Microbiology
437

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MED437
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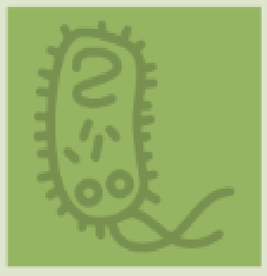
CHOLERA

BACTERIAL INFECTION OF GIT

Tip: We recommend you to start this lecture by reading the notes

Vibrio Cholera

Overview	• A waterborne live threatening diarrheal disease. • Caused by *vibrio cholera* which is a comma- shaped gram-negative rods. • Found in salt and freshwater. • Has many serotypes based on O-antigen. • O 1 and O 139. • Produce a non-invasive enterotoxin. • Leads to outbreak and epidemic. • Can be prevented by good sanitation system.
Discovery	• **John Snow** discovered an outbreak in **London 1854** • It was related to **broad street pump** sewage contamination. • Removal of the pump handle →end of the outbreak..
Epidemiology	• V. cholera O1 and O139 serogroup organisms are the causes of epidemic cholera. • O1 (from 1817 till now) • Classical: 1 case per 30-100 infections • El Tor: 1 case per 2-4 infections (Seventh pandemic) • O139 (recently in 1992 in Asia only) • Contained in India, Bangladesh. • Seven major outbreaks. • Majority in India, Sub-Saharan Africa, Southern Asia. • Endemic in > 50 countries. • Each year 3-5 millions cases result in 100,000 deaths.
Risk factors	• Children, elderly and people with less gastric acidity are at higher risk than others • Blood group O>> B > A > AB.
Transmission	• Fecal- oral transmission through contaminated food or water. • Common in summer grows in brackish estuaries and coastal seawaters, often in close association with copepods or other zooplankton. • Sewage or infected person contaminate water supply. • Not well established sewage system and water treatment. • Undercooked shellfish.

