INFECTIOUS DISEASES

Cholera
(霍乱）

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Aim and Requirements

1. Grasp the clinical manifestations, diagnosis and differential diagnosis, treatment of cholera.

2. Familiar the epidemiology, pathogenesis for common cholera.

3. Familiar the the pathogen, the prevention of cholera.

Definition(定义）

Cholera is an acute diarrheal disease caused by Vibrio cholera(霍乱弧菌） that infect the small intestine.

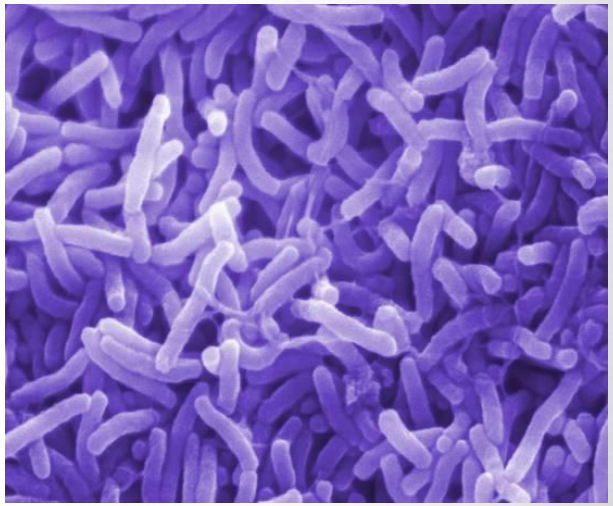
In our country, cholera is a kind of category A infectious disease.

Typical symptoms include large amounts of watery diarrhea（水样便）, vomiting（呕吐）, dehydration（脱水） and muscle cramps（肌肉痉挛）. Circulation failure（循环衰竭）and acute renal failure（急性肾衰竭）often happened in severe cases.

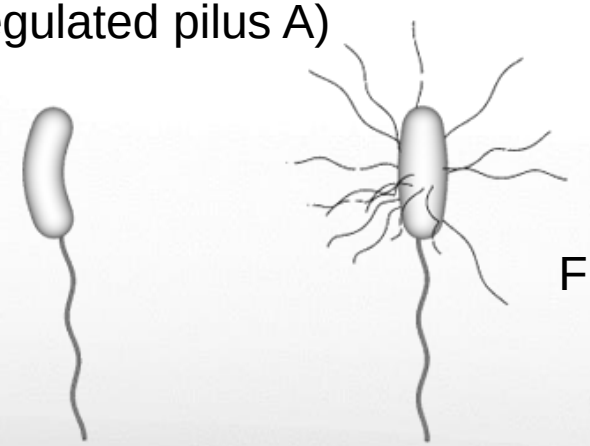
Up to 80% of cases can be successfully treated with oral rehydration salts (ORS).

Etiology（病原学）

- **Gram-negative, curved rod**
- **Motile, single polar flagellum**
- **They tolerate alkaline media that kill most intestinal commensals, but they are sensitive to acid.**



TcpA (toxic coregulated pilus A)



Flagellum

Etiology（病原学）

- O antigen（菌体O抗原）：somatic antigen, antigenic specificity in different serotype.

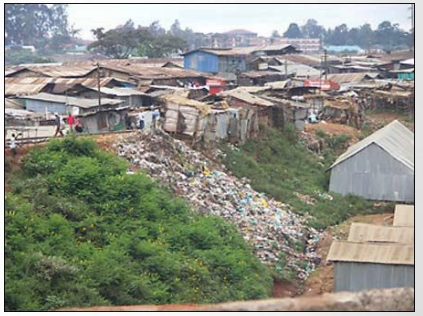
- H antigen（鞭毛H抗原）：flagellar antigen, common

Etiology（病原学）

- **O1：** the main pathogenic bacteria. Until 1992, cholera was caused by only three serotypes, Inaba (AC) and Ogawa (AB), Hikojima (ABC)and two biotypes, classical and El Tor.
- **Atypical O1:** nonpathogenic
- **O2~O200:** nonpathogenic or weak pathogenic
- **O139:** pathogenic, found in Indian and Bangladesh in 1992

