

# CHOLERA

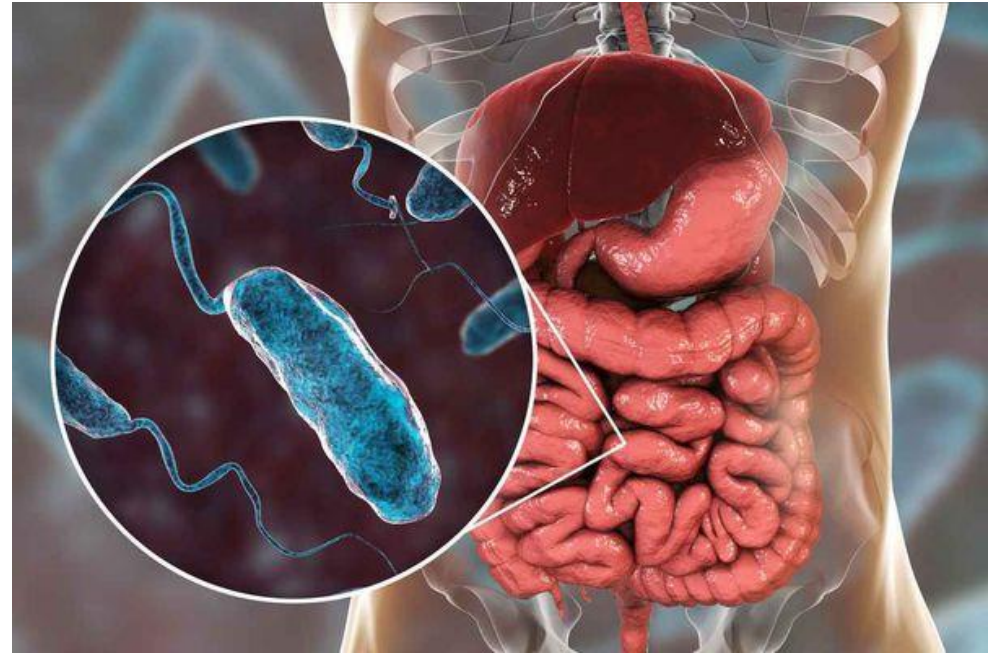


WARNING  
**CHOLERA**

**Cholera** (from the ancient Greek χολή «bile" and ῥέω «flows") - an acute intestinal sapronotic infection caused by bacteria species **Vibrio cholerae.**

***Cholera (cholera)*** is an acute anthroponotic infectious disease with a fecal-oral mechanism of pathogen transmission, which is characterized by profuse diarrhea with rapid development of dehydration.

*Due to the possibility of mass spread, it is classified as a quarantine dangerous infection.*



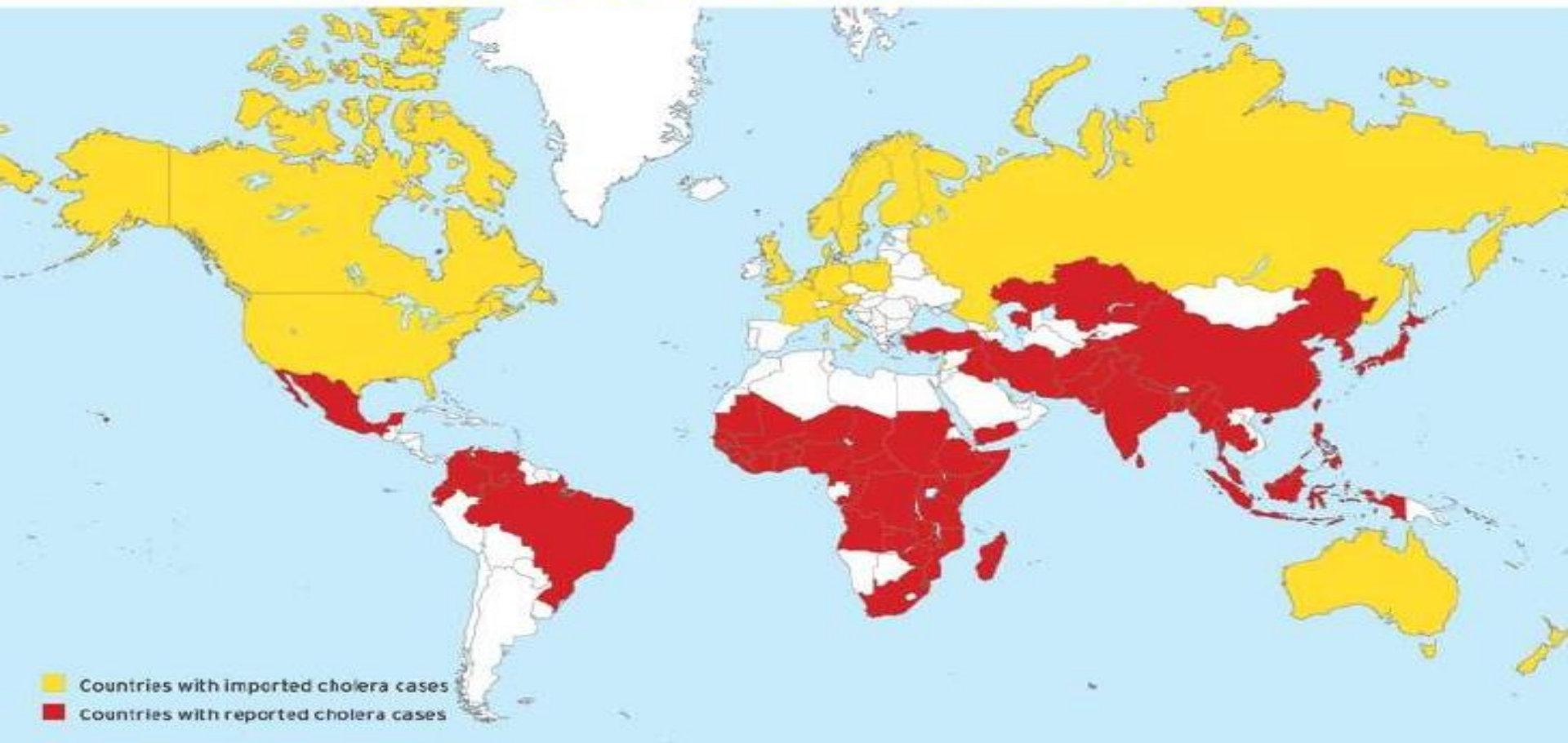
# Cholera can be an endemic, epidemic, or a pandemic disease.