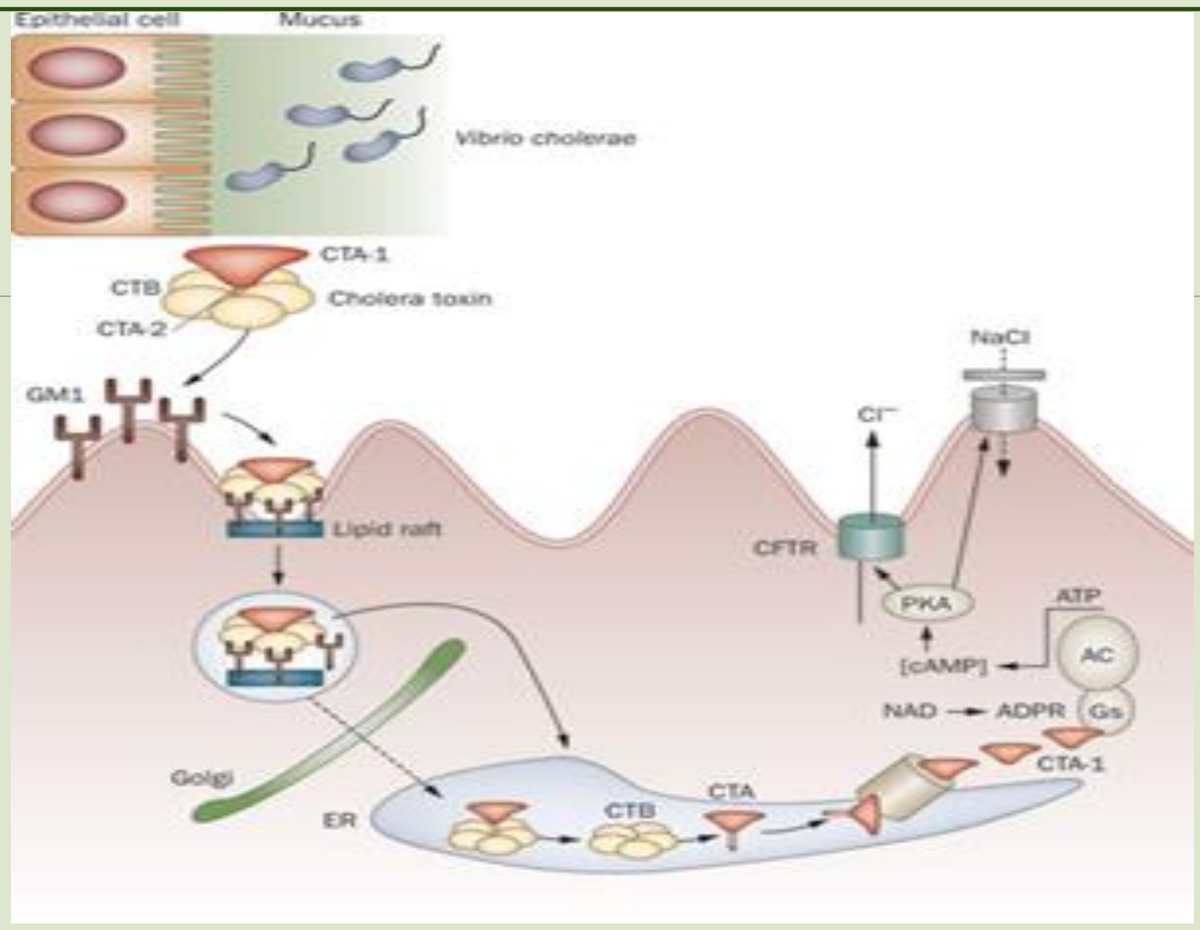
Infectivity

- Period of infectivity during acute stage till recovery (end one to three wks)
- Infected person can produce up to 20 L of 10^9 CFU/ml /day
- Has high infectious dose NOT like Shigella
- Infectious dose **10^6-10^{11}** colony-forming units (not highly virulent)
- Due to harsh environment of the intestine i.e. temperature and stomach acidity and Bile salts, organic acids in the intestine.

Pathogenesis (previous lecture)

- Vibrio cholerae uses toxin-coregulated pili (TCP) to colonize the human intestine.
- Cholera results from secretory diarrhea caused by the actions of cholera toxin (Enterotoxin) on intestinal epithelial cells.
- CT is an adenosine diphosphate–ribosylating enzyme that leads to chloride, sodium, and water loss from intestinal epithelial cells. → leads to rice water diarrhea
  - GM1, a glycosphingolipid on the surface of epithelial cells
  - Enzymatic A subunit of cholera toxin mediates
  - Nicotinamide adenine dinucleotide (NAD) → Adenosine diphosphate (ADP)-ribose → G protein → Regulates adenylyl (adenylate) cyclase activity (AC) → elevation in the intracellular cyclic adenosine monophosphate (cAMP) concentration

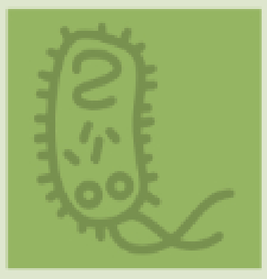
❖ Monosialoganglioside (GM1) receptor



Clinical Manifestations:

- ❖ Ranges from a few hours to 5 days(range 1-3 days).
- ❖ Depending on gastric acidity (antacids) and initial infectious dose.
- ❖ Majority have mild, or no symptoms at all
- 75% asymptomatic
- 20% mild disease
- 2-5% severe

20% mild disease	• Vomiting, • Cramps • Watery diarrhea (1L/hour) with flecks of white mucus (rice water stool) with a fishy odor (no fever)
2-5% severe symptoms **Cholera gravis:**	• More severe symptoms due to Rapid loss of body fluids (6 liters/hour, 10^{7-9} vibrios CFU/mL) → hypovolemic shock(severe metabolic acidosis due to inadequate O) and electrolytes imbalance(↓ Ca^{++} and K can lead to ileus, muscle pain and spasm, and even tetany)→multi failure organ (Cardiac and Renal failure). • Rapidly lose more than 10% of body weight • Dehydration and shock • Sunken eyes, and ↓skin turgor (tenting), cold and clammy. • Anuric and lactic acidosis (Kussmaul breathing). • Hypoglycemia leads to seizure or comma. • Aspiration pneumonia
Prognosis	• **Mild disease**→Death occurred in 18 hours-several days if not treated due dehydration. • **Severe symptoms**→•Death within 2-12 hours or less. •Mortality 50-60% without treatment •Mortality <1% with redehydration.

