Frequently Asked Questions

Below are answers to some common questions about cholera and oral cholera vaccines (OCV). Please use the links in the right sidebar to navigate between frequently asked questions (FAQ) categories. In addition to the information below, an excellent source of general cholera information is the CDC cholera FAQ website [1].

Cholera basics

What is cholera?

Cholera is an acute diarrheal disease that in severe cases rapidly leads to dehydration and death if appropriate treatment is not provided immediately.

Cholera is a disease in which the bacterium *Vibrio cholerae* colonizes the small intestine and produces a toxin which leads to massive secretion of water and salts. This huge amount of fluid from the intestinal cells is much more than the intestine can reabsorb and so the fluid comes pouring out as watery diarrhea. The loss of fluids is so great that the patient can quickly become severely dehydrated, go into shock, and die within a few hours. The diarrhea fluid is teeming with huge numbers of the bacteria and these can rapidly spread to others, leading to epidemics.

What are the symptoms of cholera?

Cholera patients commonly present with diarrhea and vomiting. In severe cases, diarrhea is voluminous, resulting in dehydration and shock within a few hours.

Symptoms can range from mild diarrhea to very severe diarrhea. Severe cases are generally accompanied with severe vomiting, weakness, and shock. Muscle cramps in the legs and arms are also common because of the electrolyte imbalance. With shock, the patient may lose consciousness and this may lead to death.

What causes cholera?

The causative organism, *Vibrio cholerae*, is a gram-negative, comma-shaped bacillus known to have more than 200 serogroups. Only serogroups O1 and O139 have been associated with epidemics.

The causative bacterium (*Vibrio cholerae*) produces a toxin called cholera toxin which stimulates adenylate cyclase, increasing the level of intracellular cyclic AMP, which leads to the fluid secretion from intestinal cells that is much faster than it can be reabsorbed. Thus, the disease is actually caused by the toxin rather than the bacteria itself.

Who is most susceptible?

Cholera transmission occurs where there is unsafe water and poor sanitation. In areas where cholera is common, children aged <5 years have the highest rates of infection, but all age groups are at risk. Household contacts of cholera patients are at increased risk of developing the disease.

How is the disease transmitted?

Ingestion of fecally contaminated water is the most common source of transmission of cholera; therefore, it can easily spread in highly populated communities where access to clean water and sanitation are poor and when hygiene is compromised by insufficient hand washing and during food preparation. Cholera may also be transmitted via contaminated shellfish and food.

Are there mild and severe cases of cholera, or are they all the same intensity?

Most cholera infections (about 80%) are mild or unapparent. Among those who are infected, some develop severe dehydration from profuse, acute, watery diarrhea.
After an incubation period of 1-3 days, about 20% will develop diarrhea which may be severe, along with severe vomiting. As the illness progresses, the stools become like water with little flecks of mucus (called rice-water stool). The diarrhea is usually painless and may have a fishy smell. Patients may also have severe muscle cramps and spasms which can be very painful.

What exactly do the bacteria do to cause such severe diarrhea?

If a large enough dose of the bacteria is ingested and survives the acidity of the stomach, the bacteria then colonize the small intestine where they release cholera toxin. This toxin triggers mechanisms which eventually leads to massive purging of electrolyte-rich fluid in the small intestine that exceeds the absorptive capacity of the colon and is expelled as diarrhea. This loss of fluid and depletion of electrolytes can lead to rapid dehydration.

After ingestion of a large enough dose of the bacteria that are able to survive the gastric acidity, the Vibrio organisms then colonize mucosal cells of the small intestine. During this time, the organisms release cholera toxin that bind to the small intestinal epithelial cells. The release of the A subunit of the cholera toxin stimulates the enzyme system of the intestinal cells leading to the increase in chloride secretion by the crypt cells, which in turn leads to inhibition of absorption of sodium and chloride by the microvilli. These events eventually lead to massive purging of electrolyte-rich isotonic fluid in the small intestine that exceeds the absorptive capacity of the colon, resulting in rapid dehydration and depletion of electrolytes, including sodium, chloride, bicarbonate, and potassium.

Cholera diagnosis, treatment, and prevention

What methods are available for diagnosing the presence of Vibrio cholera?

The gold standard for diagnosing cholera is bacteriological culture of a stool specimen of a patient with diarrhea.

Rapid tests (e.g., dipsticks) can also assist in surveillance for cholera in areas without bacteriology. The rapid tests sometimes give positive results when the culture is negative, so if there is doubt, a standard culture should be carried out with a few specimens to be sure of the diagnosis. Newer methods, using preincubation in enrichment broth for a few hours, may eliminate these false positives, making these dipstick tests more reliable.

Once contracted, how soon can a person die from the disease?

