels
  - Home chlorination of water

- **Long term: “Sanitary Reform”**
  - Maintain and upgrade water systems
  - Build sewage treatment systems
  - Implement shellfish sanitation
Laboratory Diagnosis
Uses of Laboratory Diagnosis of Cholera

- To confirm individual cases in a previously unaffected area
- To monitor antimicrobial resistance patterns
- To define the end of an outbreak
- To support epidemiologic investigations
Testing Recommendations for Haiti: Non-affected Areas

- Test patients with acute watery diarrhea
  - Inform MSPP/DELR and collect stool specimens from up to 10 patients for Rapid Diagnostic Testing (RDT) who meet these criteria
  - Send samples with positive results to the national laboratory immediately for culture confirmation

- If one or more specimens from a previously non-affected location are culture-confirmed for cholera, this area will be considered a “cholera confirmed area”
Testing Recommendations for Haiti: Cholera Confirmed Area

- Once an outbreak is confirmed, the clinical case definition of acute watery diarrhea is sufficient to diagnose

- Only periodic laboratory testing of samples will be needed for antimicrobial sensitivity testing and to confirm when the outbreak has ended
  - The decision will be made by MSPP as to which departments are affected areas
Microbiological Diagnosis

- **Culture of rectal swab or stool specimen**
  - Transport medium: Cary Blair
  - Selective agar: TCBS
    - Thiosulfate
    - Citrate
    - Bile salts
    - Sucrose
  - Takes 2-3 days
Rapid Diagnostic Test (Crystal VC Dipstick)

Rapid Diagnostic Test (RDT) for screening

- Test fresh stools in the field can be read within 15-20 minutes
- Early presumptive diagnosis
- Not definitive
Serologic Diagnosis

- Serologic diagnosis is done in specialized laboratories
  - Acute and convalescent vibriocidal titers
    - Increase in 2 weeks after exposure
    - Decrease in 2 months after exposure
Surveillance in Haiti
Cholera - Haiti

- October 21, 2010 – toxigenic Vibrio cholerae O1, serotype Ogawa, biotype El Tor identified by national lab and confirmed by CDC
- Immunologically naïve and highly vulnerable population
- As of October 27, 2010 - 4,722 confirmed cases and 303 deaths
- Mainly reported from Artibonite Department, but spread to 5 departments including Port-au-Prince
- Preventive measures and appropriate case management is critical to prevent spread and reduce mortality
A case of cholera should be suspected when:
A patient aged 5 years or more develops acute watery diarrhea, with or without vomiting.

A case of cholera is confirmed when:
*Vibrio cholerae* O1 is isolated from any patient with diarrhea.
Surveillance Case Definitions: Haiti, 2010

- **Suspect case**: acute watery diarrhea in a non-affected Department

- **Case**: acute watery diarrhea in an affected Department

- **Affected Department**: a Department where one or more cholera cases have been confirmed by laboratory testing (isolation of V. cholerae O1) that have no history of travel to affected departments in the 5 days before onset.

- Designation of affected and non-affected Departments is ultimately determined by MSPP.
Data Collection and Reporting

- **For ALL health facilities:**
  - Maintain records daily on new number of cases and deaths at health facility
  - It is strongly recommended that each health facility record daily the new number of suspect cholera cases and deaths.
  - Please use the institution report form issued by MSPP
The Ministry of Health has instructed all health centers to use the form illustrated to the right to report suspect cholera cases (all patients with acute, watery diarrhea).

Basic information collected includes number of:

- cases less than 5 years old and greater than 5 years old
- hospitals reporting cholera cases
- cholera deaths at health centers
- cholera deaths in community
Testing Recommendations for Haiti: Non-affected Areas

- Test patients with acute watery diarrhea
  - Inform MSPP/DELR and collect stool specimens from up to 10 patients for Rapid Diagnostic Testing (RDT) who meet these criteria
  - Send samples with positive results to the national laboratory immediately for culture confirmation

- If one or more specimens from a previously non-affected location are culture-confirmed for cholera, this area will be considered a “cholera confirmed area”
Flow of Information

- Health facilities should report surveillance data from the institution report form on acute, watery diarrhea patients to your Unite Communale de Sante or the departmental epidemiologist.