Initiation and maintenance of epidemic and pandemic disease by *V.cholerae* result from human infection and poor sanitation with assistance from human migration and seasonal warming of coastal waters.






# Cholerae Outbreaks

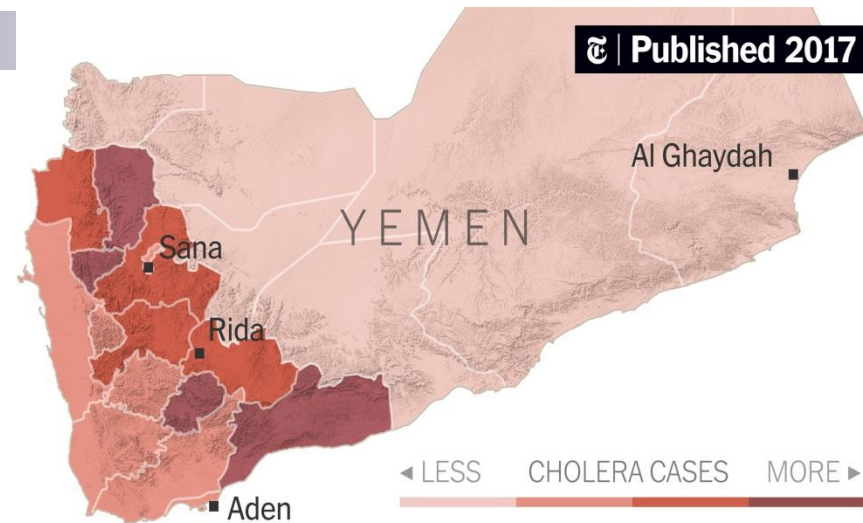


**Distributed, usually in the form of epidemics.  
Endemic foci are located in Africa, Latin America, India and  
Southeast Asia.**



***V. cholerae* has an endemic or epidemic occurrence. In countries where the disease has been for the past three years and the cases confirmed are local (within the confines of the country) transmission is considered to be "endemic." Alternatively, an outbreak is declared when the occurrence of disease exceeds the normal occurrence for any given time or location. Epidemics can last several days or over a span of years. Additionally, countries that have an occurrence of an epidemic can also be endemic.**

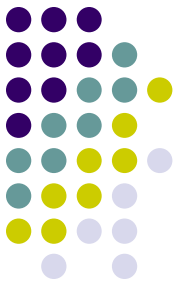
**The longest standing *V. cholerae* epidemic was recorded in Yemen. Yemen had two outbreaks, the first occurred between September 2016 and April 2017, and the second began later in April 2017 and recently was considered to be resolved in 2019. The epidemic in Yemen took over 2,500 lives and impacted over 1 million people of Yemen. More outbreaks have occurred in Africa, the Americas, and Haiti.**



**Since 1817, 7 cholera pandemics have occurred:**

- 1. The first pandemic 1817-1824 .**
- 2. The second pandemic, 1829-1851**
- 3. Third pandemic 1852-1860 .**
- 4. Fourth pandemic 1863-1875 .**
- 5. Fifth pandemic, 1881-1896 .**
- 6. The sixth pandemic, 1899-1923 .**
- 7. The seventh pandemic, 1961-1975.**

**In 1905, a quarantine station El Tor has been allocated a new kind of agent, called in honor of the station.**







# Etiology

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The causative agent is **Vibrio cholerae** represented by two biovars -

**V. cholerae biovar cholera**

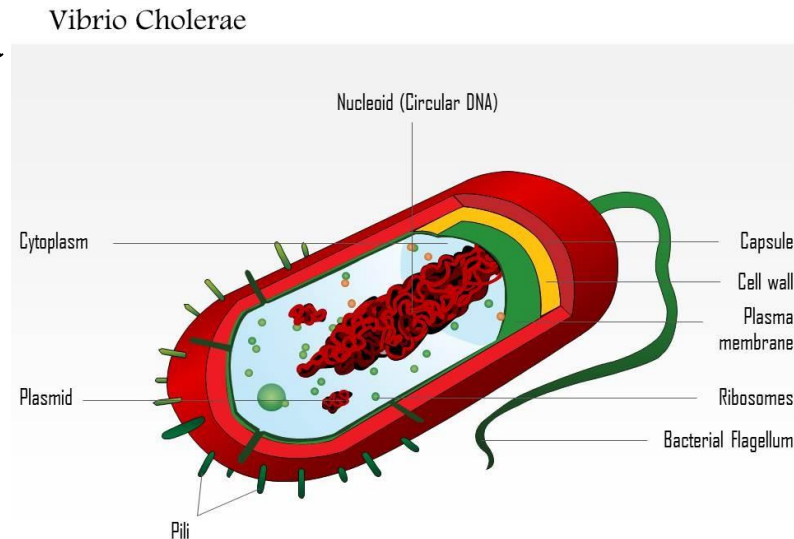
(classic) and

**V. cholerae biovar El-Tor**, similar in morphological and tinctorial properties.

# Etiology

The causative agents of cholera are

- ▶ comma-shaped (1.5-3  $\mu\text{m}$  long and 0.2-0.6  $\mu\text{m}$  in diameter),
- ▶ Gram-negative
- ▶ highly mobile due to the presence of a polarly located flagellum.
- ▶ Spores and capsules do not form,
- ▶ arranged in parallel,
- ▶ cultivated on alkaline nutrient media
- ▶ aerobic or optional anaerobic bacillus



❑ Vibrios contain thermostable **O-antigens** (somatic) and thermolabile **H-antigens** (flagellate).

