



Cholera

Laboratory Diagnosis and Management

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COMMUNICABLE DISEASES**

Division of the National Health Laboratory Service



Presentation outline

- Introduction
 - Microbiology of the organism
- Epidemiology
 - Risk factors for acquiring cholera
- Clinical Manifestations
- Laboratory diagnosis
- Management
- Prevention and Control

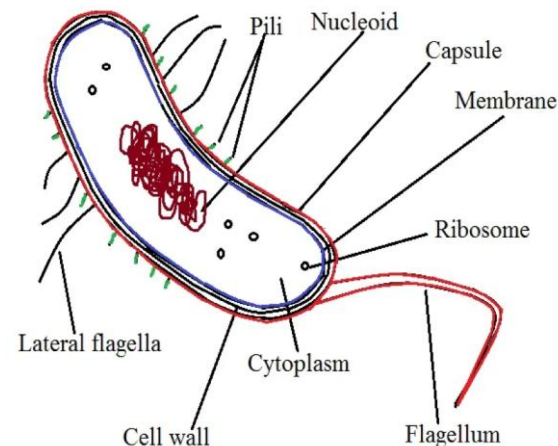
Cholera

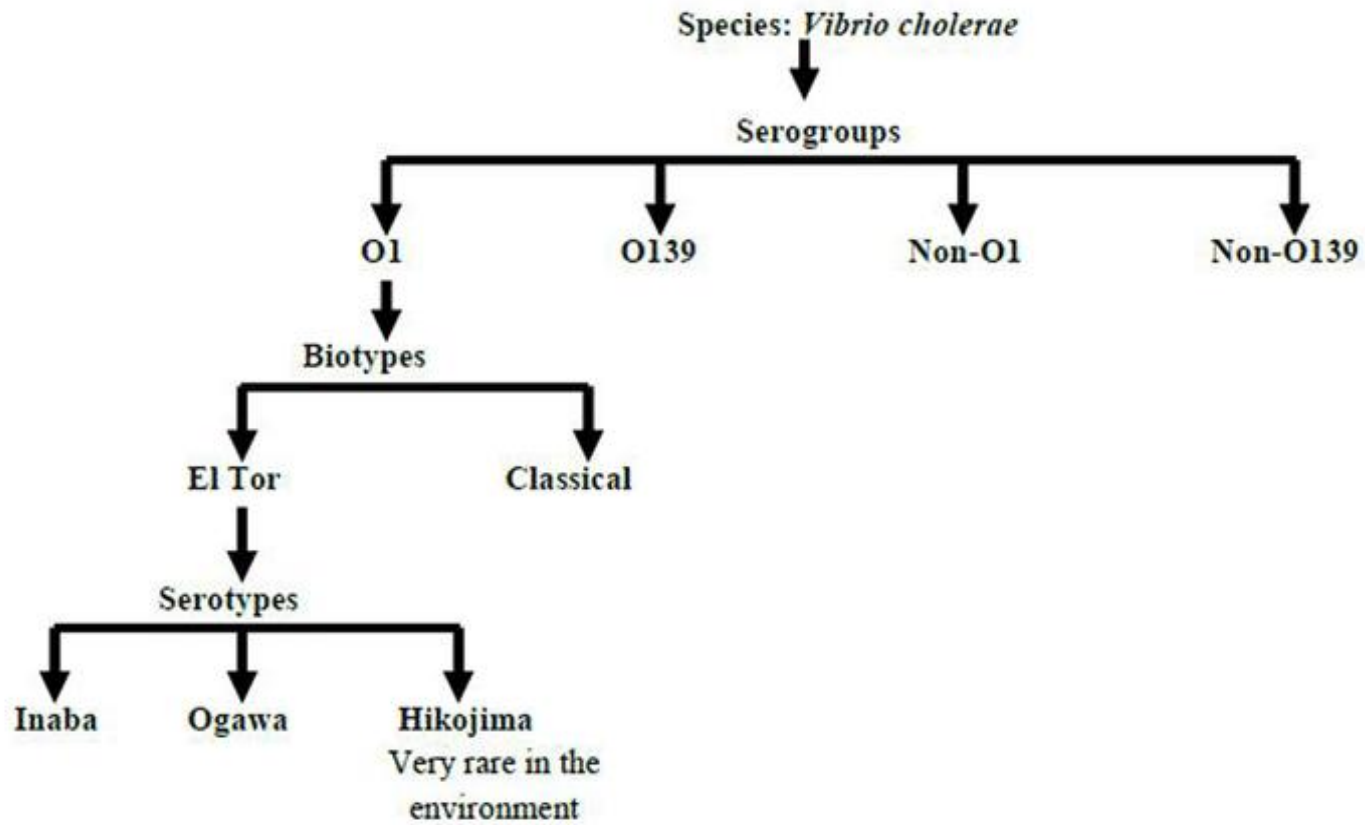
- Cholera is an acute diarrhoeal disease caused infection with the toxigenic ***Vibrio cholerae*** serogroup **O1** or **O139**.
- Seven global cholera pandemics have occurred over the last 200 years, driven primarily by trade routes, poor sanitation, and contaminated water.
- The first six took place across the 19th and early 20th centuries, while the **current seventh pandemic began in 1961 and remains ongoing today**.
- The World Health Organization classifies the seventh pandemic as ongoing, driven by climate shocks, conflict, and fragile water sanitation infrastructure in parts of Asia and Africa.