Epidemiology（流行病学）

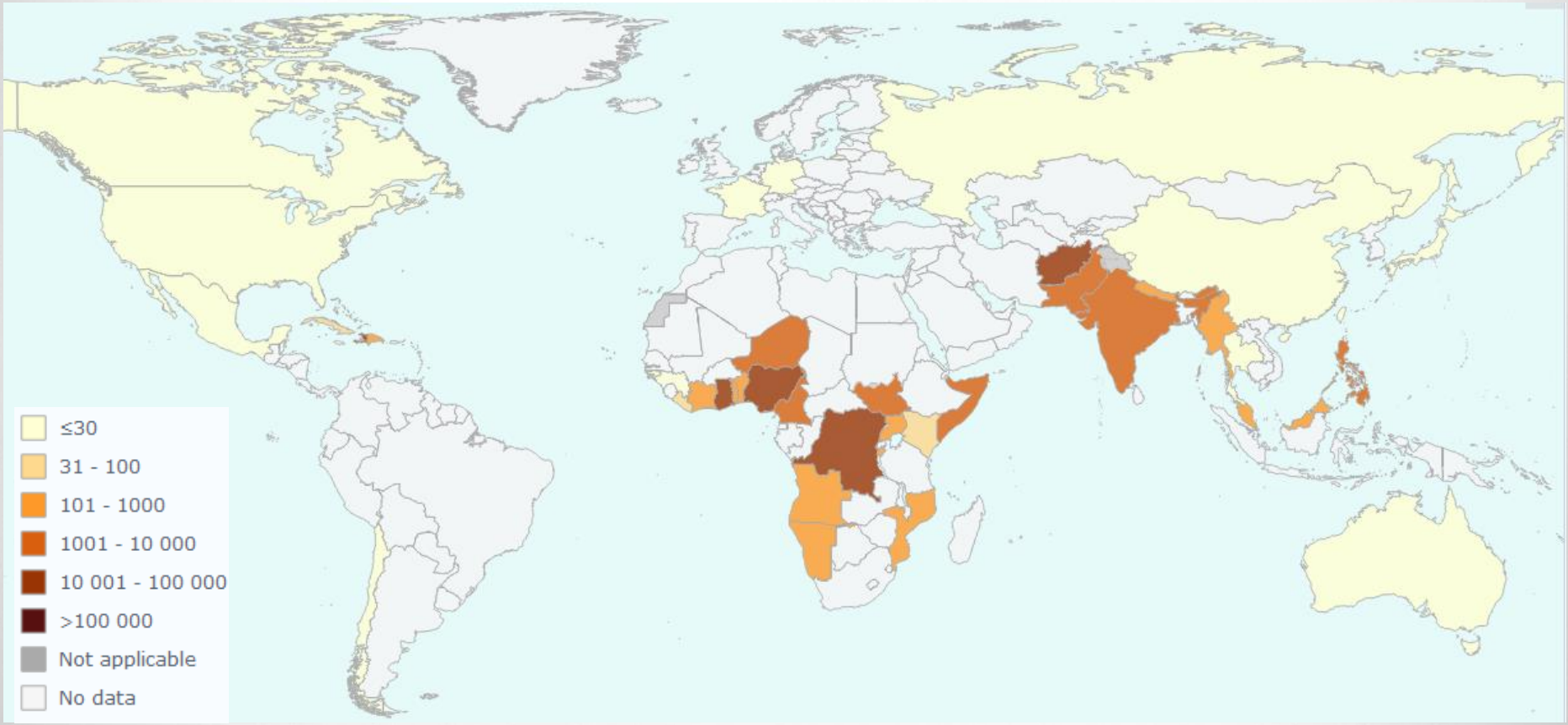
- Cholera can be spread as an endemic, epidemic, or pandemic disease.
- The disease caused by classical biotype of V cholerae swept the world in 6 great pandemics since 1817.



- In 1961, the El Tor biotype of V cholerae emerged from the Sulawesi, causing the 7th great cholera pandemic.
- In 1992, with the emergence of O139 in India and Bangladesh. It might be the 8th pandemic.

