



## Cholera

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- Cholera is an acute diarrheal disease that can kill within hours if left untreated.
  - Estimated 3–5 million cholera cases and 100 000–120 000 deaths a year.
  - Up to 80% of cases can be successfully treated with oral rehydration salts.
- Effective control measures rely on prevention, preparedness and response.
  - Provision of safe water and sanitation is critical in reducing the impact of cholera and other waterborne diseases.

Most persons infected with the cholera bacterium have mild diarrhea or no symptoms at all. Only a small proportion, about 10%, of persons infected with *Vibrio cholerae* have illness requiring treatment at a health center.

Cholera patients should be evaluated and treated quickly. With proper treatment, even severely ill patients can be saved. Prompt restoration of lost fluids and salts through rehydration therapy is the primary goal of treatment.

Antibiotic treatment, which reduces fluid requirements and duration of illness, is indicated for severe cases of cholera.

Zinc treatment has also been shown to help improve cholera symptoms in children.

### Summary recommendations

1. Oral or intravenous hydration is the mainstay of cholera treatment.
2. In conjunction with hydration, treatment with antibiotics is recommended for severely ill patients. It is particularly recommended for patients who are severely or moderately dehydrated and continue to pass a large volume of stool during rehydration treatment. Antibiotic treatment is also recommended for all patients who are hospitalized.
3. Antibiotic choices should be informed by local antibiotic susceptibility patterns. In most countries, Doxycycline is recommended as first-line treatment for adults, while Azithromycin is recommended as first-line treatment for children and pregnant women
4. None of the guidelines recommend antibiotics as prophylaxis for cholera prevention, and all emphasize that antibiotics should be used in conjunction with aggressive hydration for treatment.

## Background

### 1. Mainstay of cholera treatment is hydration

Intravenous and oral hydrations are both associated with greatly decreased mortality and remain the mainstay of treatment for cholera.

### 2. Antibiotic effectiveness for the treatment of cholera

- Antibiotics have been used as an adjunct to hydration treatment for cholera since 1964. Findings from randomized controlled trials evaluated the effectiveness of selected antibiotics on three main outcomes: stool output, duration of diarrhea, and bacterial shedding. These studies compared outcomes for cholera patients who were given both intravenous (IV) fluids and antibiotic treatment with those given IV fluids only. Findings indicate that antibiotics reduced volume of stool output by 8-92%, duration of diarrhea by 50-56%, and duration of positive bacterial culture by 26-83%.
- Antibiotic use for moderately and severely ill patients is also likely to reduce resource requirements. By decreasing duration of diarrhea and stool volume, antibiotics result in more rapid recovery and shorter lengths of inpatient stay, both of which contribute to optimizing resource utilization in an outbreak setting.
- The majority of published studies exploring effectiveness of antibiotics for cholera patients have been done in patients who were adequately rehydrated. In these studies, there was no mortality and therefore the impact of antibiotics on mortality cannot be assessed. In the absence of adequate rehydration, antibiotics alone are not sufficient to prevent cholera mortality.

### 3. Antibiotic regimens for the treatment of cholera

Tetracycline has been shown to be effective treatment for cholera, and is superior to furazolidone, cholamphenicol and sulfaguanidine in reducing cholera morbidity. Treatment with a single 300mg dose of doxycycline has shown to be equivalent to tetracycline treatment. Erythromycin is effective for cholera treatment, and appropriate for children and pregnant women. Ofloxacin, trimethoprim-sulfamethoxazole (TMP-SMX), and ciprofloxacin are effective, but doxycycline offers advantages related to ease of administration and comparable or superior effectiveness. Recently, azithromycin has been shown to be more effective than erythromycin and ciprofloxacin, and is an appropriate first line regimen for children and pregnant women.

### 4. Antibiotic resistance

Resistance to tetracycline and other antimicrobial agents among *V. cholerae* has been demonstrated in both endemic and epidemic cholera settings. Resistance can be acquired through the accumulation of selected mutations over time, or the acquisition of genetic elements such as plasmids, introns, or conjugative elements, which confer rapid spread of resistance. A likely risk factor for antimicrobial resistance is widespread use of antibiotics, including mass distribution for prophylaxis in asymptomatic individuals. Antibiotic resistance emerged in previous epidemics in the context of antibiotic prophylaxis for household contacts of cholera patients.

## 5. Summary of Antibiotic Treatment Guidelines

None of the guidelines recommend antibiotics as prophylaxis for cholera prevention, and all emphasize that antibiotics should be used in conjunction with aggressive hydration.

<b>Guidelines for Cholera Treatment with Antibiotics</b>				
<b>Organization</b>	<b>Recommendation</b>	<b>First-line drug choice</b>	<b>Alternate drug choices</b>	<b>Drug choices for special populations</b>
<b>World Health Organization</b>	Antibiotic treatment for cholera patients with severe dehydration only	Doxycycline	Tetracycline	Erythromycin is recommended drug for children
<b>Pan American Health Organization</b>	Antibiotic treatment for cholera patients with moderate or severe dehydration	Doxycycline	Ciprofloxacin Azithromycin	Erythromycin or azithromycin recommended as first-line drugs for pregnant women and children Ciprofloxacin and doxycycline recommended as second-line drugs for children
<b>International Centre for Diarrheal Disease Research, Bangladesh</b>	Antibiotic treatment for cholera patients with some or severe dehydration	Doxycycline	Ciprofloxacin Azithromycin Cotrimoxazole	Erythromycin recommended as first-line drug for children and pregnant women
<b>Medicins Sans Frontieres</b>	Antibiotic treatment for severely dehydrated patients only	Doxycycline	Erythromycin Cotrimoxazole Chloramphenicol Furazolidone	

\* Please note, due to space constraints, dosage information is not included in this table.

### Considerations

- Over-emphasizing antibiotics for treatment of cholera could divert resources from oral and intravenous rehydration.
- Antibiotics can cause nausea and vomiting. Gastrointestinal side effects should be carefully monitored, especially in dehydrated patients.
- Antibiotics are not needed and should not be given to patients with cholera who have only mild or no diarrhea and dehydration.
- Prospective surveillance for antibiotic resistance among bacterial isolates from any outbreak is essential for understanding and minimizing the spread of resistance.