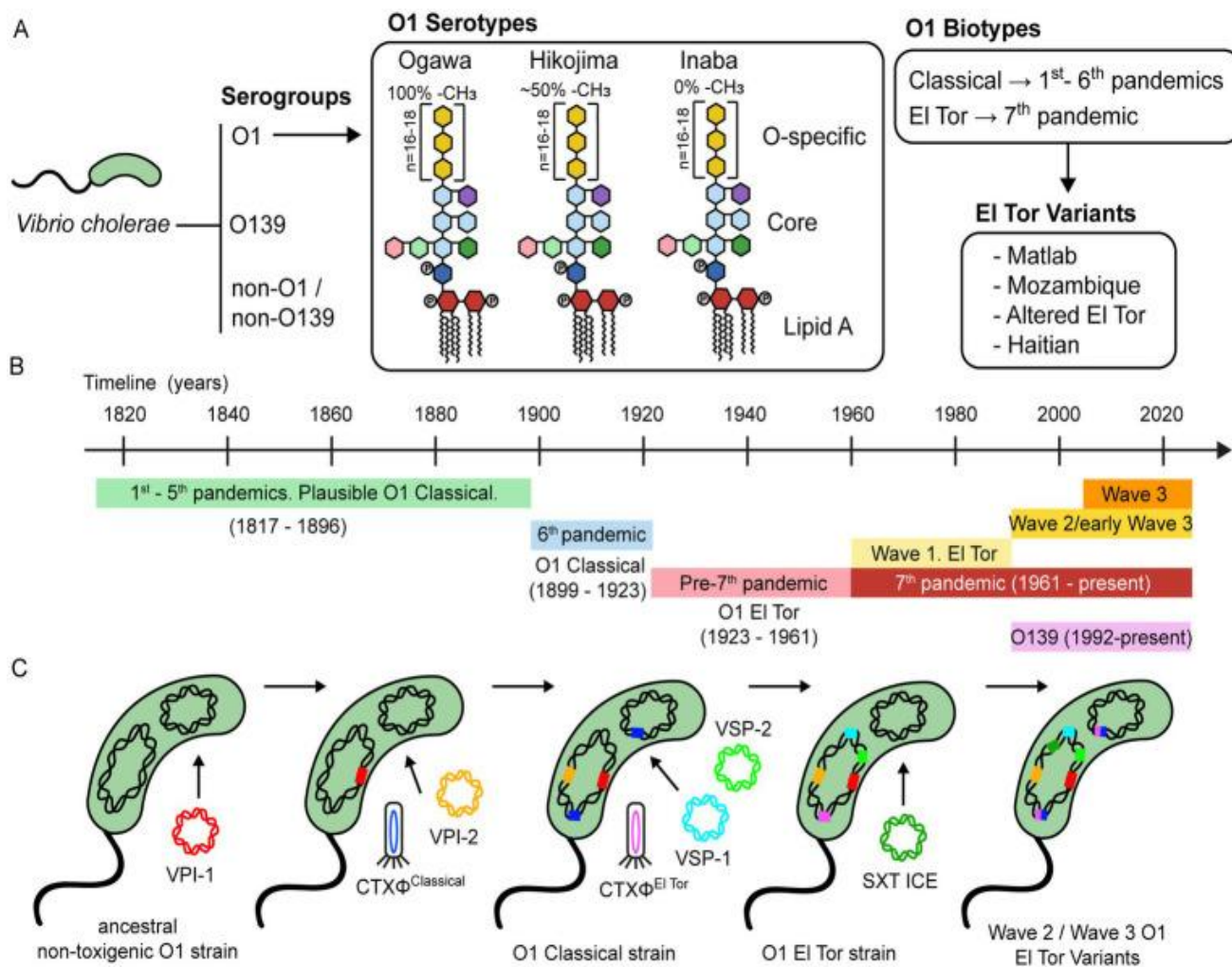
Lets break down *Vibrio. spp.*

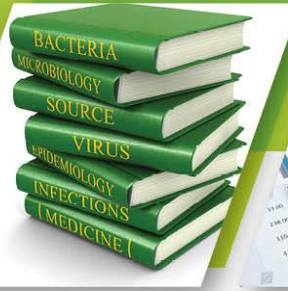
- *Vibrio spp.* that cause disease in humans are divided into 2 groups:
 - *Vibrio cholerae*
 - Non-cholera Vibrios (NOVC)
- ***Vibrio cholerae*** is the aetiologic agent of cholera epidemics and pandemics in humans.
- The different *V.cholerae* strains are divided according to differences in their cell wall structure (**somatic O antigen**) which is the basis of serotyping scheme that classifies the organism into 139 different serogroups.





- 
- **O1 serogroup**
 - Agglutinated by O1 antisera
 - All pandemics & most epidemics of cholera
 - **O139 serogroup**
 - Since 1992: several epidemics & outbreaks: India & Bangladesh
 - **Non O1/O139 serogroups (O2 –O138)**
 - occasional sporadic outbreaks of diarrhoea & extraintestinal manifestations
 - never epidemic cholera
 - Neither major serotype is inherently more severe or lethal than the other.





Epidemiology



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Core Epidemiologic Features

- Reservoir: Humans are the **primary reservoir**, along with aquatic environments where the bacteria attach to crustacean zooplankton called copepods.
- Transmission: Feecal-oral route via contaminated drinking water or food (such as raw or undercooked seafood).
- Infectious Dose: High (typically 10^3 to 10^6 organisms), though lower in achlorhydria or when ingested in food/buffer.
- Incubation Period: Range from 2 hours to 5 days, commonly 1 to 3 days.



Detailed Epidemiology

