

Clinical Updates on Cholera

Lina Traboulsi* (PharmD), Hala Sacre* (PharmD), Ayman Alameddine (PharmD), Carla Abou Selwan (PharmD), Joya Dagher (PharmD), Zeina Nahhas (PharmD, MBA) & Pascale Salameh (PharmD, MPH, PhD)

For the OPL Scientific Communication Subcommittee.

*These authors contributed equally.

After more than 30 years of eradication, culture-confirmed cholera cases and deaths threaten the resurgence of the cholera epidemic in Lebanon. The cholera outbreak first appeared in the Syrian refugee camps of Akkar, North Lebanon, as the neighboring country Syria is still struggling to contain this waterborne disease. Given the collapse of the public health system, the lack of effective sewerage networks, and the lack of access to safe water and sanitation, concerns are growing about a widespread outbreak in Lebanon^{1,2}.

A prompt awareness program on cholera transmission and an effective prevention and management strategy are essential to limit the rapid spread of cholera in Lebanon.

PATHOPHYSIOLOGY

Cholera is a potentially epidemic, life-threatening, waterborne disease caused by infection of the intestine with the toxigenic bacterium *Vibrio cholerae* serogroup O1 or O139³. It is characterized by secretory diarrhea with numerous, voluminous watery stools, often accompanied by vomiting, resulting in hypovolemic shock and acidosis⁴.

TRANSMISSION

Cholera can be contracted by drinking water or eating food contaminated with cholera. In an epidemic, feces of an infected person are usually the source of contamination and remain for 1-10 days after infection, even in asymptomatic individuals. Feces are shed back into the environment and contaminate water or food and, potentially infecting other people^{3,5}.

Thus, the disease can spread quickly in areas with inadequate sewage and drinking water treatment, poor sanitation, and poor hygiene. Because the infection is unlikely to spread from person to person, casual contact with an infected person is not a risk factor for becoming ill³.



SIGNS AND SYMPTOMS

Symptoms appear 2-3 days after ingesting contaminated food/water and include⁶:

- **Diarrhea.** Cholera-related diarrhea appears suddenly and can result in dangerous fluid loss of up to about 1 liter per hour. Cholera diarrhea has a pale, milky appearance that resembles water in which rice has been rinsed.
- Nausea and vomiting. Vomiting is expected in the early stages of cholera and can last several hours.
- **Dehydration.** Dehydration can occur within hours of the onset of cholera symptoms and can range from mild to severe. A 10% or higher loss of body weight indicates severe dehydration.

The table below describes the characteristic signs and symptoms of the different types of dehydration⁷:

Severe Dehydration	Some Dehydration	No Dehydration
One or more danger signs:	No danger signs AND at least two	Signs:
	of the following:	
 Lethargic or unconscious 		Awake and alert
 Absent or weak pulse 	 Irritable or restless 	 Normal pulse
 Respiratory distress 	Sunken eyes	 Normal thirst
	Rapid pulse	Eyes not sunken
OR at least two of the following:	 Thirsty (drinks eagerly) 	Skin pinch normal
	Skin pinch goes back slowly	
• Sunken eyes		
• Not able to drink or drinks		
poorly		
• Skin pinch goes back very		
slowly		

One in every ten people infected with cholera will develop severe symptoms such as watery diarrhea, vomiting, and leg cramps³. People living in an endemic region should seek treatment immediately in case of severe diarrhea. Rapid loss of body fluids causes dehydration, which, in turn, can lead to electrolyte imbalance due to the rapid loss of minerals in the blood that maintains the balance of fluids in the body⁴. Severe dehydration is a medical emergency that requires immediate care⁴.

Electrolyte imbalance can cause severe symptoms, such as^{3,6}:

- Muscle cramps: caused by the rapid loss of salts such as sodium, chloride, and potassium.
- Shock: one of the most severe complications of dehydration; it occurs when a decrease in blood volume causes a drop in blood pressure and a depleted amount of oxygen in the body. Death can occur within hours if electrolyte imbalance is not treated and within minutes if a severe hypovolemic shock occurs and remains untreated.