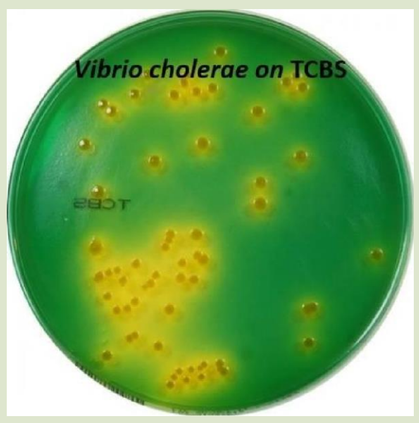



Diagnosis:

- Suspect in severe diarrhea with dehydration.
- Other non-invasive bacterial, ETEC and viral gastroenteritis might have similar presentation.
- Complete history and physical examination.
- Insert central line for IV fluid, collect blood for basic routine tests (chemistry and hematology).
- Send stool for smear and culture on special media.
- Culture not routinely performed, you have to request it.
- Dark field microscopy (shooting stars)
- Gram stain (curve Gram Negative bacilli)
- Culture on **thiosulfate citrate bile sucrose (TCBS)** agar-yellow colonies
- Recovery of organisms can be enhanced by enrichment of stool in alkaline peptone water. (60-100%).

Diagnosis/ microbiology:

- *Vibrio cholera* is highly motile, gram-negative, curved or comma-shaped rods with a single polar flagellum.



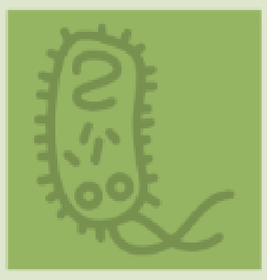
String test:
if the organism is growing it will be like a honey

Dont memorize these charts

Biotype O 1 antigen	Serotype	Antigen
Classical	Ogawa	A,B
	Inaba	A,C
	Hikojima	A,B,C
El Tor	Ogawa	A,B
	Inaba	A,C
	Hikojima	A,B,C

O 139 serogroup appeared in Bangladesh 1992
Has polysaccharide capsule but does not have O1 antigen

Non-O1, Non-O139 Serogroup
Most are CT (cholera toxin) negative and are not associated with epidemic disease.



Treatment

- Basically rehydration and antimicrobial therapy.
- Rehydration should be started immediately before confirming the diagnosis.
- Either oral rehydration if the patient can tolerate it (not vomiting or start IV rehydration).
- Decrease mortality from 50% to 1 %.
- Give 1.5 time the amount lost.
- Start when 10% of total body weight lost.
- Patients recovered within 3-6 days.
- Oral Rehydration Salt (ORS) by WHO and UNICEF
- One pack in 1 liter contain NaCl, KCl, $NaHCO_3$, glucose
- IV use either Ringer's lactate, Saline or Sugar and water.

Antibiotics:

- Reduce the recovery time to 2-3 days.
- Decrease infectivity

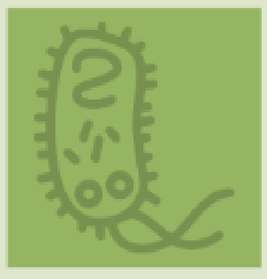
➢ **Azithromycin** single-dose is often the preferred therapy especially in children.

➢ **Ciprofloxacin**(not for pts younger than 18,but you can use it because its life saving)

➢ **Tetracycline, Doxycycline (not in patients younger than 7)**

Can be a bioterrorism agents:

- Ease of procurement
- Simplicity of production in large quantities at minimal expense
- Ease of dissemination with low technology
- Silent dissemination.

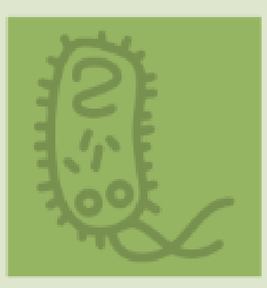
Prevention:

➔Wash your hand frequently
➔Boil water and chlorination.
➔Cook all types of food very well.
➔Avoid salad, ice and iced food
➔Water Sanitation
➔Water treatment
➔Disrupt fecal-oral transmission if present.