According to O-antigens, cholera vibrios are divided into 3 serological types:

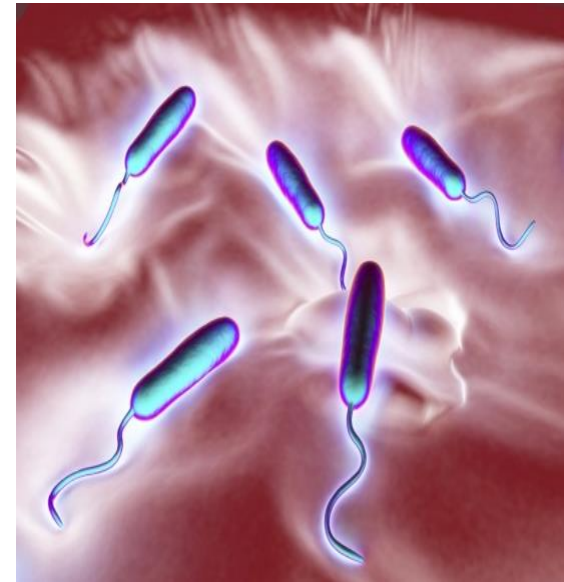
❑ **Ogawa** type (contains antigenic fraction B),

❑ **Inaba** type (contains fraction C) and

❑ **intermediate type of Hikodzima (Hikojima)** (contains both fractions - B and C).

These serological types are observed as in classical vibrios, and in the **El Tor** biotype.

There are 140 serotypes of *Vibrio cholerae*, but currently only serotype O1 causes very severe diarrhea (so-called Asiatic cholera).



# V.Cholerae Serological Classification

## Toxigenic V.cholerae

Divizion into 2 epidemic serotypes

**01**

Divizion into 2 biotypers

**0139**

Classical

El Tor

Each 01 biotype can have 3 serotypes

Inaba

Ogawa

Hikojima

A& B

A&B

A&C



**The clinical and epidemiologic features of disease caused by *V. cholerae* O139 are indistinguishable from those of disease caused by O1 strains.**

**Both serogroups cause clinical disease by producing an **enterotoxin** that promotes the secretion of fluid and electrolytes into the lumen of the small intestine.**

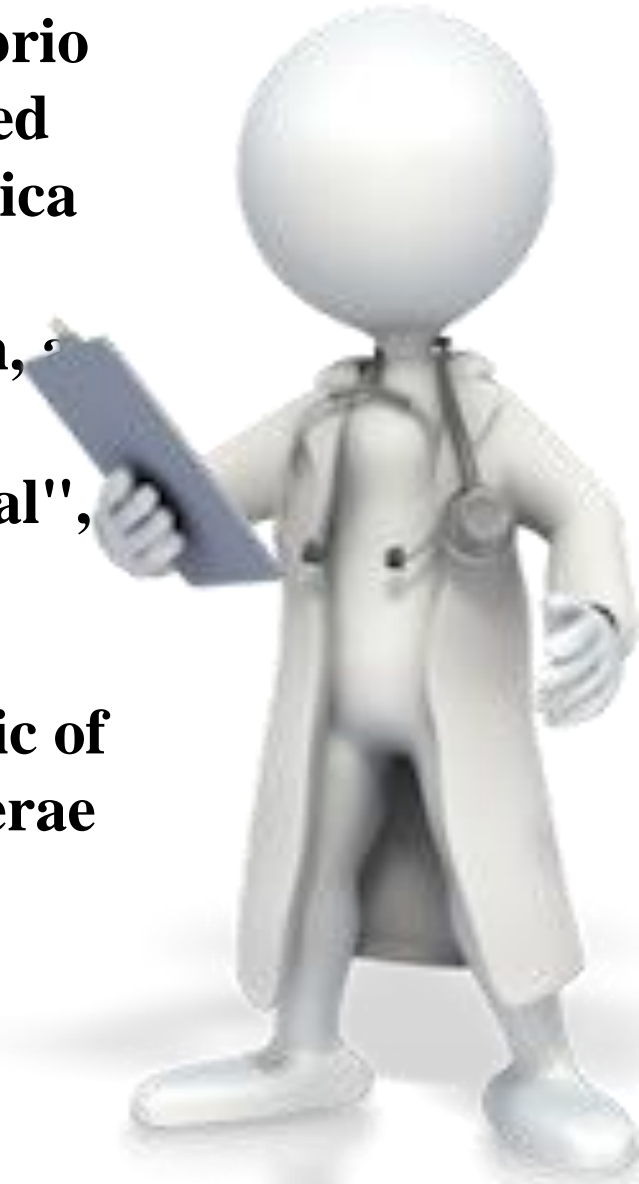



**In the 1960s, an epidemic caused by the *Vibrio eltor* (El Tor) serotype, previously considered opportunistic pathogen, spread in Asia, Africa and Europe.**