- Both O1 and non-O1 strains co-exist in the environment with non-O1 and non toxigenic strains O1 predominating over toxigenic O1 strains.
- *Vibrio cholerae* lives attached to a copepods which co-exist in a symbiotic manner.
- When conditions in the environment are suitable (temp, salinity, nutrients), *V. cholerae* can multiply and survive for years in a free living cycle without human intervention.
- Otherwise when conditions are unsuitable, it switches to a dormant state.
- When it is in a dormant state, it cannot be cultured from water and can survive harsh conditions.
- *V.cholerae* also produces biofilms (surface associated bacterial communities – survive under harsh conditions and are able to switch to active forms and induce epidemics)





Detailed Epidemiology

- Cholera is spread through the feacal-oral route, either directly from person-to-person or indirectly through contaminated fluids from an environmental reservoir, or from food and potentially flies and fomites.
- Persons with cholera infection excrete *V. cholerae* in their stool.
- The period of excretion may be as short as one day in asymptomatic infected contacts, whereas the stool of symptomatic patients may contain the bacteria prior to the illness and for up to 1–2 weeks.



Epidemiologic Features	Epidemic Pattern	Endemic Pattern
Age	All ages	Children 1 -5 years
Mode of T/M	Single introduction with feacal-oral spread	Multiple modes of introduction- water, food, feacal-oral spread
Reservoir	None	Aquatic reservoir
Asymptomatic infection	Less common	Asymptomatic people more common
Immune status of population	No pre-existing immunity	pre-existing immunity
Secondary Spread	High	Variable