International Efforts:

- **WHO:** Global Task Force on Cholera Control
- Reduce mortality and morbidity
- Provide aid for social and economic consequences of Cholera
- **CDC**
- **U.N.: GEMS/Water**
- Global Water Quality Monitoring Project
- Addresses global issues of water quality with monitoring stations on all continents

	Killed Whole-cell Vaccines	**Live Attenuated Vaccines**
Adult	50% protection for 6 months	60% protection for 2 years
children aged 2-5	< 25% protection	protection rapidly declines after 6 months
Doses	Multiple doses	3 dose
Side effects	----------	Mild diarrhea, abdominal cramping

Summary
Vibrio Cholera

Description	● A waterborne live threatening diarrheal disease. ● Caused by *Vibrio Cholera* which is a comma- shaped gram-negative rods. Which is found in salt and freshwater. ● Serotypes (O 1 and O 139). ● Produce a non-invasive enterotoxin.
Transmission	● Fecal- oral transmission through contaminated food or water. ● Sewage or infected person contaminate water supply. ● Undercooked shellfish.
Infectivity	● During acute stage till recovery (end one to three weeks) ● Infected person can produce up to 20 L of 10^9 CFU/ml /day ● Infectious dose **10^6-10^{11}** colony-forming units
Pathogenesis	● Vibrio cholerae uses toxin-coregulated pili (TCP) To colonize the human intestine. ● secretory diarrhea caused by the actions of cholera toxin (enterotoxin)
Clinical Manifestations	● Ranges from a few hours to 5 days(range 1-3 days). ● Depending on gastric acidity and initial infectious dose. ● **75% asymptomatic** ● **20% mild disease:**Vomiting -Cramps -Watery diarrhea (1L/hour) with flecks of white mucus (rice water stool) with a fishy odor ● **2-5% severe(Cholera Gravis):** More severe symptoms due to Rapid loss of body fluids Causing Hypovolemic Shock & electrolytes imbalance.
Prognosis	● **mild disease**→ Death in 18 Hours-days if not treated due dehydration. ● **severe symptoms**→ Death within 2-12 hours or less. ● Mortality 50-60% without treatment DECREASE to 1% with redehydration.
Diagnosis	● Complete history and physical examination. ● Collect blood for routine tests ● stool for smear and culture on special media. ● Dark field microscopy (shooting stars) ● Gram stain (curve Gram Negative bacilli) ● Culture on **thiosulfate citrate bile sucrose (TCBS)** agar-yellow colonies ● Recovery of organisms can be enhanced by enrichment of stool in alkaline peptone water. (60-100%).
Treatment	● Rehydration ● **Azithromycin** single-dose is often the preferred therapy especially in children. ● **Tetracycline,doxycycline**(**not** for pts younger than 7) ● **Ciprofloxacin**(**not** for pts younger than 18,but you can use it because its life saving)
Prevention	● **General prevention:**hand wash, cooking food well water cleaning...etc ● **Killed Whole Cell Vacc:**50% for adults for 6 months- 25% children -multiple doses. ● **Live Attenuated Vacc:**60% for adults for 2 years-declines after 6 months -3 doses-Side effects: mild diarrhea, abdominal cramping.

Dr's Notes

❖ **introduction**:

- Cholera is a curved gram negative bacteria,that causes rice-watery(with mucous) diarrhea usually through contaminated water**,** it lives within shellfishes it prefers in salt water, It may contaminate water after an earthquake due to the mixing between sewage and water. patients may die **why**?Because of dehydration→renal/cardiac failure.**treated** by→dehydration Can be prevented by vaccines

❖ **epidemiology:**

- Old type O1/new type O139 in india bangladesh(O=somatic antigen)
- There is an outbreak in yemen right now

❖ **Transmission:** fecal-oral

- Due to water contaminated by sewage
- Undercooked shellfish

❖ **Infectivity**: it needs a higher infectious dose than shigella and salmonella

- Period of infectivity is 1-3 weeks so you have to isolate them

❖ **Pathogenesis:** (he said just know the following)

- They have enterotoxin and it will increase cAMP leading to increased Na+ and water secretions

❖ **Clinical manifestation:**

➔It depends on gastric acidity and patients immunity

➔Most people are asymptomatic, 5% have severe symptoms

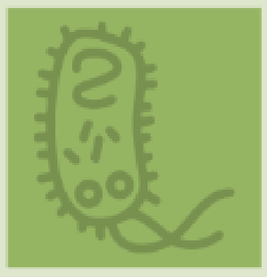
➔It causes rice water stool Patient will lose 1L/hour.