- The Unite Communale de Sante or the departmental epidemiologist will compile the daily number of suspect cases and deaths you have recorded at your CTC and report cumulative numbers of cases and deaths to MSPP.
When to Suspect a Cholera Outbreak

- **Symptoms of moderate or severe cholera:**
  - Profuse, watery diarrhea
  - Vomiting
  - Leg cramps
  - Symptoms of dehydration

- **If there is a local increase in the number of cases with these symptoms, please alert your Unite Communale de Sante or the Departmental epidemiologist immediately.**
Development and Operation of a Cholera Treatment Center (CTC)
Purpose of CTC

- A Cholera Treatment Center is a temporary center for rapid and efficient treatment for patients with cholera
- Cholera patients do not require quarantine
Location

- Health authorities and communities should be involved in the selection of sites and their preparation
- Should provide enough space and resources for adequate treatment
- Should not be close to a water source or any other functioning public structures (e.g. schools, dispensaries, markets)
- Should be in a place where patients can reach it easily (the nearer the patients, the lower the CFR)
  - Options:
    - Existing health facility
    - School
    - Community Hall
    - Other existing building
    - Tents
- If located within an existing health care facility, CTC should be separated and isolated from the rest of the in-patient wards
Planning Considerations

- Drainage
- Accessibility
- Easy to clean
- Ventilation
- Lighting
- Sanitation capabilities
- Hand-washing facilities
- Concrete floor, or plastic sheeting cover if temporary facility
Space Considerations

- 2.5 m² per ward patient
- 2 m² per observation patient
- A 29 m² tent can accommodate 10 patients and attendants
Oral Rehydration Points (ORPs)

- ORPs are satellite stations that reduce pressure on overburdened CTCs

- **Objectives:**
  - Treat patients with oral rehydration salts (ORS)
  - Refer severely dehydrated patients to the CTC

- Run by community health workers who need quick training and regular supplies

- Can have several ORPs for each CTC

- Usually operate 12 hours per day
The design may be adapted to the situation, but **four areas** have to be well delimited in order to limit spread of infection.
Triage at Treatment Center

- **Triage**
  - **No dehydration**: refer to normal dispensary
  - **Some dehydration** = “Moderate Case”:
    admit to Observation Area for oral rehydration treatment
  - **Severe dehydration and/or uncontrollable vomiting** = “Severe Case”:
    admit to Hospitalization Area for immediate IV and oral rehydration.

- **Patients are admitted with no more than 1 attendant (caregiver)**

- **Patients who are admitted are registered (cholera register).**
  - Upon Admission: record patient demographics, presenting signs and symptoms, assessment of dehydration severity, and triage status
  - Upon Exit: record outcome (discharged, died)
Observation Area

- Mild or moderate cases receive oral rehydration therapy in observation where they stay for 6 hours.
- Patients stay in tents or shelters, on mats or benches and will be discharged directly from there.
- Need 2 m² per observation patient
Hospitalization of Severely Dehydrated Patients

- Patients with severe dehydration and/or uncontrollable vomiting must be hospitalized for immediate rehydration.
- Each patient lies on a cholera cot (see next slide) with 1 bucket for stool collection underneath and 1 bucket for vomit beside the bed.
- Can run rope or wire above where severe patients are located with hooks above each patient to hang the IV bag on.
- Patients needing special management (children, elderly, pregnant women) should be grouped.
- 20 patients per ward is recommended.
Pierced Bed or “Cholera Cot”

- A bed with a hole cut out for passage of stool so patient does not have to move each time they move their bowels
- Bed is covered with plastic sheeting or reinforced plastic mats to allow for easy cleaning
• One bucket should be placed underneath the bed to collect stool and another bucket by patient’s side to collect vomit.
• Transparent buckets allow for measuring quality and quantity of stool patient is excreting.
Recovery Area

- For oral rehydration after hospitalization, when less surveillance is required.
- Patients stay on mats or benches, as in the observation area.