CHOLERA INFECTION TREATMENT

1. Rehydration therapy⁷

Rehydration therapy refers to the prompt restoration of lost fluids and salts and is the primary treatment for cholera patients.

- Rehydration (intravenous and oral) is associated with significantly lower mortality and continues to be the mainstay of cholera treatment.
- In cases of severe dehydration, IV fluids should be administered immediately. If the patient is able to drink, oral rehydration solutions (ORS) should be administered orally while the IV drip is being set up. Ringer's lactate is the best IV fluid to use. If unavailable, it can be substituted with normal saline solution.
- It is critical to monitor the fluids administered intravenously and keep track of the fluids lost through diarrhea and vomiting.
- The patient should be reassessed every 15-30 minutes while rehydration is maintained:
 - The fluid administration rate can be increased or prolonged as needed to achieve adequate rehydration. The patient may require ≥ 200ml/Kg of IV fluids during the first 24 hours of treatment.
 - The fluid administration can be decreased if rehydration is achieved earlier than anticipated.
 - The ORS prescribed quantity can be increased if requested by the patient.
- ORS can be administered through nasogastric tubes if the patient is alert but unable to drink sufficient quantities independently.
- Once hydration has improved and the patient is able to drink, switching from intravenous to oral rehydration solution is necessary to conserve IV fluids while lowering the risk of phlebitis and other complications. The signs of adequate rehydration are:
 - Skin goes back normally when pinched.
 - Thirst has subsided.
 - Urine has been passed.
 - Pulse is strong.

The table below details the rehydration treatment recommendations and administration methods according to the type of dehydration and the patient's age range⁷:

Table 2. Cholera - Fluid Replacement or Treatment Recommendations ⁷			
Dehydration Type	Treatment Recommendation	Administration Method	
Severe dehydration	Intravenous Ringer's lactate or, if not available, normal saline and ORS as outlined in the guidance above.	Age <1 year Timeframe 0-60 min 60 min-6 h 6 h-24 h	Total volume 30 ml/kg* 70 ml/kg 100 ml/kg
		Age ≥1 year Timeframe 0-30 min 30 min-3 h *Repeat once if rovery weak or not	



Some dehydration	Oral rehydration solution	signs of dehydra use ORS to repla diarrheal losses plan for no dehy Patients do not	4 hours. Then patient still shows ation, repeat. If not, ace ongoing using the treatment	
No dehydration	Oral rehydration solution	Administer afte	Administer after each loose stool:	
		Age	Volume of ORS	
		<2 years	50-100 ml	
		2–9 years	100-200 ml	
		≥10 years	As much as	
			patient wants	

Centers for Disease Control and Prevention. Cholera - Vibrio cholerae infection. Rehydration therapy. 2020. https://www.cdc.gov/cholera/treatment/rehydration-therapy.html

2. Antibiotic treatment8

Treatment with antibiotics reduces fluid requirements and the duration of illness. Antibiotics are only indicated for severe cases of cholera. They have the potential to cause nausea and vomiting; hence, side effects of the gastrointestinal tract should be closely monitored, especially in dehydrated patients. However:

- None of the guidelines recommend antibiotics as prophylaxis for cholera prevention, and all emphasize that antibiotics should be used in conjunction with aggressive hydration.
- Antibiotics should not be given to cholera patients who have only mild or no diarrhea and/or dehydration.
- Surveillance of antibiotic resistance among bacterial isolates from any outbreak is critical for understanding and limiting the spread of resistance.