Clinical Manifestations

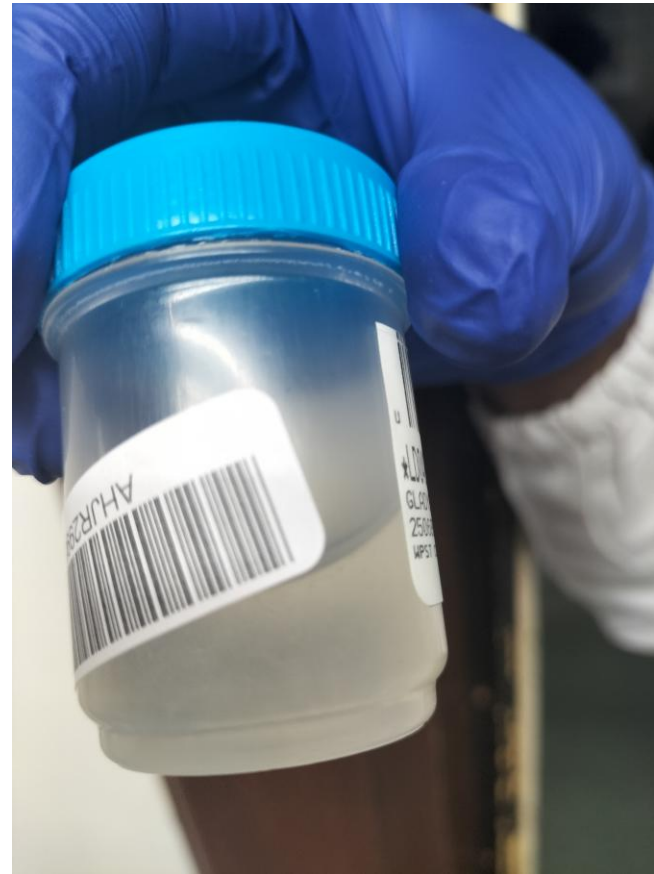
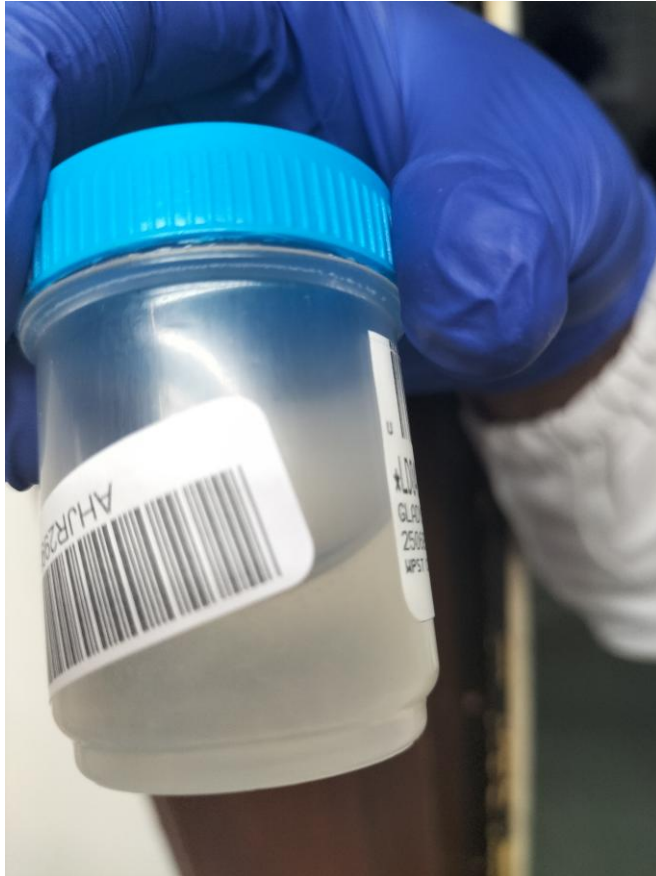
- Cholera can cause severe acute watery diarrhoea, which can be fatal within hours if untreated.
- Most people infected with *V. cholerae* do not develop symptoms or have mild or moderate symptoms but can spread the bacteria through their faeces for **1–10 days**.
- A minority of patients develop severe acute watery diarrhoea and life-threatening dehydration.
- The median time from infection to onset of disease (incubation period) is 1.4 days, with 5% of cholera cases developing symptoms by 12h and 95% by 4.4 days after infection.
- **Diarrhoea is usually painless** and may contain bile or faecal matter in the early stages of infection.