Diagram:

- **Hospitalization Area**
  - Patients with severe dehydration and vomiting
  - Treatment: IV and ORS

- **Morgue**

- **Waste Area**

- **Recovery Area**
  - Patients with no remaining signs of dehydration
  - Continue ORS

- **Neutral Area**
  - Staff only
  - Stocks, supplies, staff kitchen, staff showers and latrines

- **Observation Area**
  - Patients with moderate dehydration
  - Treatment: ORS

- **Admission**

- **Screening**

- **Door**

- **Exit**
Neutral Area

- For staff only
- Includes office space, rest area, changing room for staff, pharmacy and logistic stores, water storage, preparation and storage of chlorine solutions, kitchen
- Logistic store and pharmacy must be organized to ensure sufficient supply for at least 7 days function.
Other Required Components

- **Infection Control**
  - Washing and cleaning areas, laundry area
  - Convenient hand-washing stations
  - Water treatment (preparation of chlorine solution)

- **Environment and waste**
  - Well-maintained toilets (latrines) for staff and public
  - Safe disposal of medical waste (incinerator, dustbins)
  - Rapid burial or a Morgue that allows for effective cleaning

- **Security**
  - Watchman for information and patient flow control
  - fences
  - protection of stocks (food, drugs, supplies)
Supplies and Resources

Key principle: Avoid any shortage
One Cholera Kit Provides Treatment for:

- 100 severe cases of cholera: IV fluids, ORS, and antibiotics at the beginning of the treatment and ORS during the recovery phase

  **AND**

- 400 mild or moderate cases of cholera in a CTC or ORP

- Each Kit consists of 4 modules: Basic, ORS, Infusion, and Support
Basic Module of Cholera Kit

- ORS and Ringer’s Lactate for 10 severe cases only (8L per patient)
- Doxycycline (65 adults), Doxycycline (100 children); zinc tablets (250 children)
- Disinfectant
- Renewable supplies, including culture swabs
- Equipment (e.g. scissors, forceps, stethoscope, etc.)
- Documents on diarrheal disease management in emergencies
ORS Module of Cholera Kit

- ORS for 400 patients with no, mild, or moderate dehydration
- This material covers the needs for two ORPs
Infusion Module of Cholera Kit

- Ringer’s Lactate with IV sets for 90 severe cholera cases (8L per patient)
- If purchasing supplies locally, must purchase Ringer’s Lactate and infusion AND IV sets
- Other IV fluids should not be purchased for care of cholera patients
Support Module of Cholera Kit

- Non-medical items necessary for running a CTC such as:
  - Bucket
  - Ladle
  - Jerrican
  - Chlorine test kit
  - Gloves
Human Resource Needs

- Health workers trained in case management of diarrhea
- Health workers also have important responsibilities in infection prevention and control activities
- Auxiliary staff: patient attendants, drivers, cleaners, cooks and general helpers
Minimum staff requirements to treat 100 patients/day in a 20-bed CTC:

- Medical Officer: 3
- Nursing staff: 2
- Cleaner: 2
- Health educator: 2
- Cook: 1
- Logistics Officer/Storekeeper: 1
- Sprayer/Watchman: 1

Total minimum staff requirement: 12 persons
Management

- **Regular team meetings are necessary to:**
  - Provide regular feedback on work performed in the treatment center
  - Provide updates on epidemic progress (graphs) and discuss information
  - Discuss and resolve management problems
  - Re-organize, explain and redistribute tasks and responsibilities if needed
  - Train and/or retrain personnel for precise tasks and responsibilities
  - Ensure that working conditions are adequate (furniture, clothes, food, rest room space) especially if personnel live far away from home during the epidemic
  - Ensure that regular rest periods are scheduled
Infection Control Measures at Entry/Exit Point(s):

- Install a sprayer or foot bath with 0.5% chlorine solution (1:10 bleach dilution) with obligation to sterilize soles of shoes
  - Watchman monitors adherence, reminding everyone to sanitize as they pass from one area to another

- Prepare new solution at least 3 times a day

- Hand-washing stations should also be available
Infection Control Measures: On Admission