Age group	First-line drug choice	Alternate drug choices
Children <12 years old	Doxycycline 2–4 mg/kg by mouth (per os, p.o.) single dose	Azithromycin 20 mg/kg (max 1 g p.o. single dose, or ciprofloxacin 20 mg/kg (max 1 g) p.o. single dose
Childen ≥12 years old and adults, including pregnant women	Doxycycline 300 mg p.o. single dose	Azithromycin 1 g p.o. single dose or ciprofloxacin 1 g p.o. single dose



3. Zinc

Treatment with zinc has been shown to improve cholera symptoms in children. When available, supplementation with 20 mg zinc per day should be started immediately in children 6 months or older⁹.

Special Considerations:

- Administering zinc with some antibiotics, such as ciprofloxacin, may reduce the absorption of these antibiotics. In these circumstances antibiotics should be administered 2 hours before or 4-6 hours after taking zinc⁹.
- Treatment with proton pump inhibitors causes severe hypochlorhydria and leads to bacterial colonization and increased susceptibility to enteric bacterial infection, including an increased vulnerability to cholera infection¹⁰.

CHOLERA PREVENTION^{11,12,13}

Preparing safe water

- If the water is cloudy, **filter** (using a clean cloth, paper towel, or coffee filter) before disinfecting, or allow it to settle.
- Bring the clear water to a rolling **boil** for at least 3 minutes. Let it cool and store it in clean, sanitized containers with tight covers.
- If boiling is not possible, disinfect with **chlorine**. Use commercially available chlorine food disinfection solutions or tablets and follow the manufacturer's instructions. Wait for at least 30 minutes before use.
- If a chlorine product is unavailable, use **household bleach** as per the table below (this technique also applies to sanitizing water tanks). Wait for at least 30 minutes before use.

Table 4. Preparing Safe Water According to Bleach Concentration				
<5% (50,000 ppm)	5%-10% (50,000 ppm-100,000 ppm)			
Add 0.2 ml (4 drops) to 1 liter of water	Add 0.1 ml (2 drops) to 1 liter of water			
(200 ml/m³)	(100 ml/m³)			
If the water is cloudy, murky, colored, or very cold, add double the amount of bleach				

Food and drinks

- Use safe (bottled, boiled, or treated) water to drink, brush teeth, wash and prepare food, and make ice cubes.
- Wash and scrub hands for at least 20 seconds before preparing food or after going to the toilet.
- Clean food preparation areas and kitchenware with soap and safe water and let them dry completely before reuse.
- Cook food well for at least 15 minutes (especially **seafood**); keep it covered, and eat it hot.
- Avoid eating raw foods.
- Peel fruits and vegetables.
- Do not share food, drinks, utensils, and cutlery.
- Do not use drinking fountains.



Hygiene and use of toilets for people living in community and camps

- Do not defecate in any body of water (well, lake, etc.).
- Use latrines/toilets or bury your excrement.
- Clean latrines/toilets and surfaces contaminated with feces using a solution of household bleach diluted as follows: 1 part of household bleach to 9 parts of water.
- If latrines/toilets/chemical toilets are not available.
 - Defecate at least 30 meters from any body of water and then bury excrement.
 - Dig new latrines or temporary pit toilets at least a half-meter deep and at least 30 meters away from any body of water.
- Wash patients' clothes with a 2% chlorine solution. If chlorine is not available, patients' bedding and clothing should be stirred for 5 minutes in boiling water and dried in direct sunlight, or washed with soap and dried thoroughly in direct sunlight.

Note¹⁴:

- Food, daycare, and healthcare workers should be tested regularly.
- If positive, they should be excluded from employment until all the following have been confirmed:
 - The case has been asymptomatic for at least 24 hours.
 - One negative stool culture has been confirmed.
 - The case has been counseled about preventive measures, such as hand washing procedures, that must be followed to prevent transmission of disease.