**Appearing in 1992 in India and Bangladesh, a new serotype**

***Vibrio cholerae* O139, also known as "Bengal", led to the development of an extensive 8 epidemic by water.**

**The causative agent of the seventh pandemic of cholera are toxigenic strains of *Vibrio cholerae* O1 of the serogroup El Tor biovar, and also probably *Vibrio cholerae* O139 of the serogroup.**





**Vibrio cholerae survive well at low temperatures; kept on ice for up to 1 month in sea water - up to 47 days, in river water - from 3-5 days to several weeks, in soil - from 8 days to 3 months, in feces - up to 3 days, on raw vegetables - 2-4 days, on fruit - 1-2 days.**

**Vibrio cholerae at 80 ° C die after 5 minutes, at 100 ° C - instantly;**

**highly sensitive to acids, drying and exposure to direct sunlight, under the action of chloramine and other disinfectants, they die after 5-15 minutes, persist for a long time and even multiply in open reservoirs and wastewater rich in organic substances.**

# **EPIDEMIOLOGY**

**In recent years, there has been an increase in the number of countries in the world where the incidence and outbreaks of cholera are recorded**

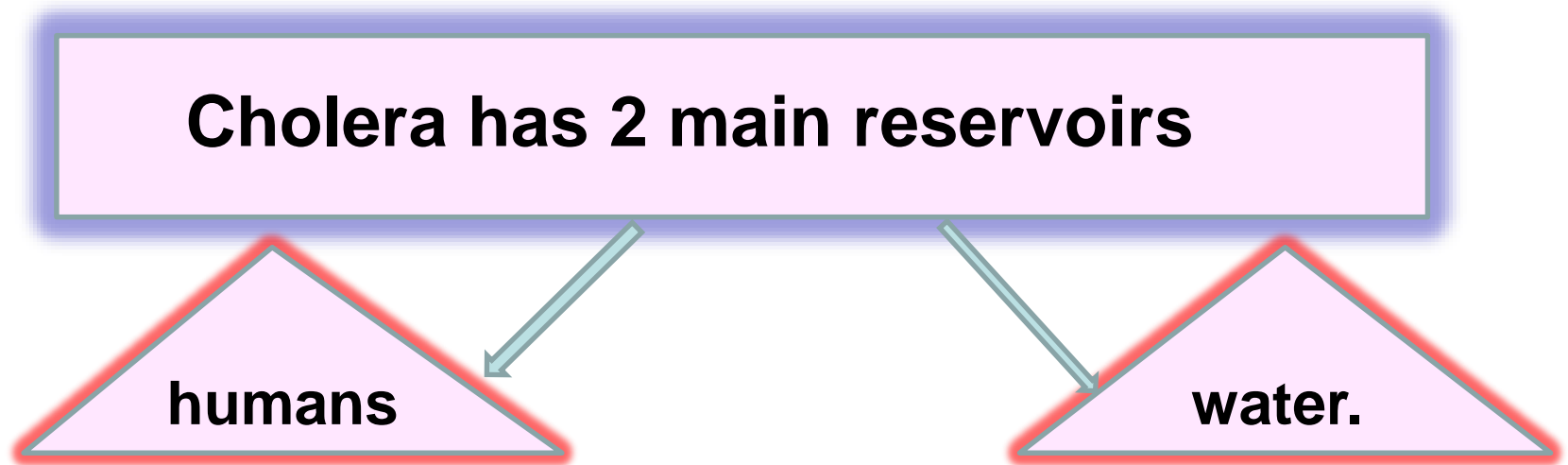
**The most disadvantaged for cholera are currently:**

- ✓ **on the European and Asian continents:  
India, Laos, Indonesia, Iran, Iraq, Turkey,  
Afghanistan;**
- ✓ **on the American continent: Bolivia, Brazil, Guatemala,  
Honduras, Mexico, Nicaragua, Peru, El Salvador;**
- ✓ **on the African continent: Angola, Burundi, Ghana, Guinea,  
Nigeria, Somalia, Chad, Uganda, Tanzania, Sierra Leone.**



# Environmental factors

*V.cholerae* is a saltwater organism, and its primary habitat is the marine ecosystem where it lives in association with plankton.



*V cholerae* is rarely isolated from animals, and animals do not play a role in transmission of disease.

# EPIDEMIOLOGY

**The source of the infection** is a person (a patient and a vibrio-carrier).

Patients with mild and erased forms of the disease who remain socially active are especially dangerous.

**The mechanism of transmission of infection** is fecal-oral.

**Ways of transmission** - water, alimentary, contact-household. The waterway is critical to the rapid epidemic and pandemic spread of cholera.


**At the same time, not only drinking water, but also using it for household needs (washing vegetables, fruits, etc.), bathing in an infected reservoir, as well as eating fish, crayfish, shrimp, oysters caught there and not thermally processed, can lead to cholera infection.**






**Vibrio-carrier convalescents secrete pathogens on average within 2 to 4 weeks,  
Transient carriers - 9 - 14 days.**

**After an illness, with a favorable course of the infectious process, immunity is developed in the body of those who have been ill.  
It is short - repeated cases of cholera seen after 3-6 months.**