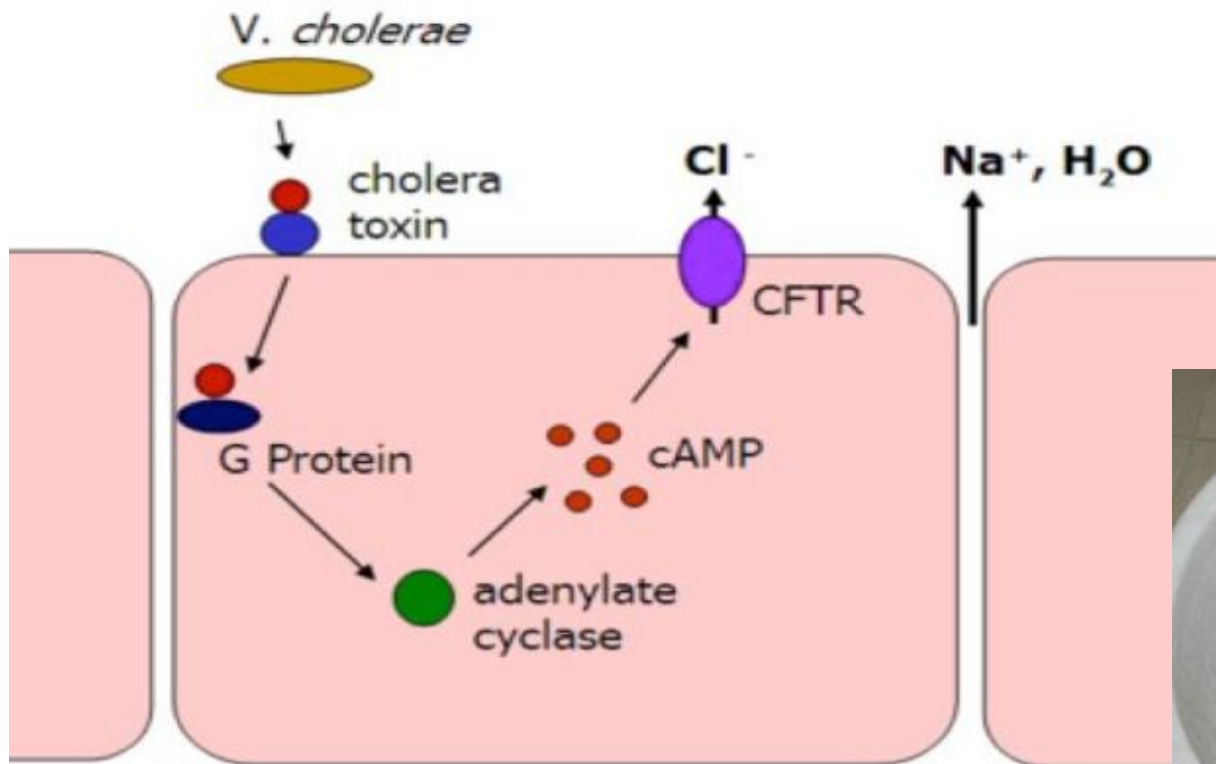
- **“Rice water stools”** are unique to cholera patients
- They are starchy in colour, look more like water that has been used to wash rice and have a fishy odour.
- An adult cholera patient can produce up a litre per hour of loose watery stool, leading to hypovolemia, shock, and death.
- Signs of dehydration (e.g., sunken eyes, tears, dry mouth, thirst, rapid pulse, lethargy, cold skin, loss of skin elasticity, or crumpled hands and feet) are present due to profuse watery diarrhoea.
- Hyperventilation and acidosis are some of the striking features of severe cholera.
- Symptomatic cholera patients can shed bacteria in their stool for 2 days to 2 weeks from the onset of infection, whereas asymptomatic carriers shed for only a few days.

Cholera stool appearance

- The rice-water appearance



Pathophysiology



Cholera Dehydration Assessment Quick Reference



World Health
Organization

Adults & Children



Degree of Dehydration	Signs	Treatment	Admission to CTU/CTC
Severe Dehydration	One or more danger signs: • Lethargic or unconscious • Absent or weak pulse • Respiratory distress OR at least 2 of the following: • Sunken eyes • Not able to drink or drinks poorly • Skin pinch goes back very slowly	PLAN C	Yes
Some Dehydration	No danger signs AND at least 2 of the following: • Irritable or restless • Sunken eyes • Rapid pulse • Thirsty (drinks eagerly) • Skin pinch goes back slowly	PLAN B	Yes
No Dehydration	• Awake and alert • Normal pulse • Normal thirst • Eyes not sunken • Skin pinch normal	PLAN A	No

References (scan QR code)
1. World Health Organization. Cholera control



Notification

- Cholera is a **category 1** Notifiable Medical Condition in South Africa.
- Immediate reporting telephonically followed by written or electronic notification on the **NMC App** within 24hrs of diagnosing a case.
- Early notification of suspected cases will ensure that the diagnosis is confirmed early, and that measures are implemented to prevent additional cases.
- The healthcare worker who identifies a suspected case should notify health authorities immediately.
- Healthcare workers should **NOT** wait for laboratory confirmation before notifying cases.

NMCSS accounts that have not logged in for more than 12 months may be locked. Please log in at least once a year to keep your account active. Contact the NMCSS Technical Team for assistance if your account is locked.