Epidemiology（流行病学）

Cholera in World



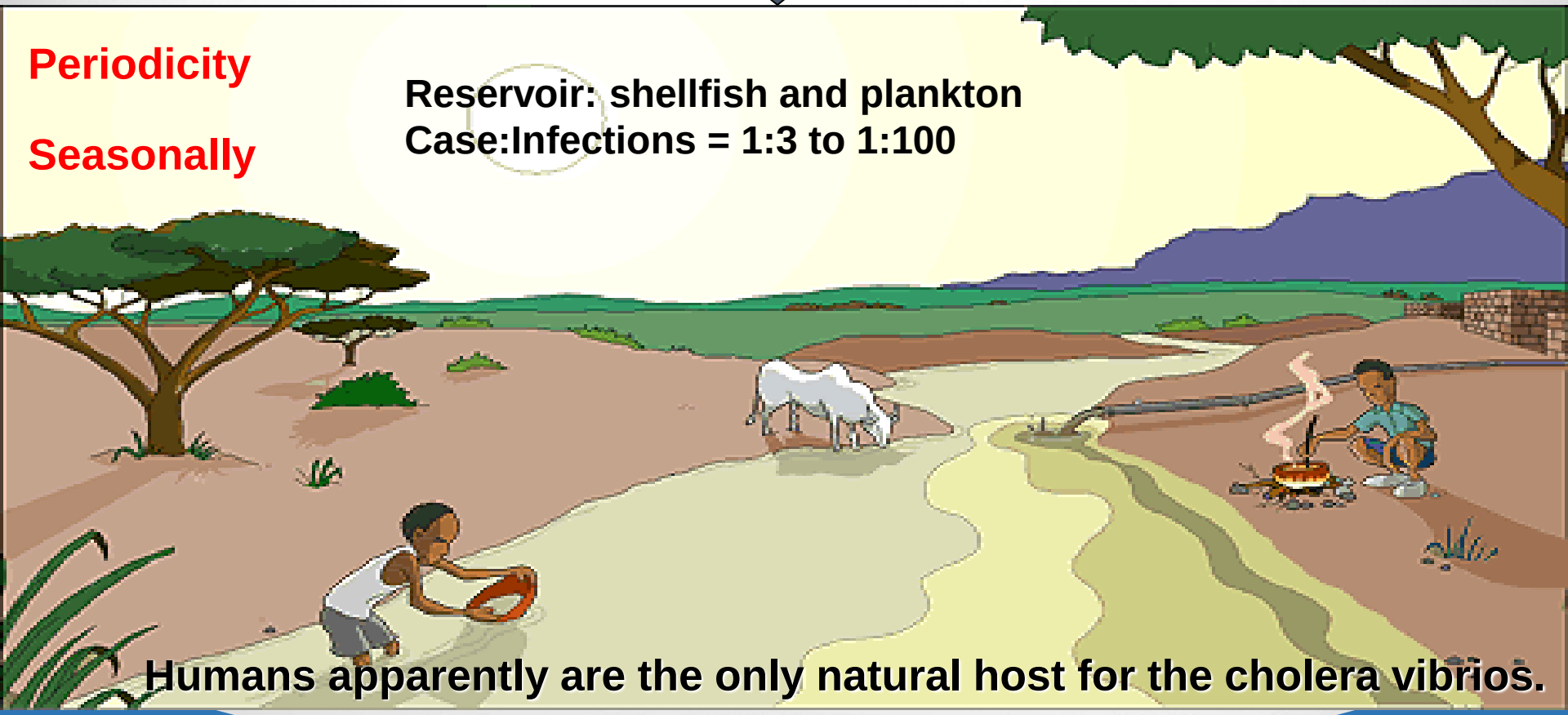
Epidemiology（流行病学）

symptomatic cases & asymptomatically infected individuals

Periodicity

Seasonally

Reservoir: shellfish and plankton
Case:Infections = 1:3 to 1:100



Humans apparently are the only natural host for the cholera vibrios.