Patients can die in 4 to 18 hours if fluid and electrolyte losses from diarrhea and vomiting are not replaced.

Dehydration, electrolyte abnormalities (especially hypokalemia—low potassium concentration in the blood), metabolic acidosis, and hypovolemic shock may occur within 4 to 18 hours if diarrheal and vomiting losses are not replaced.

How do you treat someone who has cholera?

Adequate rehydration followed by maintenance hydration to replace ongoing fluid loss is the most important treatment. If the patient is severely dehydrated or is in shock, rapid administration of intravenous fluids is needed. Oral rehydration solution (ORS) may be given to patients with mild or moderate dehydration who are able to drink. Rice-based ORS has been shown to be superior to regular ORS for cholera patients and this should be used whenever available. Antibiotic treatment is recommended for patients with severe or moderate dehydration. For children <5 years of age, daily zinc should also be given for 10-14 days.

For patients with severe dehydration, rapid administration of intravenous fluids is needed. Ringers lactate is generally used because it has the appropriate mix of electrolytes which are needed to replace those being lost in the diarrhea stool. Ringers has less potassium than is ideal but this can be compensated by starting ORS as soon as the patient is able to drink. Patients with severe...
dehydration require large volumes given rapidly—generally 10% of their body weight over 2 to 4 hours. Thus, a 50kg patient needs 5 liters quickly. Additional fluids are needed to keep up with ongoing losses, using either ORS or IVs as tolerated. Patients with cholera should be monitored closely, especially in the first 24 hours of illness as the severe purging and vomiting may continue. Ideally, patients should be placed on cholera cots so that stool outputs can be more easily monitored, and they must be reassessed every 1-2 hours or more frequently if purging continues. There is no restriction on feeding, and small frequent feedings may be continued, if tolerated, during treatment. Antibiotic treatment is recommended for patients with severe or moderate diarrhea and should begin as soon as vomiting stops, which is usually 4-6 hours after initiation of rehydration therapy.

Zinc should be given to children <5 years old as soon as vomiting stops. Zinc supplementation has been shown to shorten the duration of diarrhea and reduce diarrhea episodes when given for 10-14 days.

How effective are antibiotics in treating cholera?

Antibiotics decrease the passage of diarrheal stools, thereby decreasing fluid losses. Antibiotics also result in decreasing the fecal excretion of vibrios. However, some strains of V.cholerae are resistant to certain antibiotics, such that the choice of which antibiotic to use is very important.

Antibiotics reduce the purging by about 50% and shorten the illness by about 50%. This means less time in the hospital, fewer supplies needed for treatment, and less work for the hospital staff. This is important during outbreaks when hospitals can be overwhelmed with patients. The antibiotic must be appropriate, however, and some strains are resistant to commonly-used antibiotics. Thus, samples should be obtained periodically from different patients to determine antibiotic sensitivity of the outbreak strains to be sure the bacteria have not become resistant. If the strains are sensitive, doxycycline is the preferred antibiotic for both children and adults. If strains are resistant to tetracycline, azithromycin is generally used. Antibiotics also shorten the period of Vibrio excretion and thus limit the spread to the family members and neighbors.

What is the best way to prevent contracting cholera?

Cholera will not occur if people have safe water and safe food. Thus, improved water and sanitation is the long term solution to preventing cholera. However, for many developing countries, this goal is a long way off. In these areas where there is a high risk of cholera, people need to use only safe water, but they should also consider cholera vaccine.

If the cholera vaccine were available in unlimited quantities and very inexpensive, then most people in developing countries should receive it. Currently the cost is about $1.70 - $1.85 per dose when purchased through agencies. Formerly, the supply was very limited but now the production is rapidly expanding and the cost is expected to decrease.

How effective is sari filtration?

One study [2] has demonstrated that the risk of cholera can be reduced by about 50% if the household water is filtered through sari material. Use of sari filtration is based on the idea that many of the cholera bacteria are attached to plankton and these can be filtered out with the sari material. The bacteria which are not attached to plankton can slip through a sari filter easily. Thus, this method is worthwhile but it is best used with other water purification methods (e.g. chlorination).

Where can I find more information on cholera?

For a training program for managing cholera outbreaks, see the COTS website [3]. For other materials see the WHO [4], UNICEF [5], and CDC [6] websites.

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How many people are affected annually, and how many die?

Each year about 2.7 million people suffer from cholera and about 90,000 of them die from this preventable disease. Cholera has been reported in much of the developing world, and an estimated 1.4 billion people are said to be at risk of developing cholera in endemic countries alone. In 2015, 172,000 cases were reported to the World Health Organization, including 71,000 from Africa, 65,000 from Asia, and 36,000 from Haiti. WHO publishes an annual report in the *Weekly Epidemiology Report* each year. While useful, these reports are believed to significantly underestimate the disease burden since many countries with very large numbers of cases do not report.

