

Vibrio cholerae

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Objectives

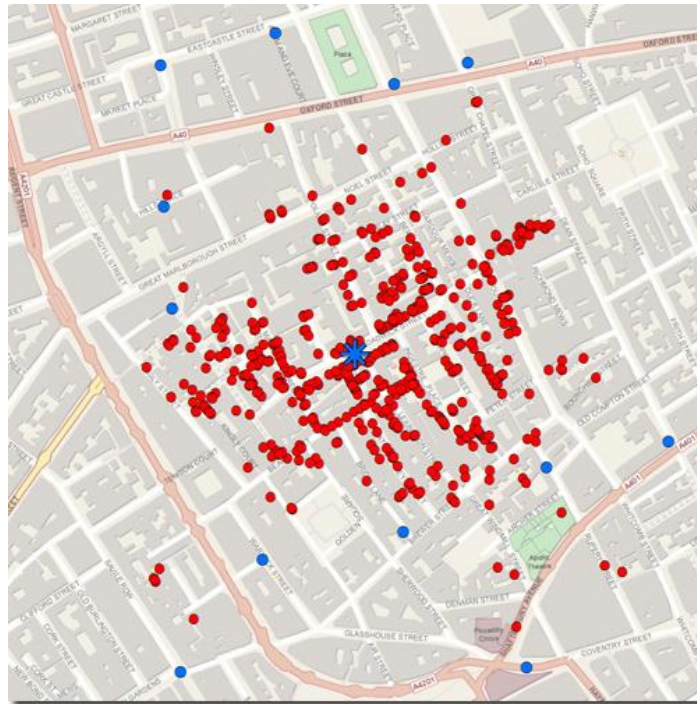
- Recall the epidemiology of cholera and history of cholera
- Recall the microbiological characteristic of *V. cholerae*
- Describe the pathogenesis of cholera
- Describe the clinical features of cholera
- Describe the methods for laboratory diagnosis
- Recall the management of cholera and control of outbreak

Introduction

- A water born live threatening diarrheal disease.
- Caused by *vibrio cholerae* which is a comma- shaped gram-negative rods.
- Found in salt and fresh water.
- 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

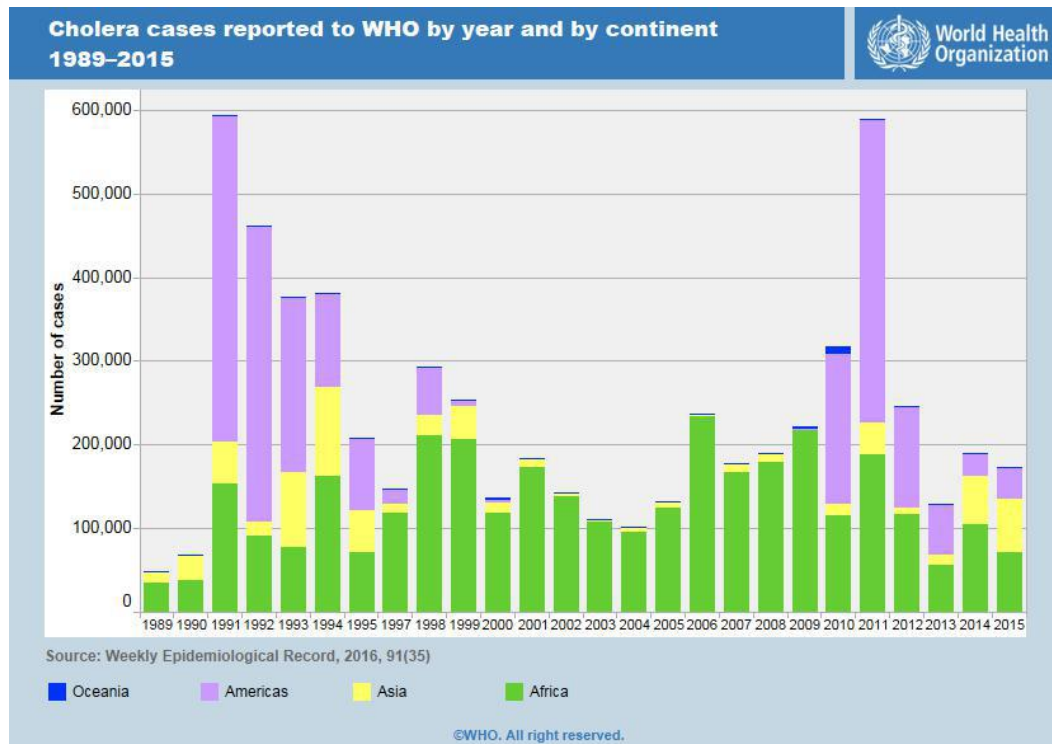
- **John Snow** discovered an outbreak in **London 1854**
- It was related to **broad street pump** sewage contamination.
- Removal of the pump handle → end of the outbreak.



Epidemiology

- *V. cholerae* 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.