- Spray or bathe the patient and his companion (skin, clothes, sheets, ....) with 0.05% chlorine solution (1:100 bleach dilution)
- Disinfect the means of transport of the patient with the 0.5% solution (stretcher, bed, vehicle,…)
- Dip the clothes of the patient in a 0.05% solution for 30 minutes, then rinse with clean water and dry under the sun.
- Restrict and control movements into and within the wards as much as possible, with foot spraying or bathing at each area entrance
- Keep water and soap for hand-washing
- Wash hands with soap or chlorine solution (0.05%) before and after examining each patient
- Those caring for patients should not be allowed to prepare or serve food
- One relative attends each patient
Infection Control Measures: During Hospitalization

- Disinfect the shelters, beds and floor at least twice daily with sprayers and squeeze-mops using 0.5% chlorine solution.
- Disinfect the showers, the latrines and the washing area with at least 0.5% chlorine solution.
- Dispose of stools or diarrhea of patients from buckets in a specific, regularly disinfected (2% chlorine, or 1:1.5 bleach dilution), latrine.
- Wash and disinfect (0.5% chlorine) the clothes and bed linen of cholera patients frequently and separately.
Infection Control Measures: At Discharge

- Spray or bathe the person, his hands and his clothes with the 0.05% chlorine solution
- Disinfect any other items which exit from the DTC with the 0.5% chlorine solution
- In case of death, see slides on preparing the body and mortuary guidelines
Visitors

- If a family member will stay with the patient to provide general nursing care and feed the patient, you may need less staff.
- Clinical staff should concentrate on the treatment of patients, and look for others who can temporarily take over routine or clerical work.
- Professional staff must teach and closely supervise nonprofessional caretakers.
Caretaker Education

- Caretakers spend the most time with the patients
- All caretakers should be obliged to attend a short training on: importance of ORS, hand hygiene, and infection control
- Nurse or healthcare worker can train caretakers in small groups
Water Quantity

- **60** liters of safe (chlorinated) water are needed per CTC patient per day (this includes needs for drinking water, food, hygiene of the patient and the caregiver).
- **10** liters/patient/day for Oral Rehydration
- Sufficient water storage capacity for **3** days must be ensured in order to avoid a shortage.
- Label and clearly differentiate each container (drinking water, ORS, chlorine solutions)
- Different colored containers can also be used to call attention to the different concentrations
Water Quality

- All drinking-water is treated
  - Levels of chlorine are tested regularly
  - Chlorine residual protects from secondary contamination

- Drinking-water is stored separately from water for other uses.

- If drinking-water is stored in containers, only safe containers are used and there is a safe way to take water from the containers.
  - All containers used should be fitted with a lid and tap for hygienic access to the solutions.

- It is advisable that only one person is in charge of preparing the different solutions per shift.
Water Quality

- **Hand Washing**
  - Water concentration: 0.05% chlorine solution
  - Provide soap for effective hand-washing
  - Teach and encourage all patients, caretakers and visitors to wash their hands
  - All staff must wash their hands before and after examining patients

- **Provision of appropriate containers**, preferably with a tap or a narrow neck, to enable safe storage, protection
Disinfection

- **Disinfecting solutions**
  - 0.05% chlorine (1:100 bleach dilution): hand washing, laundry, dish rinsing and bathing of soiled patients
  - 0.5% chlorine (1:10 bleach dilution): floors, beds, latrines, showers, and footbaths
  - 2% chlorine (1:1.5 bleach dilution): vomit, feces and corpses

- **Maintain stocks of each chlorine solution concentration**
Hygiene Promotion for Staff and Caregivers

- Hand-washing after dealing with each patient or after handling contaminated items
- Hand-washing after defecation and before handling or eating food
- Changing into protective clothing upon entering the area. On leaving, protective clothing should be removed in the CTC for washing on site and not taken home.
- Only kitchen staff allowed into the kitchen area.
- Caregivers should learn to clean the patient/care giver’s home that has been soiled with excreta/vomit (0.5%)
Protective Clothing