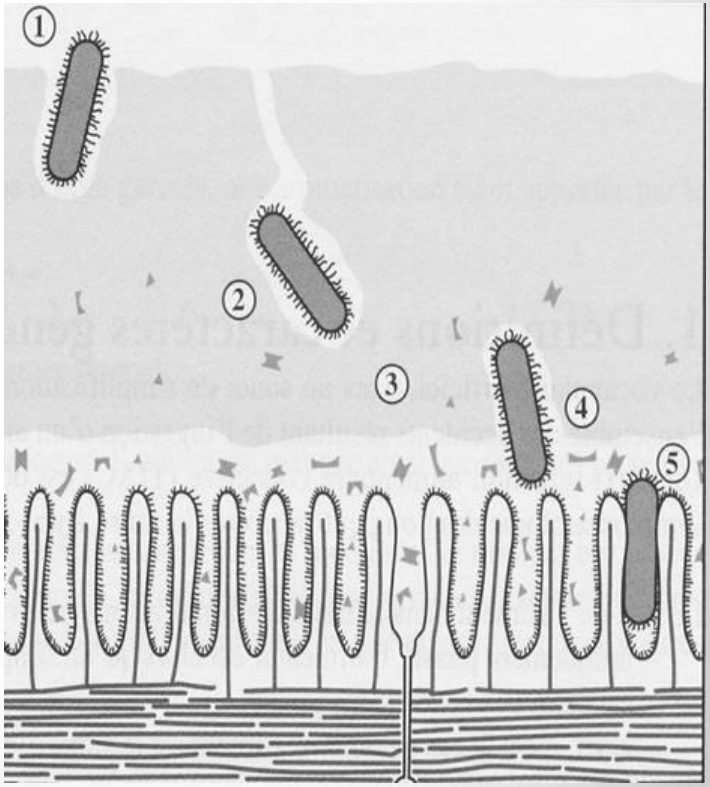
Pathogenesis（发病机理)

- **Immunologic status of host: gastric acidity, vaccine**
- **Amount of bacteria: 10^8-10^9**
- **Virulence**

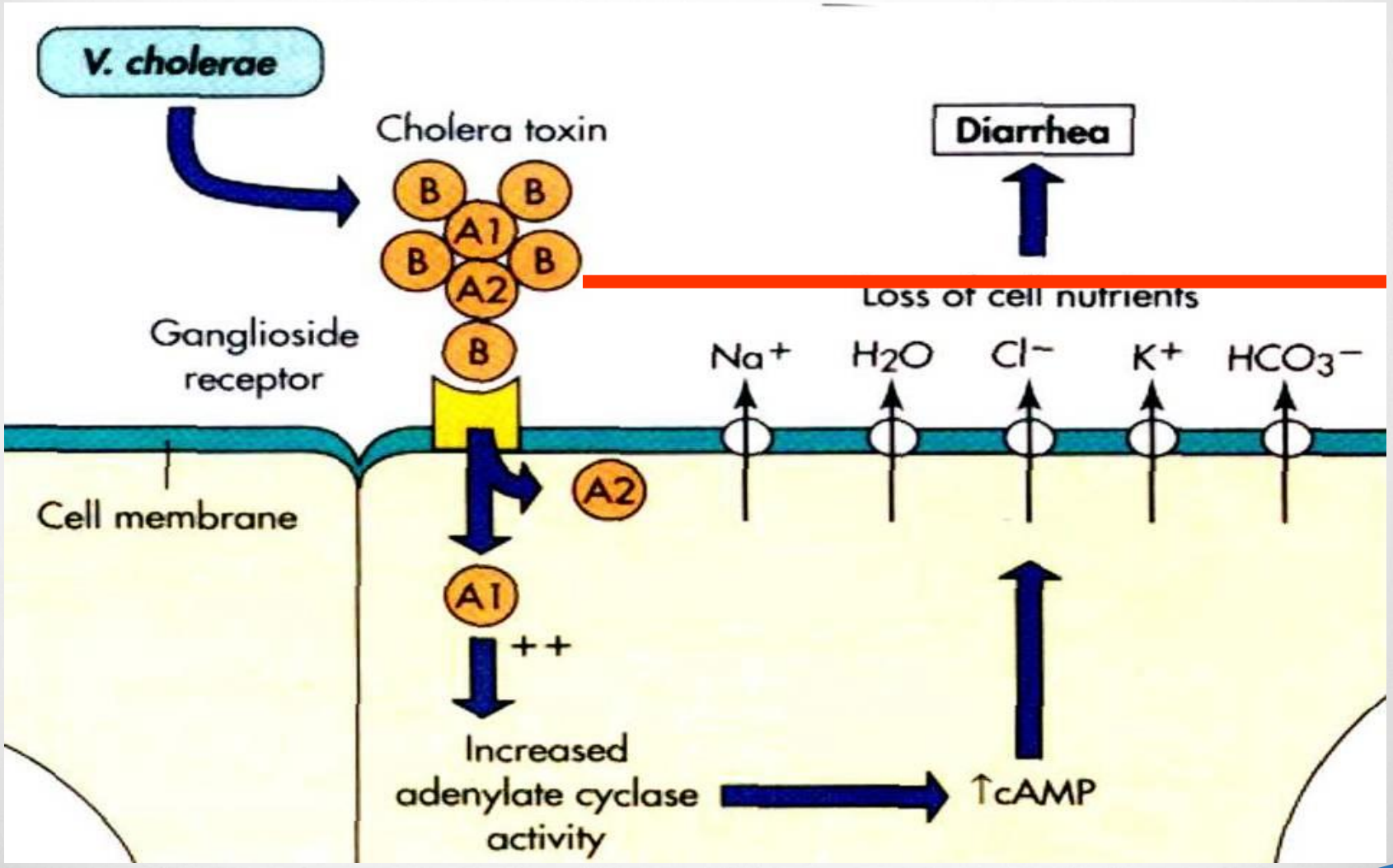
Pathogenesis（发病机理)