Epidemiology



- In 2016 in Haiti after Hurricane Matthew, in South Soudan and Yemen and many other African countries

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.
- Under-cooked shellfish.
- Children, elderly and people with less gastric acidity are at higher risk than others
- Blood group O >> B > A > AB

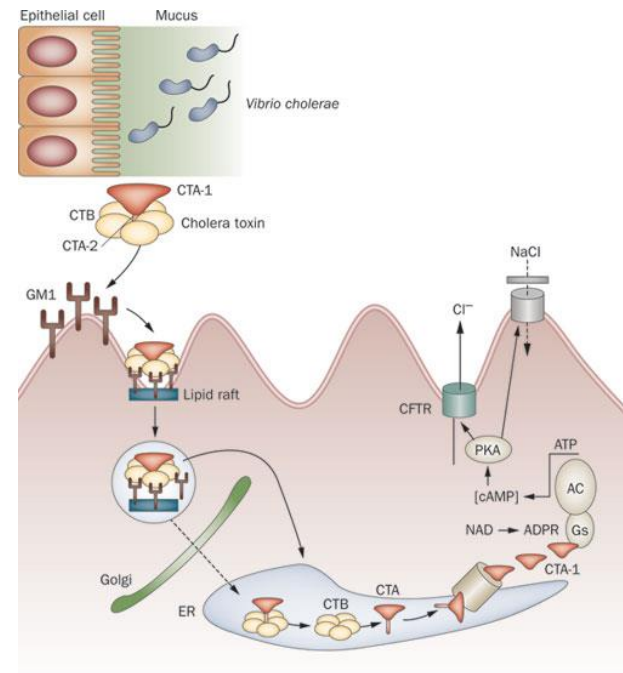
Infectivity

- 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
 - Due to harsh environment of the intestine ie 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 (CT) on intestinal epithelial cells.
- CT is an adenosine diphosphate–ribosylating enzyme that leads to chloride, sodium, and water loss from intestinal epithelial cells.
- 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 adenine monophosphate (cAMP) concentration

Monosialoganglioside (GM1) receptor



Clinical Manifestations

- Ranges from a few hours to 5 days (range 1-3 days).
- Depending on gastric acidity and initial infectious dose.
- Majority have mild, or no symptoms at all
 - 75% asymptomatic
 - 20% mild disease
 - 2-5% severe
- Vomiting, Cramps and Watery diarrhea (1L/hour) with flecks of white mucus (rice water stool) with a fishy odor
- Death occurred in 18 hours-several days if not treated due dehydration.
- ↓ Ca^{++} and K can lead to ileus, muscle pain and spasm, and even tetany

Clinical Manifestations

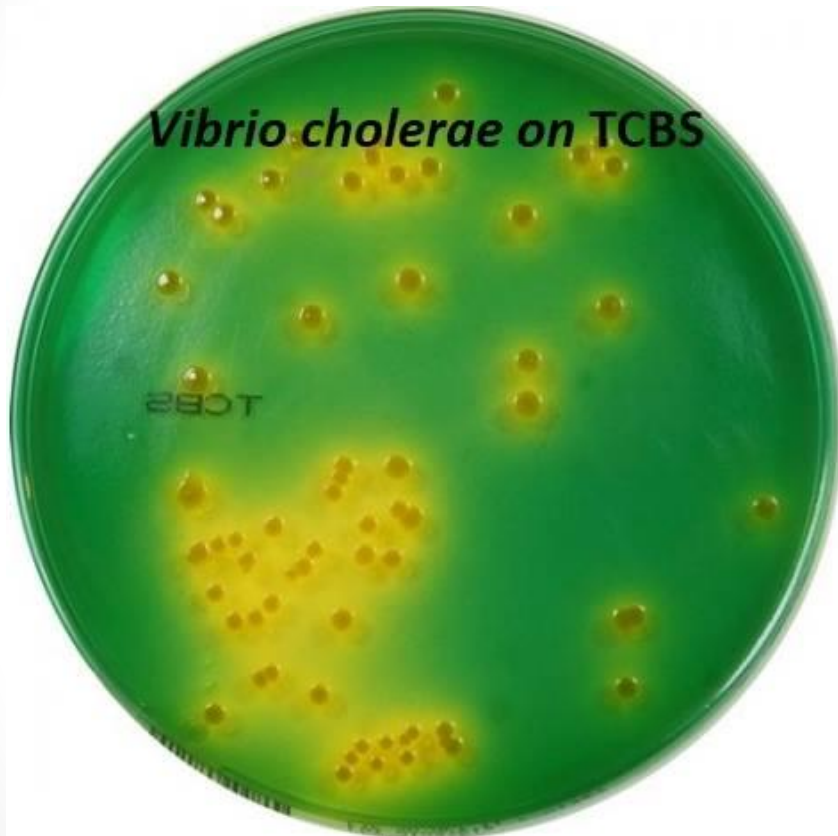
- **Cholera gravis:**
- More severe symptoms due to Rapid loss of body fluids
- 6 liters/hour
- 10^{7-9} vibrios CFU/mL
- Rapidly lose more than 10% of bodyweight
- Dehydration and shock
- Sunken eyes, and ↓skin turgor (tenting), cold and clammy.
- Anuric and lactic acidosis (Kussmaul breathing).
- Hypoglycemia leads to seizure or comma.
- Cardiac and Renal failure.
- Aspiration pneumonia
- Death within 2-12 hours or less.
- Mortality 50-60% without treatment
- Mortality <1% with rehydration



Diagnosis

- Suspect in sever 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%)

Microbiology



Diagnosis/ microbiology

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

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 poly saccharide 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, NaHCO₃, 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.

Or

- **Ciprofloxacin**

Or

- **Tetracycline, Doxycycline**

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

	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	
Side effects	-----	Mild diarrhea, abdominal cramping

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