What parts of the world are most likely to experience cholera?

The home of cholera is the area around the Bay of Bengal, but cholera now affects most countries of South and Southeast Asia and most countries of Sub-Saharan Africa. In 2010, cholera spread to Haiti, and temporarily to Mexico and Cuba. Outbreaks have also occurred recently in Afghanistan, Iraq, and Somalia.

What is a cholera outbreak?

According to the WHO, countries are said to be endemic for cholera if cholera cases have been reported in 3 out of the previous 5 years. An outbreak of cholera occurs when a higher than expected number of cases are reported in a given area for a specific period of time. Outbreaks may occur in endemic or non-endemic areas and are more limited in scope compared to epidemics. In Africa, some countries appear to have cholera nearly every year, while other countries suffer from outbreaks every few years.

How effective is surveillance in containing cholera outbreaks?

In areas at risk for cholera, surveillance is critical so that outbreaks can be detected early and control strategies can be employed.

Improved surveillance is a critical component for cholera control that is missing from many countries with cholera. Since cholera tends to occur in remote areas of poor countries, cases may go undetected until a major outbreak has already begun. Some constraints to carrying out proper surveillance include the lack of good laboratory facilities in these remote locations and the lack of infrastructure to report suspected cases.

Is it a problem for travelers?

Cholera is rare in travelers because they are usually careful about consuming only safe foods and safe water. However, cholera does happen among travelers to developing countries. They have no immunity and are susceptible. Travelers should therefore be advised to drink only safe water and safe food. During the cholera outbreak in Cuba, some travelers from Europe to Cuba developed cholera, presumably due to insufficient care in food and water precautions.

Click here for a case report (PDF format) of a traveler to Cuba who contracted cholera.

Oral cholera vaccine (OCV) basics

**What kinds of cholera vaccines are available?**

There are five licensed vaccines for cholera. Four of these are killed oral vaccines (Dukoral, Euvichol, Shanchol, and mORCVAX) and one is an attenuated liver oral vaccine (Vaxchora). Dukoral, Euvichol, and Shanchol are approved (prequalified) by the World Health Organization. These are licensed and available in certain countries. Dukoral is available in many travel clinics in Europe, as well as many developing countries but are not licensed in the USA. Vaxchora is licensed in the USA in 2016. A comparison of currently manufactured killed oral cholera vaccines can be found here.

**Who can receive the oral cholera vaccine?**
Euvichol and Shanchol are most often provided through campaigns organized by the national ministry of health during cholera outbreaks or to prevent cholera in areas at risk. The ministries obtain the vaccine through an application to the global stockpile [10]. For travelers who wish to take oral cholera vaccine, Vaxchora is available in travel clinics in the USA, and Dukoral is widely available in travel clinics in many countries, but not the USA.

Why use oral cholera vaccine?

As with other vaccines, oral cholera vaccine helps to reduce the risk of getting the disease should one be exposed. In the case of cholera vaccine, vaccine reduces this risk by about 65-75%.

In addition to reducing the risk to individuals who may be exposed, the vaccine also induces herd protection, meaning that if a large proportion of the population is immunized, the spread of the infection is reduced. This lowers the risk of cholera for persons who may not have received the vaccine, and it also lowers the risk further for those who do receive it.

Where can I find more information on oral cholera vaccine?


In addition, the package inserts provided by the manufacturers of the vaccines also provide helpful information and can be found at these links:

- **Dukoral** [12]
- **Euvichol** [13]
- **Shanchol** [14]

How can I contact an expert in cholera or oral cholera vaccine?

The DOVE project has experts who can advise about cholera and are available to assist in planning for oral cholera vaccine.

OCV efficacy and safety

How effective is the oral cholera vaccine at protecting against cholera?

Vaccine reduces the risk of getting sick with cholera by 65-75%, and a recent study has found that protection lasts 5 years.

How many days after vaccination does it take to establish protection against cholera?

Based on clinical studies and immunological tests, protection starts 7 to 10 days after the first dose. Currently, the standard practice is to give two doses, but a single dose does provide short term protection (at least 6 months) in endemic settings.

Does the oral cholera vaccine need to be taken separately from the oral polio vaccine?

Currently, the manufacturers caution that there should be two weeks between rounds of oral vaccines for polio and cholera. Whether this is necessary or not is not known. Until we have data to show that there is no interference between the two vaccines, it is best to separate the two vaccines by at least two weeks.

It seems likely that studies will show that the two vaccines can be given at the same time, but there are no studies to show this can be done without interaction.