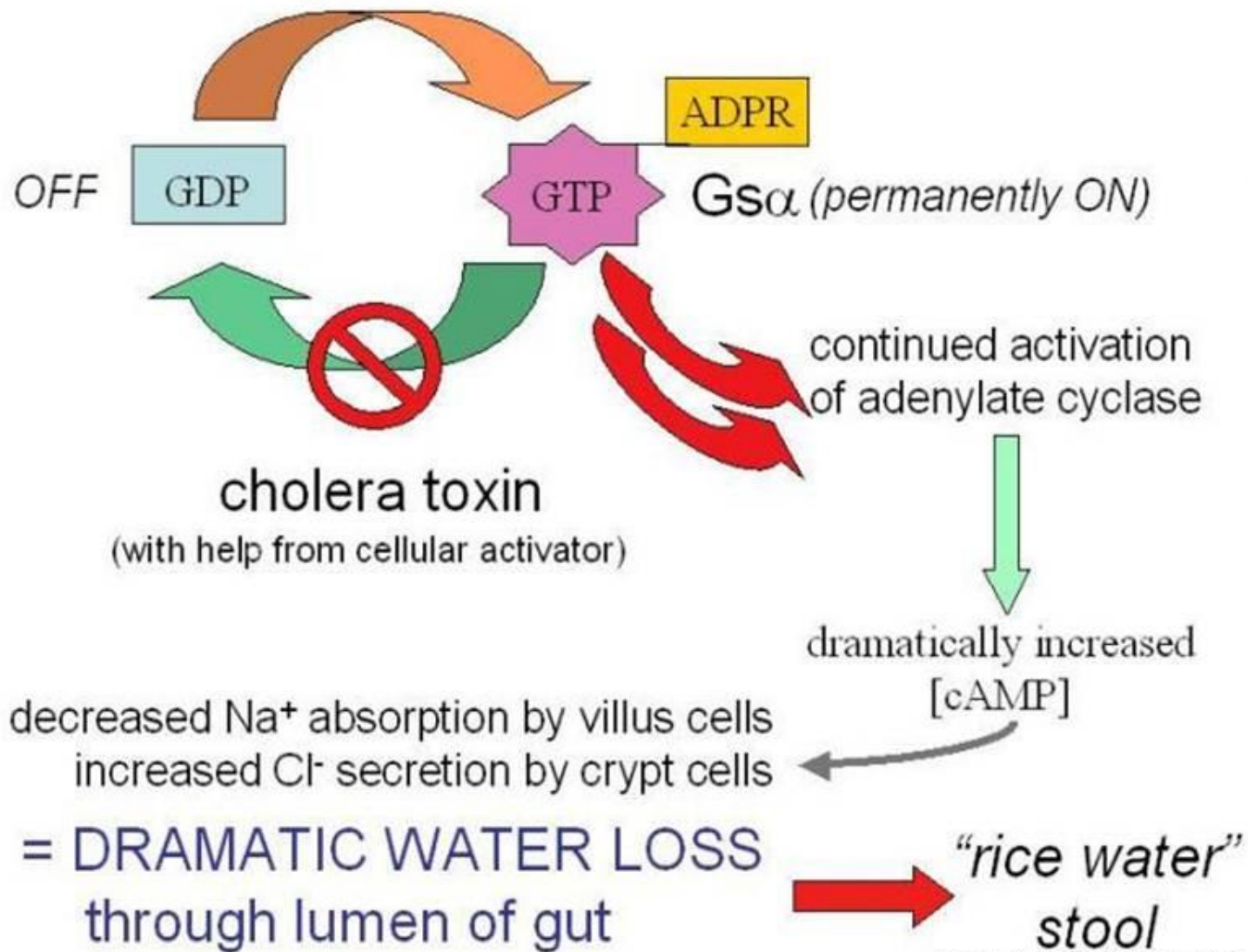
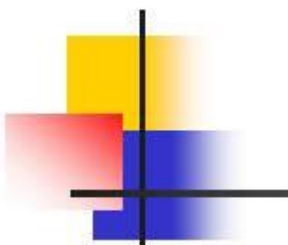


**The use of antacids, histamine receptor blockers, and proton pump inhibitors increases the risk of cholera infection and predisposes patients to more severe disease as a result of reduced gastric acidity. The same applies to patients with chronic gastritis secondary to *Helicobacter pylori* infection or those who have undergone a gastrectomy.**

# Pathogenesis

***V. cholerae* is not acid-resistant, it depends on its large inoculum size to withstand gastric acidity. *V. cholerae* cause clinical disease by producing an enterotoxin that promotes the secretion of fluid and electrolytes into the lumen of the small intestine.**

**Enterotoxin is responsible for the increase in cyclic adenosine monophosphate (cAMP). cAMP blocks the absorption of sodium and chloride and promotes the secretion of chloride and water by the crypt cells. The result is watery diarrhea with electrolyte concentrations isotonic to those of plasma. The large volume of fluid produced in the upper intestine overwhelms the absorptive capacity of the lower bowel, resulting in severe diarrhea. Unless the lost fluid and electrolytes are replaced adequately, the infected person may develop shock from profound dehydration and acidosis from loss of bicarbonate.**



# Clinical features

**According to the severity of clinical manifestations, there are:**

- ▶▶ an erased form of the disease**
- ▶▶ mild**
- ▶▶ moderate,**
- ▶▶ severe**
- ▶▶ very severe forms, defined degree of dehydration.**

## **Dehydration levels:**

- **I degree of dehydration - losses up to 3% of body weight.**
- **II degree of dehydration -loss of 4-6% of body weight.**
- **III degree of dehydration - loss of 7-9% of body weight.**
- **IV degree of dehydration or decompensated dehydration -losses of more than 10% of body weight.**

# The incubation

The incubation period lasts from several hours to **5 days, usually 24-48 hours**. The severity of the disease varies - from erased, subclinical to severe conditions with a severe dehydration and death within 24-48 hours.

According to WHO, "many patients infected with *V. cholerae*, cholera do not develop in spite of the fact that bacteria are present in their faeces for 7-14 days.