➔Death may occur due to dehydration

- **Cholera gravis(severe):**

➔Death will be fast he will lose 10% of his weight

➔They will have signs of dehydration:sunken eye ,turgor(elastic) skin. They will be anuric and hypoglycemic) so you need to rehydrate them very fast

❖ **Diagnosis:**

- Suspected if severe diarrhea or pts(patient) is coming from an endemic area other non-invasive bacteria may produce non-invasive diarrhea but it won't be as severe is cholera
- **Stool smear and culture:**
- microscope will show shooting stars gram -ve curved bacilli
- culture media is TCBS(thiosulfate citrate bile sucrose for all vibrio not just V.cholera)
- string test: if organism is growing it will be like honey

❖ **Treatment** :

- Rehydration and antibiotics
- Rehydration: more important than antibiotics we gave it IV if pts is vomiting
- Antibiotics:

➔Azithromycin(patient younger than 7 because others are contraindicated)

➔Ciprofloxacin(not for pts younger than 18,but you can use it because its life saving)

➔tetracycline(**not** for pts younger than 7)

❖ **Prevention:**

- **2 vaccines killed and live attenuated**

➔**Killed vaccine: -less** efficient **-less** side effect **-**we **used for travelers**

➔**Live-attenuated: -more** effective **-more** side effects **-used in outbreaks**

❖ **Summary:**

★ **V.cholera:** a Gram negative, motile, lactose non-fermentative bacteria

★ **Source:** shellfish

★ **transmitted:** fecal orally by drinking contaminated water

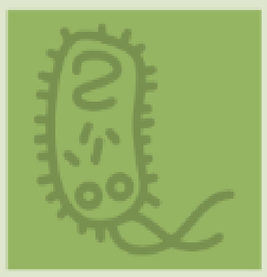
★ **leading to:** severe watery diarrhea

★ **Diagnosis:** by smear→ shooting stars

★ **The culture media:** TCBS ,results can be confirmed by string test

★ **Treated:** by rehydration and azithromycin/ciprofloxacin/tetracycline

★ **prevented:** by killed and live attenuated

QUIZ:

1.Which of the following is true about cholera?
A-non-motile
B-gram - curved rods
C-low infection dose
D-transmitted sexually

2.Which of the following is high risk for v.cholera infection ?
A-overcooked shellfish
B-low gastric acidity
C-low infection dose
D-good hygiene

3.In cholera gravis how many litter of the fluid is lost ?
A-6L/H
B-1L/H
C-3L/H
D-4L/H

4-A tsunami tidal wave hits the east coast of South America and the people living there are forced to drink unclean water. Within the next several days, a large number of people develop severe diarrhea and about half of these people expire. Samples of drinking water are positive for Vibrio cholerae. Which of the following types of ion channels is most likely to be irreversibly opened in the epithelial cells of the crypts of Lieberkühn in these people with severe diarrhea?
A) Calcium channels
B) Chloride channels
C) Magnesium channels
D) Potassium channels

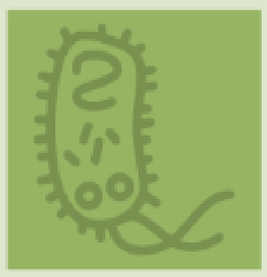
Case:A middle-aged man returns from a trip to yemen and immediately begins passing voluminous, watery diarrhea. When he is seen in the emergency department, he is suffering from dehydration and has tachycardia but no fever. While in the emergency department, he is given fluids and electrolytes.

5.What is the most likely etiology?

6.Which of the following should have been given before traveling?

A-prophylaxis antibiotics
B-live attenuated vaccine
C-killed vaccine
D-I.V. normal saline

1/B 2/B 3/B 4/B 5/V.cholera 6/C

THANK YOU!

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