You can help **contain** the spread of an **Outbreak**

Viruses don't **discriminate** and neither should we. It's personal, yet **global**. Let's fight it **together**



PREVENT



DETECT &
REPORT



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 Overview



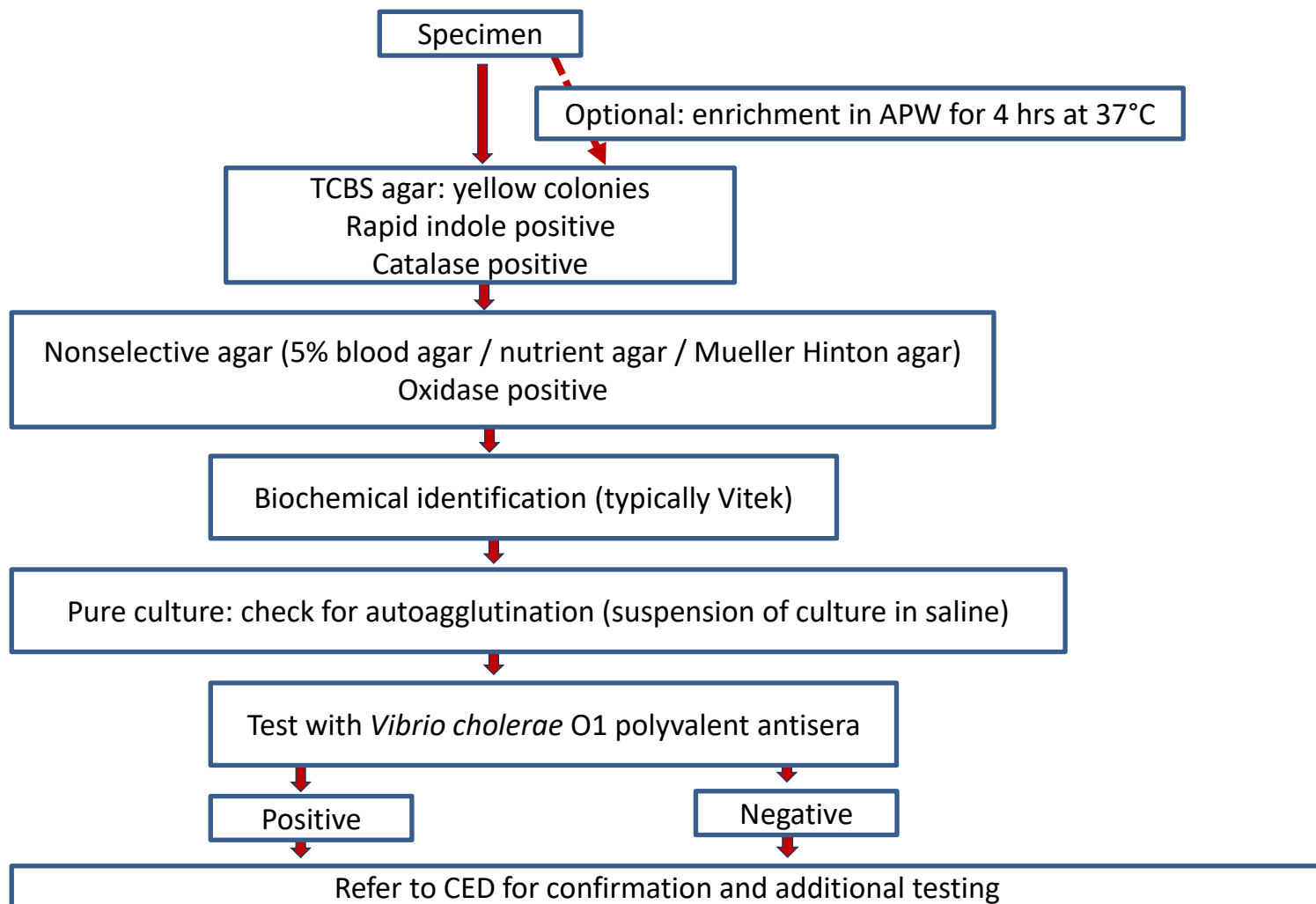
Sample collection

- Obtain specimen collection material from the laboratory (universal specimen container, rectal swab).
- If the laboratory is on-site, collect stool specimen in universal specimen container and submit immediately.
- If a delay of >2 hours between specimen collection and processing at the laboratory is likely, obtain transport media from the laboratory (**Cary-Blair transport media is recommended**).
- Dip a swab into the stool specimen and place the swab into the bottle of Cary-Blair transport medium.
- Mark specimen clearly: '**suspected cholera**'!!!