In 80-90% of cases when the disease develops, it takes the form of mild or moderate severity that are difficult to distinguish clinically from other types of acute diarrhea. Less than 20% of ill persons develop typical cholera with signs of moderate or heavy dehydration.

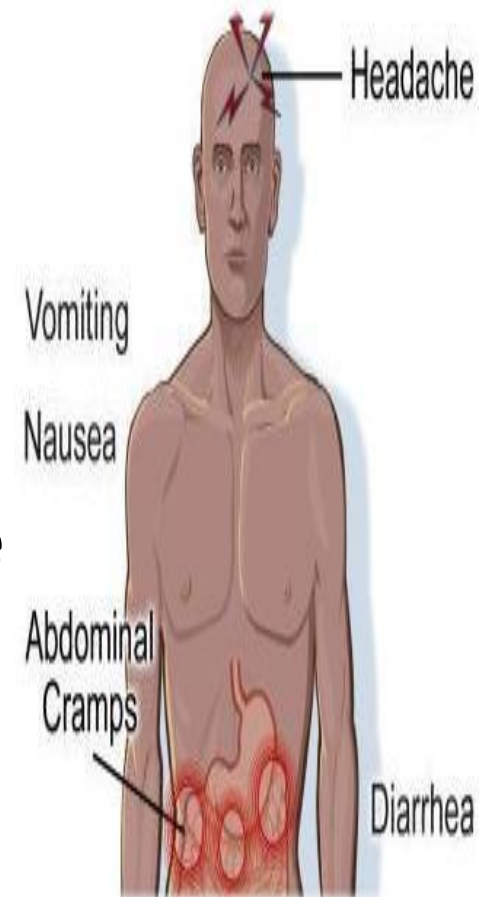


After a 24- to 48-hour incubation period, symptoms begin with the sudden onset of painless watery diarrhea that may quickly become voluminous and is often followed by vomiting. The patient may experience accompanying abdominal cramps, probably from distention of loops of small bowel as a result of the large volume of intestinal secretions. Fever is typically absent.

However, most *Vibrio cholerae* infections are asymptomatic, and mild to moderate diarrhea due to *V.cholerae* infection may not be clinically distinguishable from other causes of gastroenteritis.

An estimated 5% of infected patients will develop cholera gravis, ie, severe watery

**diarrhea, vomiting, and dehydration.**



# Diarrhea

Profuse watery diarrhea is a hallmark of cholera. Cholera should be suspected when a patient older than 5 years develops severe dehydration from acute, severe, watery diarrhea (usually without vomiting) or in any patient older than 2 years who has acute watery diarrhea and is in an area where an outbreak of cholera has occurred.

Stool volume during cholera is more than that of any other infectious diarrhea. Patients with severe disease may have a stool volume of more than 250 mL/kg body weight in a 24-hour period. Because of the large volume of diarrhea, patients with cholera have frequent and often uncontrolled bowel movements.

The stool may contain fecal material early in the course of clinical illness. The characteristic cholera stool is an opaque white liquid that is not malodorous and often is described as having a “**rice water**” appearance (ie, in color and consistency, it resembles water that has been used to wash or cook rice).



**Typical "rice water" diarrhea**





**As a result of dehydration, facial features are sharpened, the eyes sink, the skin becomes cold to the touch, easily gathers in folds and slowly straightens.**

**The voice becomes hoarse and disappears, shortness of breath appears,  
body temperature falls below normal.**



**In patients with a mild form of cholera, defecation is repeated no more than 3-5 t/ day, general health remains satisfactory, slight sensations of weakness, thirst, dry mouth. The duration of the disease is limited to 1-2 days.**





## **With moderate severity (dehydration of the II degree),**

**the disease progresses, vomiting joins diarrhea, becoming more frequent. The vomit has the same kind of rice water as the stool. It is characteristic that vomiting is not accompanied by any tension and nausea. With the addition of vomiting, exsiccosis progresses rapidly. Thirst becomes excruciating, the tongue is dry, with a "chalky coating", the skin, mucous membranes of the eyes and oropharynx turn pale, skin turgor decreases. Stool up to 10 t / day, plentiful, does not decrease in volume, but increases. There are single convulsions of the calf muscles, hands, feet, chewing muscles, unstable cyanosis of the lips and fingers, hoarseness of the voice. Moderate tachycardia, hypotension, oliguria, hypokalemia develop.**

**The disease in this form lasts 4-5 days.**



**The severe form of cholera (III degree of dehydration) is characterized by pronounced signs of exsiccosis due to abundant (up to 1-1.5 liters per defecation) stool, which becomes so already from the first hours of the disease, and the same profuse and repeated vomiting. Patients are concerned about painful cramps in the muscles of the limbs and abdomen, which, as the disease progresses, change from rare clonic to frequent and even give way to tonic convulsions. The voice is hoarse, quiet. The turgor of the skin decreases, the skin gathered in a fold does not straighten out for a long time. The skin of the hands and feet becomes wrinkled**

**("the washerwoman's hand").**

**The face takes on a characteristic appearance: pointed features, sunken eyes, cyanosis of the lips, auricles, earlobes, nose.**



**A very severe form of cholera (formerly called algid) is characterized by a rapid sudden development of the disease, starting with massive continuous bowel movements and profuse vomiting. After 3-12 hours, the patient develops a severe condition of algid, which is characterized by a decrease in body temperature to 34-35.5 ° C, extreme dehydration (patients lose up to 12% of body weight - IV degree dehydration), shortness of breath, anuria, and hemodynamic disturbances by type hypovolemic shock. By the time patients arrive at the hospital, they develop paresis of the muscles of the stomach and intestines, as a result of which vomiting stops (it is replaced by convulsive hiccups), an anus gapes, free flow of intestinal contents from the anus with light pressure on the anterior abdominal wall.**