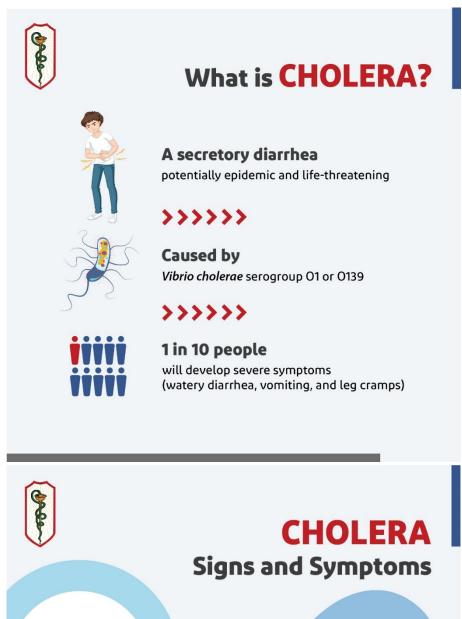


REFERENCES

- Reuters. Lebanon announces first death from cholera since detecting the disease in October. Reuters [Internet].
 2022 Oct 12. Available from: https://www.reuters.com/world/middle-east/lebanon-announces-first-death-cholera-since-detecting-disease-october-2022-10-12/
- 2. Stephan L. In Syria and Lebanon, cholera epidemic highlights lack of drinking water. Le Monde.fr [Internet]. 2022 Oct 15. Available from: https://www.lemonde.fr/en/environment/article/2022/10/15/in-syria-and-lebanon-the-reappearance-of-cholera-reveals-the-water-crisis 6000400 114.html
- 3. Centers for Disease Control and Prevention. Cholera Vibrio cholerae infection. General Information. September 2022. Available from: https://www.cdc.gov/cholera/general/index.html
- 4. Finkelstein RA. Cholera, Vibrio cholerae O1 and O139, and Other Pathogenic Vibrios. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 24. Available from: https://www.ncbi.nlm.nih.gov/books/NBK8407/
- 5. World Health Organization. Cholera [Internet]. 2017. Available from: https://www.who.int/news-room/fact-sheets/detail/cholera
- Mayo Clinic. Cholera Symptoms and causes. Mayo Clinic. 2022. Available from: https://www.mayoclinic.org/diseases-conditions/cholera/symptoms-causes/syc-20355287
- 7. Centers for Disease Control and Prevention. Cholera Vibrio cholerae infection. Rehydration Therapy. 2020. https://www.cdc.gov/cholera/treatment/rehydration-therapy.html
- 8. Centers for Disease Control and Prevention. Cholera Vibrio cholerae infection. Antibiotic Treatment. 2022. https://www.cdc.gov/cholera/treatment/rehydration-therapy.html
- 9. Centers for Disease Control and Prevention. Cholera Vibrio cholerae infection. Zinc Treatment. 2020. https://www.cdc.gov/cholera/treatment/zinc-treatment.html
- 10. Bavishi C, Dupont HL. Systematic review: the use of proton pump inhibitors and increased susceptibility to enteric infection. Aliment Pharmacol Ther. 2011 Dec;34(11-12):1269-81. https://doi.org/10.1111/j.1365-2036.2011.04874.x
- 11. Centers for Disease Control and Prevention. Cholera Vibrio cholerae infection. Five Basic Cholera Prevention Steps. 2022. https://www.cdc.gov/cholera/preventionsteps.html
- 12. Centers for Disease Control and Prevention. Water, Sanitation, & Hygiene (WASH)-related Emergencies & Outbreaks. Making Water Safe in an Emergency. 2022. https://www.cdc.gov/healthywater/emergency/making-water-safe.html
- 13. Global Task Force on Cholera Control. Cholera Outbreak Response Field Manual. [Internet]. 2019. Available from: https://www.gtfcc.org/wp-content/uploads/2020/04/gtfcc-cholera-outbreak-response-field-manual.pdf
- 14. Indiana State Department of Health; Cholera; specific control measures. 410 IAC 1-2.5-90; filed 11/25/2015, 2:54 p.m.: 20151223-IR-410150039FRA. Readopted filed 11/12/2021, 8:41 a.m.: 20211208-IR-410210385RFA. Available from: <a href="https://casetext.com/regulation/indiana-administrative-code/title-410-iindiana-department-of-health/article-1-communicable-disease-control/rule-410-iac-1-25-disease-reporting-and-control/section-410-iac-1-25-90-cholera-specific-control-measures