- Protective clothing should be made available for all staff working in the center, including boots and overalls.
- Gloves should also be made available for those manipulating blood, chlorine, and the chlorinated solutions.
- Gowns or clothes should be made available for hospitalized patients after bathing.
- Gowns or clothes should be made available for hospitalized patients after bathing. Sets of clothing should also be made available for caregivers and visitors to the center.
- These should also be kept and washed in the center.
Food Hygiene

- Upon entering the kitchen (each time), hand-washing must be carried out.
- Food must be stored so that it is only handled by kitchen staff.
- Only kitchen staff allowed inside the kitchen.
- Only kitchen staff may serve food.
- Dishes must be rinsed initially in a 0.05% solution then washed by normal methods.
- Food provided by relatives should be handled following the same hygiene criteria.
Laundry

- Should be located near the area producing the most contaminated waste and should wash soiled materials from the entire center including blankets, gowns, protective clothing

- Where sinks are not available, large plastic tubs will need to be made available

- Materials should be immersed and disinfected first in 0.2 % chlorine solution for 10 minutes, then washed as usual and hung to dry
Cleaning the Facility

- Squeeze-mops or similar should be used with 0.2 % chlorine solution to disinfect the ward floors, ideally as often as 4 times per day
- Walls around patients, where not solid, can be cleaned as necessary using 0.2 % chlorine solution in a sprayer
- Cholera cots should be sprayed with 0.2 % chlorine solution as appropriate and between each occupancy
Showers

- 1 shower room per 25 patients or caregivers of each gender in each area of CTC
- Minimum 2 shower rooms (m/f) for staff in neutral area
- The patient shower areas should be big enough for a minimum of 2 persons (caregiver and patient)
- If possible, bathing areas should be connected to a grease trap and a soakaway contained inside the CTC to prevent solid waste from being released into the environment
- The use of a sprayer may be useful for cleaning patients and initially soaking clothes in a tub on arrival

**Soakaway** (also known as a leach pit): A covered, porous-walled chamber that allows water to slowly soak into the ground
Latrines

- Should be cleaned several times a day with 0.2 % chlorine solution with mops and or/sprayed
  - Includes the slabs and the walls up to 1 m (or height of splashes)
  - No need to pour additional chlorine into the latrine.
- 1 / 25 persons + 1 or 2 in the neutral area for the staff
- All liquid human waste is disposed of in a toilet, flush pit or a latrine
- Toilets should be independent and not connected to the main sewer system (this helps to contain the *Vibrio cholerae*)
- For latrines or toilets connected to a septic tank, it is preferable empty the buckets with 2% chlorine solution into a temporary pit (natural decomposition will be disrupted by chlorine’s bactericidal activity)
  - Latrines should be at least 30 meters and downhill if appropriate, from water sources.
Waste Area

- **Waste area comprises of:**
  - Drum burner (to burn softs)
  - Organic pit with lid
  - Sharps pit

- **After CTC closure, sharps pit should be filled with concrete or similar to encapsulate sharps**
Decease Patients

- Disinfect bodies with a 2% chlorine solution
- Body-carriers should wear gloves during transportation
- Bodies should be carefully wrapped in sheet soaked in 2% chlorine solution

Patients’ Family

- If possible, physical contact between the family and the body should be prevented
- If this is not possible, the family should:
  - Wash hands with soap after touching the body
  - Avoid putting hands in the mouth after touching the body
Washing and Preparing the Body

- Wear apron, gloves, and mask
- Disinfect bodies with 2% chlorine solution
- Fill mouth and anus with cotton wool soaked with 2% chlorine solution
- Disinfect the deceased patient’s clothing and bedding by stirring in boiling water for 5 minutes or by drying them thoroughly in the sun before and after normal washing
Mortuary

- Should be located alongside the waste zone
- A closed plastic tent should be designated for to prevent access to bodies
- The structure should enable effective cleaning inside, with drainage canals that flow into a soakaway pit
- Should have an entrance from inside the CTC and an exit to allow collection of the body
- If a CTC does not have the possibility to build up a Morgue, rapid burial should be promoted
Mortuary (continued)