**In those who died from cholera algid, due to severe dehydration and demineralization, a characteristic “**Hippocratic facies**” is noted with sunken eyes and sharpened features, earthy skin color, sometimes taking on a bluish tint.**







**(a symptom of "sunglasses"), the eyeballs are turned up, the cheeks tumble in, the nose, chin, cheekbones sharply protrude forward - Facies cholericæ. The face expresses pain. The whole face of the patient is crying out for help.**

# Complications

**renal failure due to acute tubular necrosis.**

**Due to violations of hemostasis and microcirculation in patients of older age groups, myocardial infarction, mesenteric thrombosis, and acute cerebrovascular insufficiency are observed. Phlebitis is possible (with vein catheterization), pneumonia often occurs in severe patients.**





# Diagnostics

## Clinical diagnostics

**Clinical diagnosis in the presence of epidemiological data and a characteristic clinical features**

**(the onset of the disease with diarrhea followed by the addition of vomiting, the absence of pain and fever, the nature of vomit) is not complicated, however, mild, erased forms of the disease, especially isolated cases, are often not determined. In these situations, laboratory diagnosis is crucial.**



The main method of specific diagnosis of cholera is **bacteriological**, aimed at isolating a culture of pathogens from feces and vomit masses, and in case of fatal outcomes of the disease - from segments of the small intestine.



**Serological methods are of secondary importance and can be used mainly for retrospective diagnosis.**

**For this purpose, microagglutination in phase contrast, *IHAR* can be used, but it is better to determine the titer of vibriocidal antibodies or antitoxins (antibodies to cholero-gen are determined by ELISA or immunofluorescent method).**

**Recently, data have been obtained on a high sensitivity and specificity of PCR in the study of feces of patients**



# TREATMENT

**The primary task with any diarrhea is to compensate for the loss of fluid and salts in accordance with the degree of dehydration.**

**Therefore, patients with all forms of cholera are subject to mandatory hospitalization in specialized or temporary hospitals), where they undergo pathogenetic and etiotropic therapy.**



**Mandatory hospitalization of patients.**

**The basis of the treatment of cholera is pathogenetic therapy - rehydration. Patients with cholera need a special diet, and after the cessation of vomiting should receive normal food. Rehydration is carried out in two stages.**

**Stage I - rehydration.** The main task of this stage is to replenish the existing deficit of water and electrolytes based on signs of dehydration.

**Stage II - supporting.** The task of this stage is to compensate for the ongoing loss of fluid and electrolytes due to ongoing diarrhea to prevent return dehydration





**Oral rehydration is needed for cholera patients who do not vomit.**

**The WHO Expert Committee recommends the following composition: 3.5 g sodium chloride, 2.5 g sodium bicarbonate, 1.5 g potassium chloride, 20 g dextrose (Glucose\*), 1 liter of boiled water (solution oralit \*).**







**Vibrio cholerae is not capable of invasion of epithelial cells, fluid loss is associated only with the action of a toxin that causes the development of secretory diarrhea, accompanied by significant fluid loss and electrolytes in a relatively short period of time, which leads to severe dehydration, determines the severity and outcome of the disease.**

**▶ ▶ ▶ In this regard, antibacterial therapy is not leading in the treatment of cholera, since it only indirectly affects the main mechanism for the development of diarrhea. Nevertheless, antibiotics for cholera are absolutely indicated, regardless of the severity of the disease. Since they, firstly, affect the excretion of vibrio with feces, and secondly, they reduce the duration of the period of diarrhea.**



**In the treatment of cholera,  
traditionally used antibiotics,  
such as**

**tetracyclines, co-trimoxazole, nitrofurans.**

**Traditionally, doxycycline is prescribed at 0.1 g orally 2 times a day or tetracycline 0.5 g orally 4 times a day for 5-7 days.**

**Recently, there is an indication of the effectiveness of shorter courses of antibiotic therapy, while doxycycline is prescribed at a dose of 0.3. once.**



Rx

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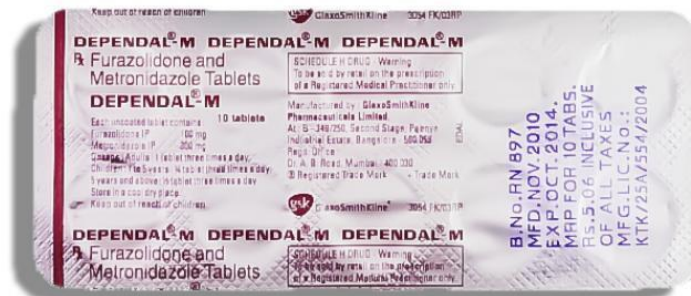
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**In the presence of resistance to traditional drugs, which is recorded quite rarely, it can be used (it is considered quite effective to reduce the course of therapy to 1 day).**

**fluoroquinolones: **ciprofloxacin** 0.5 - 1 g once for 3 days  
or**

****norfloxacin** 0.4 g twice a day for 3 days.**

**Against the background of taking antibiotics, the severity of diarrheal syndrome becomes smaller, and therefore the need for rehydration solutions is almost halved.**



# Prevention

**The basis of prevention are anti-epidemic measures to identify and eliminate the source of cholera:**

- imposition of quarantine;**
- Identification and isolation of persons (5 days) who had contact with infected people and environmental objects;**
- treatment of patients and vibriocarriers;**
- preventive treatment;**
- current and final disinfection.**





For specific prophylaxis, is used **cholera vaccine** and **cholero-gen toxoid**.