Laboratory diagnosis

- The diagnosis of cholera is frequently based on clinical signs and symptoms and a positive travel history.
- For the diagnosis of cholera, stool or rectal swab culture is the specimen of choice.
- Stool/rectal swab culture remains the gold standard method to detect cholera.
- *V. cholerae* diagnosis using PCR is highly sensitive, but this technique needs an enhanced laboratory capacity, which is often lacking in most LMICs.
- Culture media: TCBS media and Alkaline peptone water (enrichment broth)

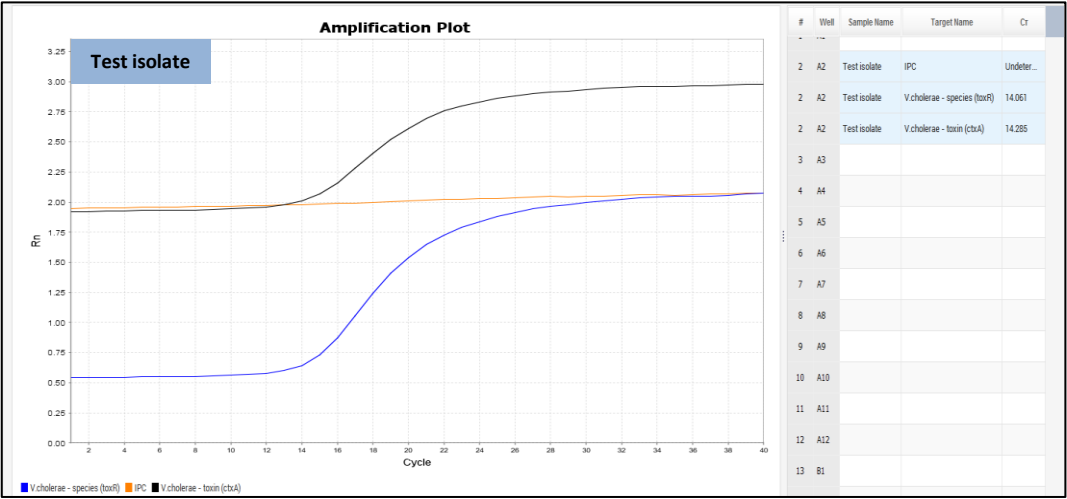
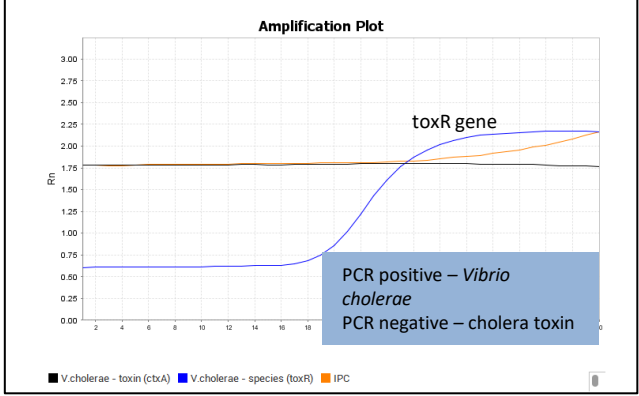
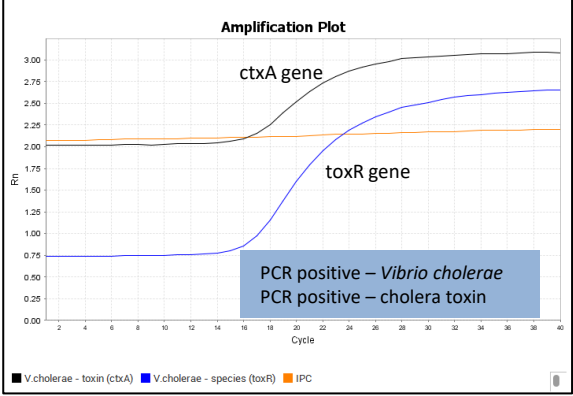
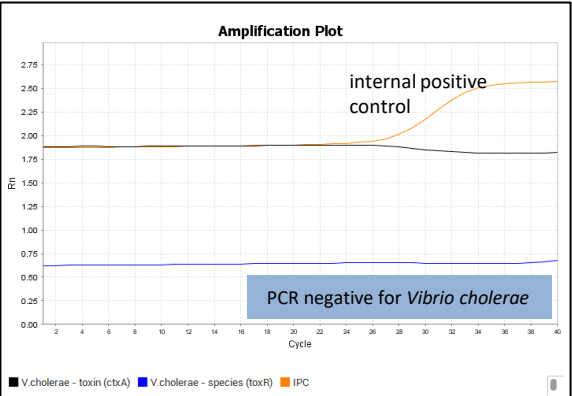