Small intestine is the place for the attachment of vibrio cholerae.

- Cholera toxin (CT, Choleragen，霍乱毒素)
- Toxin-coregulated pilus A(TcpA，毒素协同调节菌毛)
- Motility of the vibrios
- Hemagglutinins
- Mucinolytic enzymes
- Neuraminidase
- Proteases



Pathogenesis



Clinical manifestations（临床表现）

- Cholera is an extremely virulent disease.
- After infected with V. cholerae, 75% do not develop any symptoms.
- People who develop symptoms, 80%: mild or moderate symptoms; 20%: watery diarrhea with severe dehydration.
- People with low immunity (such as malnourished or with HIV) : greater risk of death if infected.
- Voluminous watery diarrhea and vomiting result in hypovolemic shock, electrolyte disturbance and acidosis .

Clinical manifestations

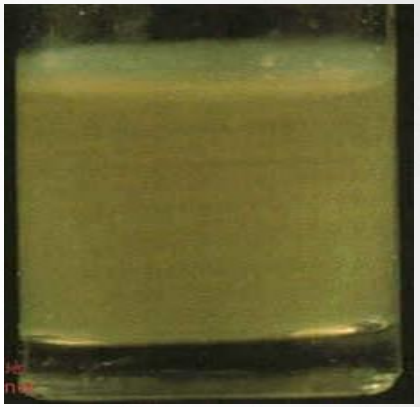
Stage 1: Diarrhea and Vomiting(泻吐期）

- Abrupt onset of diarrhea
- “Quiet” diarrhea
- Vomiting after diarrhea

Clinical manifestations

- V cholerae does not elicit an inflammatory response. few leukocytes and no erythrocytes in stool
- frequent and often uncontrolled bowel movements. abdominal cramps
- O139: 40-50% abdominal cramps and fever
- acute, severe, watery diarrhea
- The stool may contain fecal material early in the course of disease. a rice water appearance

Clinical manifestations



“rice water”

Clinical manifestations

Stage 2: Dehydration （脱水期）

Mild (1000 ml) thirst develops, dry skin, skin elasticity ↓

Moderate (3000-3500 ml) thirsty, skin elasticity ↓ ↓, sunken eyes, tachycardia, blood pressure↓, urine ↓

Severe (4000ml) Lethargic , weak or absent pulses, very sunken eyes, wrinkled skin, urine ↓ ↓ ↓, coma

Clinical manifestations

Stage 2: Dehydration （脱水期）

- Muscle cramps （肌肉痉挛）： Loss of electrolyte
- Hypopotassemia（低血钾）
- Metabolic acidosis（代谢性酸中毒）, uremia（尿毒症）
- Hypovolemic shock （低血容量性休克）， circulatory failure(循环衰竭）

Clinical manifestations

Stage 3: Convalescence（恢复期）

if the patient is adequately treated with fluid and electrolytes, complications are averted and the process is self-limited, resolving in a few days.

Clinical manifestations

Cholera sicca（干性霍乱）

- This is an uncommon, severe form of cholera.
- There is massive outpouring of fluid and electrolytes into dilated intestinal loops.
- No diarrhea and vomiting.
- Toxic shock and die.