CHOLERA VISUALS



CHOLERA Signs and Symptoms Dehydration (mild to severe) Can lead to electrolyte imbalance and death if untreated Nausea & Vomiting in early stages of the disease CHOLERA Signs and Symptoms **Diarrhea** **Sudden milky-appearance diarrhea with dangerous fluid loss (about 1L/hour) **Housea** **Provident Stages of the disease of the dis





MODE OF TRANSMISSION



Drinking contaminated water

Eating contaminated food





SOURCE OF THE CONTAMINATION

DISEASE SPREAD

Areas with:

- inadequate treatment of sewage and drinking water
- poor sanitation
- inadequate hygiene



Infection is **NOT** likely to spread directly from person to person



Rehydration theray

is the primary treatment



Antibiotic treatment

reduces fluids requirements and duration of illness and is indicated for severe cases



Zinc treatment

has been shown to improve symptoms in children



PPIs Severe hypochlorhydria generated by PPI use leads to bacterial colonisation and increased susceptibility to enteric bacterial infection

TREATMENT





1 FILTER
BEFORE DISINFECTING

If the water is cloudy



THEN, draw off the clear water and proceed with the disinfection





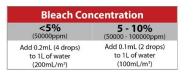
If boiling is not possible

before you drink it.



If a chlorine product is not available

Treat water with household bleach. This technique also applies for sanitizing water tanks.



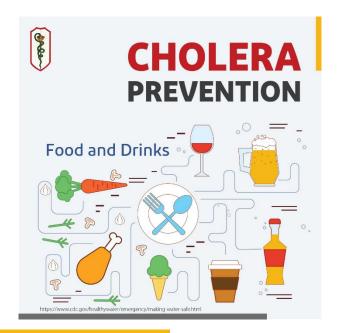




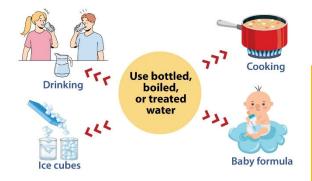
- Wait for at least 30 minutes before drinking/using.
 If the water is cloudy, double the bleach dose.

4 DISINFECT WITH HOUSE BLEACH





1 USE SAFE WATER



Wash and scrub hands with safe water for at least 20 seconds





before preparing foods after going to the toilet

2| WASH YOUR HANDS

3 | CLEAN UP SURFACES



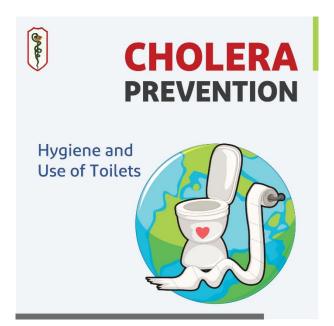
Clean food preparation areas and kitchenware with soap and safe water

Let them dry completely before reuse



4| COOK SAFELY





1 | CLEAN UP SAFELY

Where the family





bathes & washes clothes

Use available latrines/toilets

30m

Defecate at least 30 meters away from any body of water

2| RESPECT THE ENVIRONMENT

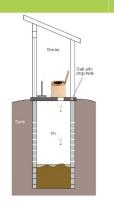
31 DIG NEW LATRINES

For people living in community and camps

Dig new latrines or temporary pit toilets at least **0.5 meter** deep

æ

at least **30 meters** away from any body of water



Clean latrines/toilets and surfaces contaminated with feces using household bleach

Dilution

- > 1 part of bleach
- > 9 parts of water



4 CLEAN UP SURFACES