After being vaccinated, why should a person continue to take precautions with clean water,
sanitation, and hygiene?

The vaccine works best if other actions are taken to prevent cholera's spread. If a person consumes a very large dose of bacteria, this large number of bacteria can overwhelm the intestinal immunity, resulting in the patient developing cholera in spite of being vaccinated. Thus, the vaccine works best when water is as safe as is reasonably possible.

Vaccine and safe water interventions work synergistically. Safer water improves the effectiveness of the vaccine and the vaccine reduces the number of *Vibrio cholerae* shed in feces and contaminating environmental water. Thus, when deciding how to control cholera, these are not two competing strategies—they work together. Also, many diseases, not only cholera, can be spread by contaminated food and water. The vaccine is only against cholera, so you still need to take precautions to avoid these other infections.

Does the vaccine have any side effects? How safe is the vaccine?

The vaccine is safe and there have been no serious side effects from it. Being a killed oral vaccine, there is no reason to expect it to be risky. While safe, a few people who have taken the vaccine have noted experiencing a brief period of upset stomach. Also, the taste of these vaccines is not pleasant.

Extensive safety studies have been conducted and there have been no serious adverse events associated with the vaccine. A few people have experienced some mild stomach discomfort, but these symptoms occurred in subjects receiving a placebo as well. The vaccine has now been given to several million people and there continues to be no evidence of safety issues.

How many doses of oral cholera vaccine are needed, and what is the recommended schedule to receive each dose?

The current recommendations are for two doses of killed oral cholera vaccine to be given with an interval of 2 to 6 weeks.

The schedule using a two week interval was designed to speed the process of immunization as much as possible during campaigns when there is urgency to get people immunized as quickly as possible. For travelers who delay getting the vaccine until shortly before the trip, the two week schedule was appropriate. From an immunological standpoint, a shorter interval may not be as effective since the vaccine stimulates local intestinal immunity and a booster response is better if the interval is not too close together. In some situations, a longer interval (up to 8 weeks) may be logistically more convenient and is also acceptable. Studies will be conducted soon to determine if the interval between doses should be extended so that the second dose can be given 3 to 12 months after the first.

How important is it to receive the second dose?

The majority of the studies that document vaccine efficacy have used two doses. However, recent studies show that a single dose is effective in the short term (6 months). Future studies are planned to determine how long protection lasts after a single dose.

How much vaccine is available?

In the past few years, the supply of vaccine was very limited (about 2 million doses per year). Now that two companies are manufacturing the vaccine the supply is increasing greatly (with capacity of up to 25 million doses per year). This will allow vaccine to be given to more people who will benefit.
provision of high-quality medical care for those who do develop cholera. Recent experiences demonstrate that these activities can reinforce each other.

In the past, there was a concern that if a cholera vaccine campaign was implemented, that this would interfere with other interventions such as improved water and sanitation. From a biological standpoint, both types of interventions reduce the threat of cholera, but there was still concern that the logistical and resource requirements of the two programs might compete. Recent experience with vaccine campaigns have demonstrated that this concern is not warranted, and in fact, with careful planning, the types of activities can reinforce each other. More information about an integrated approach to cholera control can be found here [15].

**How much does oral cholera vaccine cost per dose?**

The current price when purchased through the UN system is $1.70 to $1.85 per dose. When vaccines are provided through travel clinics, the price is much higher.

With increasing production, we anticipate that the price of the vaccine will come down.

When attempting to control a cholera outbreak, how should donors distribute the funding resources between programs for safe water and programs for vaccine?

Each outbreak must be assessed as to its risk to the population. For outbreaks that can be controlled rapidly with improved safe water, this may be the best strategy. However, for outbreaks that put many people at risk, an integrated strategy that provides vaccine along with safe water will save money as well as lives. The DOVE project consultants can help assess these situations. Please send an email to info@stopcholera.org [16] with your request.

Integration of vaccine and safe water programs begins with donors providing humanitarian funding for cholera control.

**How can oral cholera vaccines be accessed by governments for vaccination campaigns?**

Vaccine is now available through the stockpile at the World Health Organization [17].

Decisions about use of cholera vaccine depend on the cholera situation in the country. The DOVE project has a process for assessing the risk of cholera and whether vaccine makes sense for use in given situations. Some countries with a consistently high cholera rate will find that use of vaccine will save money as well as lives. For low risk countries, vaccine may not be cost effective relative to other strategies.

**What is the WHO cholera vaccine stockpile?**

The World Health Organization (WHO) has a stockpile of vaccine that can be made available very rapidly during emergency situations. Countries can access vaccine from the stockpile by applying to WHO through their website [17].
Frequently Asked Questions
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[16] mailto:Info@stopcholera.org