The vaccine is administered subcutaneously according to epidemiological testimony.



**A vaccine containing 8-10 vibrios per 1 ml is injected under the skin, the first time - 1 ml, the second time (after 7-10 days) - 1.5 ml.**

**Children 2-5 years old are administered 0.3 and 0.5 ml, 5-10 years old - 0.5 and 0.7 ml, 10-15 years old - 0.7-1 ml, respectively. Cholero-gen-anatoxin is injected once a year strictly under the skin below the angle of the scapula. Revaccination is carried out according to epidemic indications no earlier than 3 months after primary immunization. Adults are administered during vaccination and revaccination 0.5 ml of the drug, children from 7 to 10 years old - 0.1 and 0.2 ml, respectively, 11-14 years old - 0.2 and 0.4 ml, 15-17 years old - 0, 3 and 0.5 ml. The International Certificate of Vaccination against Cholera is valid for 6 months after vaccination or revaccination.**

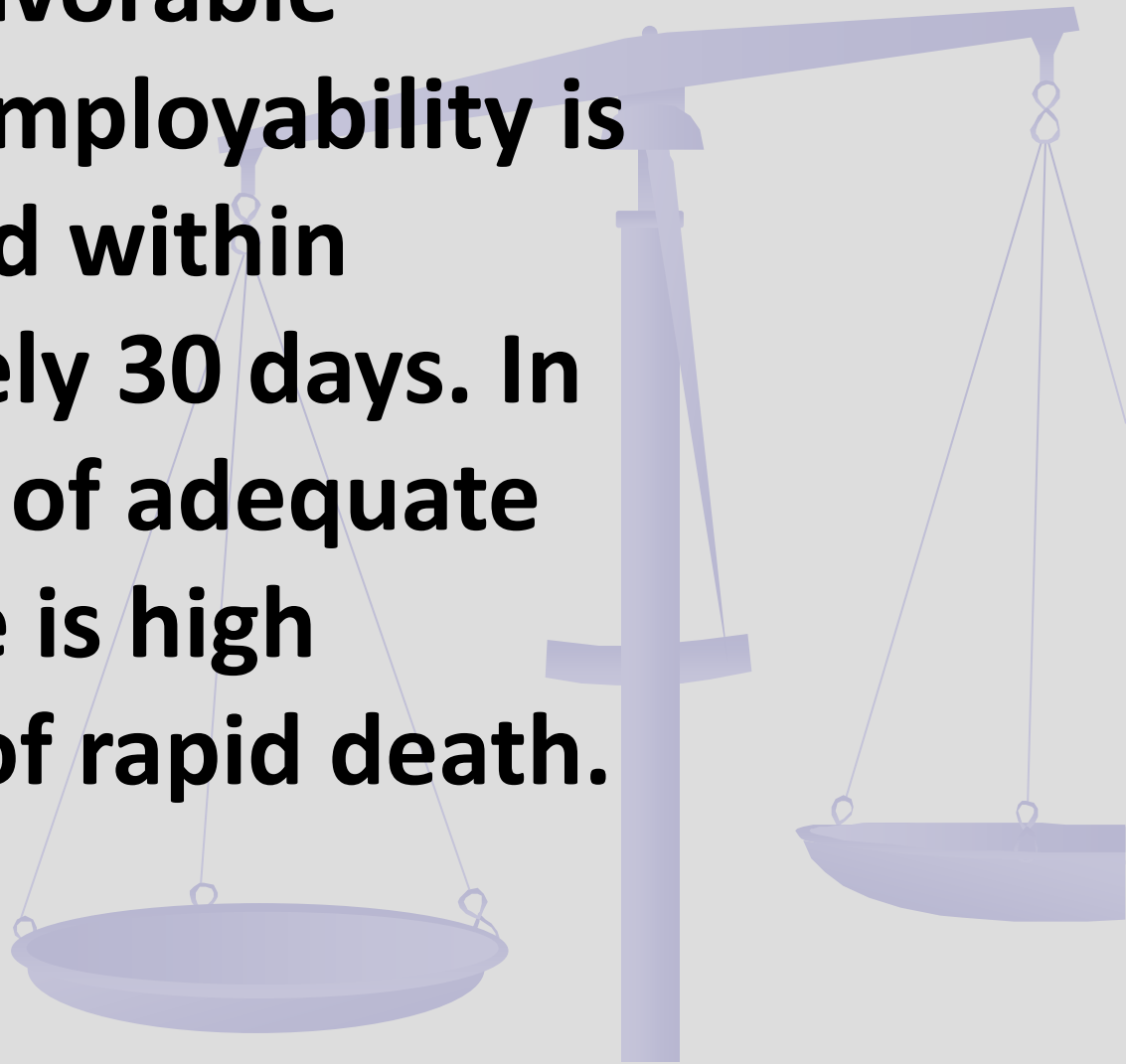


# *Forecast.*

**With timely and adequate therapy, favorable, lethality is close to zero, but it can be significant with fulminant form and delayed treatment.**

# Prediction

**With timely and adequate treatment favorable prognosis. Employability is fully restored within approximately 30 days. In the absence of adequate medical care is high probability of rapid death.**





# STOP CHOLERA

*it's in your hands!*

DRINK CHLORINATED OR  
BOILED WATER

WASH HANDS WITH SOAP AFTER  
USING THE TOILET AND BEFORE EATING

ALWAYS USE A LATRINE OR TOILET

EAT HOT, COOKED FOOD

WASH FRUITS AND PLATES  
IN CHLORINATED WATER

**PROTECT  
YOURSELF**



MEDECINS  
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