Accessory Examination（辅助检查）

Hematological tests

- **Hemoconcentration*:*** **Hematocrit, serum-specific gravity, and serum protein are elevated .**
- **First observed, they generally have a leucocytosis without a left shift.**

Accessory Examination

Serum electrolytes

- Sodium: 130-135 mmol/L
- Potassium : normal or ↓.
- Bicarbonate : less than 15 mmol/L in severely dehydrated patients .

Accessory Examination

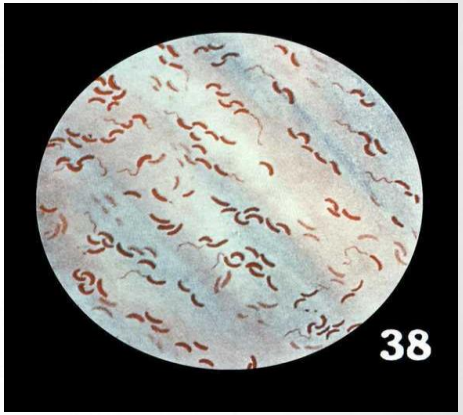
Renal profile

Blood urea nitrogen and serum creatinine are elevated, reflecting the decrease in glomerular filtration.

WBC, RBC and protein can be positive in urine.

Accessory Examination

Etiological examination



- Direct microscopic examination:

  cholerae is a gram-negative curved bacillus .

- Dark field organism:

  The characteristic motility can be examined easily by direct dark field examination of the stool.

  Moreover, it can be confirmed by adding Vibrio antisera, which results in cessation of motility of only the homologous organism.

Accessory Examination

Etiological examination

Culture:

Alkaline enrichment media: As Vibrio species has the ability to grow at a high pH or in bile salts, peptone water (pH 8.5-9) or selective media containing bile salts are recommended to facilitate isolation and lab diagnosis.

Accessory Examination

Etiological examination

Rapid bacteriologic diagnosis:

offers relatively little clinical advantage to the patient with secretory diarrhea.

Nevertheless, rapid identification of the agent can profoundly affect the subsequent course of a potential epidemic outbreak.

Complications（并发症）

- **Acute renal failure:** prerenal, and then renal tubular necrosis, azoyemia and even uremia

- **Acute pulmonary edema:** metabolic acidosis → pulmonary hypertension

Diagnosis（诊断）

1. Epidemiologic data and history

2. Clinical features: symtoms and signs

3. Lab findings

Differential Diagnosis（鉴别诊断）

- **Bacterial food poisoning**
- **Bacillary dysentery**
- **Bacterial diarrhea caused by *E. Coli*, salmonella**
- **Viral gastroenteritis caused by Rotavirus.**

Treatment（治疗）

Principle:

- **Strict quarantine（严格隔离）**
- **Rehydration in time（及时补液）**
- **Antibiotics adjuncts（抗菌治疗）**
- **Symptomatic treatment （对症治疗）**

Treatment

- **Rapid correction of hypovolemia and metabolic acidosis and prevention of hypokalemia are important.**
- **Oral administration of a glucose-electrolyte solution is effective in replacing stool losses and may be used after initial IV rehydration.**

Treatment

The oral solution(ORS) recommended by the WHO :