- The body should be moved as soon as possible to the mortuary as fluids will start to evacuate the body.
- Disinfection of the body should be done inside the mortuary.
- Where body bags are available, they should be used to transport the body for burial. If not available, the body can be wrapped in a cloth sheet soaked in 2% chlorine.
- Where many bodies must be stored, quicklime (calcium oxide) can be used to dry up and neutralize liquids and reduce the odors produced.
CTC Summary

- Cholera patients can easily contaminate the environment: isolation and hygiene are priority rules.
- The design of CTC should follow standard rules in order to control contamination between steps of patient management: screening, admission, observation, hospitalization, and recovery.
- Human resources organization, training and management are key activities, especially in CTCs.
- CTCs must be well-staffed and supplies must be organized in order to avoid any shortage.
Using the Rapid Diagnostic Test
Laboratory Diagnosis - Limitations

- Stool culture is “gold standard” but
  - Difficult in resource limited or remote settings
  - Requires specialized equipment, media, and reagents
  - Results – turnaround 2-3 days
Rapid Diagnostic Test
(Crystal VC Dipstick)

Rapid Diagnostic Test for screening

- Test fresh stools in the field can be read within 15-20 minutes
- Early presumptive diagnosis
- Not definitive
Crystal VC® Dipstick

Control region

Test region
- Membrane coated with monoclonal antibodies to Vc O1 and O139 (separate bands)

Conjugate Pad
- Contains colloidal gold coupled to anti-Vc O1/O139 LPS monoclonal antibodies

Sample Pad

Crystal VC® Test Strip (Nitrocellulose membrane)
Rapid Test - Procedure

1. Fill dropper halfway

2. Transfer 200 µl

3. Put tube in Styrofoam stand

Dropper

Test tube

Test tube stand

Patient ID
Rapid Test – Interpretation

Results should be read ≥15-20 minutes but not after 30 min

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- Positive *V. cholerae* O1
- Positive *V. cholerae* O139
- Positive *V. cholerae* O1 and O139
- Negative *V. cholerae* O1 and O139
- No control band
  Test did not perform correctly
Specimens for Testing I

Suitable specimens for testing:
- Liquid fecal specimens “rice-water” stool
- Viscous, mucoid or semi-solid stools are acceptable but must be diluted with normal sterile saline or sterile distilled water
- Rectal swab enriched in alkaline peptone water (Bhuyian et al. 2003)

Unacceptable specimens for testing:
- Solid stools
  - Particulate matter from these specimens may clog the nitrocellulose membrane
  - Rectal swabs (direct)
Specimens for Testing II

- Stool specimens should be collected from up to 10 persons who meet the following criteria:
  - Currently have watery diarrhea
  - Onset of illness is less than 4 days before sampling
  - Not initiated antimicrobial therapy

- Stools collected from patients in clean containers
  - No disinfectant or detergent residue
  - Do not collect specimens from bedpans

- Collect stool for culture of *V. cholerae* simultaneously
  - process stool within 24 hrs or place in transport medium (store between 24-26°C) for process as soon as possible
Quality Control

- The Crystal VC® dipstick contains an “internal” control band to validate the test procedure.

- Controls should be run when new shipments arrive, new lot numbers are used, or when new personnel perform the test.

- The kits are stored at refrigerated temperature (4°C) and never be frozen.

- Discard the kits after expiration dates and do not mix controls or reagents from different kit lots.
Rapid Test – Limitations

- Not for use for individual patient diagnosis
- Specificity is not optimal
  - More likely to see false positives
- Sensitivity is good but not perfect
  - Cholera should not be ruled out unless cultures are negative
- Indeterminate result
  - Weak or faint band
When to Use RDT?

- In outbreaks of watery diarrhea where an outbreak of cholera is suspected
  - Test up to 10 individuals with illness onset less than four days. If 30% or more samples are positive by RDT, cholera is suspect. Send cultures for confirmation.

- RDT does not replace stool culture
  - Any suspect cholera specimen screened by the rapid test should be confirmed by lab culture
  - RDT does not allow determination of serotype, biotype, detection of cholera toxin, PFGE or antimicrobial susceptibility profiles