Glucose: 20 g

Sodium chloride: 3.5 g

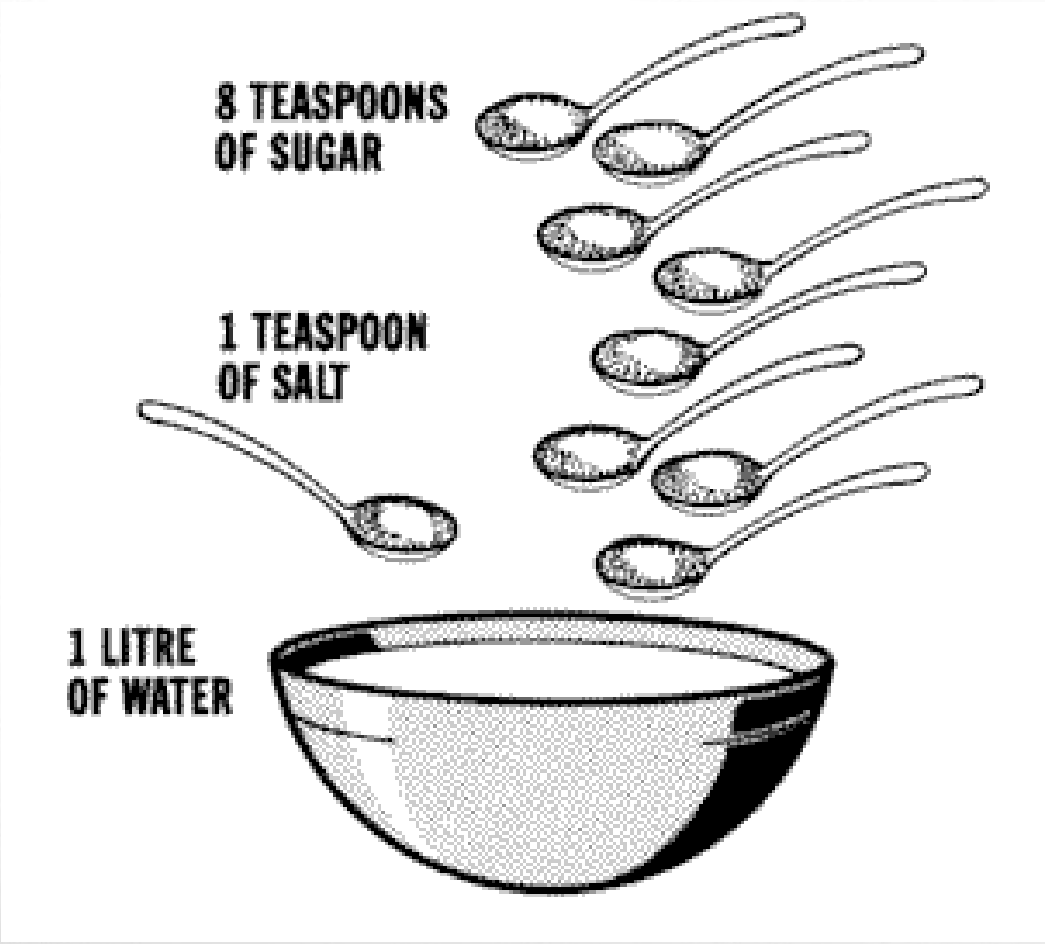
Sodium bicarbonate: 2.5 g

Potassium chloride:1.5g

per liter of water.

Treatment

A simple way to prepare “ORS”



Treatment

SOLUTION 541 with glucose for IV infusion:

Sodium chloride	5g	0.9%NaCL	550ml
Sodium bicarbonate	4g	5%$NaCO_3$	80ml
Potassium chloride	1g	10%KCL	10ml
Glucose	10g	10%GS	140ml

Treatment

Mild dehydration:

- 3000~4000ml in 24 hours
- 3~5ml/min
- Patients who are first observed with no signs of dehydration can be treated with ORS packets .
- In the first 6 hours, ORS 750 ml / h

Treatment

Moderate dehydration :

- 4000~8000ml in 24 hours
- 5~10 ml/min
- 2000ml in 2 hours
- 2000ml +total loss in 12 hours
- Administer ORS solution according to the condition of dehydration

Treatment

Severe dehydration

- Administer IV fluid immediately to replace fluid deficit. 8000~12000ml/d
- First 2 hours: 40~80 ml/min,then 20~30 ml/min
- Monitor the patient very frequently. After the initial administration, the pulse should be strong and blood pressure should be normal.
- Reassess the patient after 3 hours.

Treatment

Use of oral antibiotics in patients with severe dehydration:

- reduce the volume of diarrhea
- shorten the period during which V cholerae O1 is excreted.
- shortening the period of hospitalization.

Treatment

- **Begin antibiotic therapy after the patient has been rehydrated (usually in 4-6 h) and vomiting has stopped.**
- **The choice of antibiotics is determined by the susceptibility patterns of the local strains of V cholerae O1 or O139.**
- **Ciprofloxacin, Norfloxacin, doxycycline, SMZ**

Prevention（预防）

- **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.**
- **Oral cholera vaccines are considered an additional means to control cholera, but should not replace conventional control measures.**

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The end