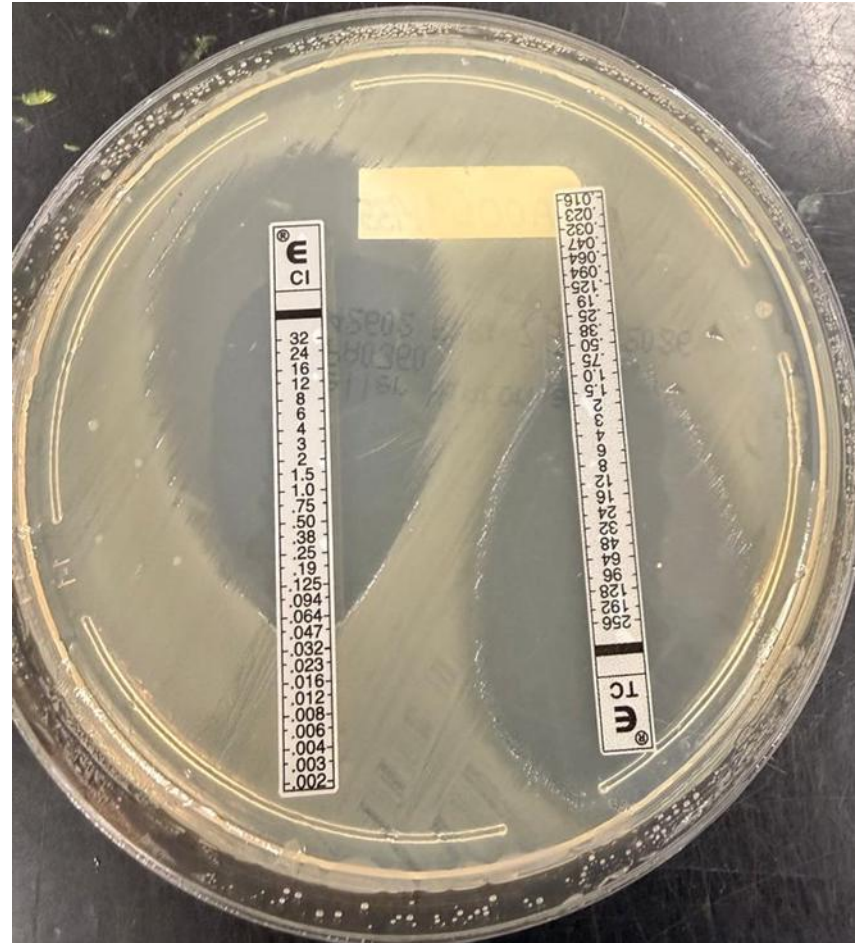




Laboratory diagnosis

- Serotyping is then performed to further identify O1 and the serogroups Inaba and Ogawa.
- PCR for toxin testing is then performed to establish if the organism is toxigenic or not.
- Antimicrobial susceptibility testing is performed at peripheral laboratories and confirmed at NICD
- Whole genome sequencing is subsequently performed to identify the specific strain.
- Direct PCR on stool specimens is available in private laboratories although it is highly sensitive and must be interpreted with caution.





CENTRE FOR ENTERIC DISEASES

SANAS Accredited Testing Laboratory, No. M0029E



Specimen received: Stool

Tests requested: ESURV

Surveillance Report:

Tested for *Vibrio cholerae*

V. cholerae Serotype *V. cholerae* O1 serotype Ogawa (VCOGA)

Vibrio cholerae Result PCR positive for *Vibrio cholerae*; PCR positive for cholera toxin

Authorised by: SL Williams (Medical Scientist) ESURV

A	B	C	D	E	F	G
SampleID	Species_Identifier	refseq_closest_match	Genera_present	ContaminationPresent	kraken2_match_#1	kraken2_match_#2
Control-04	<i>Vibrio cholerae</i> (100%)	<i>Vibrio cholerae</i> O1 biovar El Tor str. N16961	<i>Vibrio</i>	False (0%)	<i>Vibrio cholerae</i> (83.57%)	<i>Vibrio cholerae</i> (83.57%)
Control-05	<i>Vibrio cholerae</i> (100%)	<i>Vibrio cholerae</i> O1 biovar El Tor str. N16961	<i>Vibrio</i>	True (10.17%)	<i>Vibrio cholerae</i> (84.70%)	<i>Vibrio cholerae</i> (84.70%)
YA	<i>Vibrio cholerae</i> (100%)	<i>Vibrio cholerae</i> O1 biovar El Tor str. N16961	<i>Vibrio</i>	True (9.55%)	<i>Vibrio cholerae</i> (85.97%)	<i>Vibrio cholerae</i> (85.97%)
YA	<i>Vibrio cholerae</i> (100%)	<i>Vibrio cholerae</i> O1 biovar El Tor str. N16961	<i>Vibrio</i>	True (7.40%)	<i>Vibrio cholerae</i> (83.97%)	<i>Vibrio cholerae</i> (83.97%)

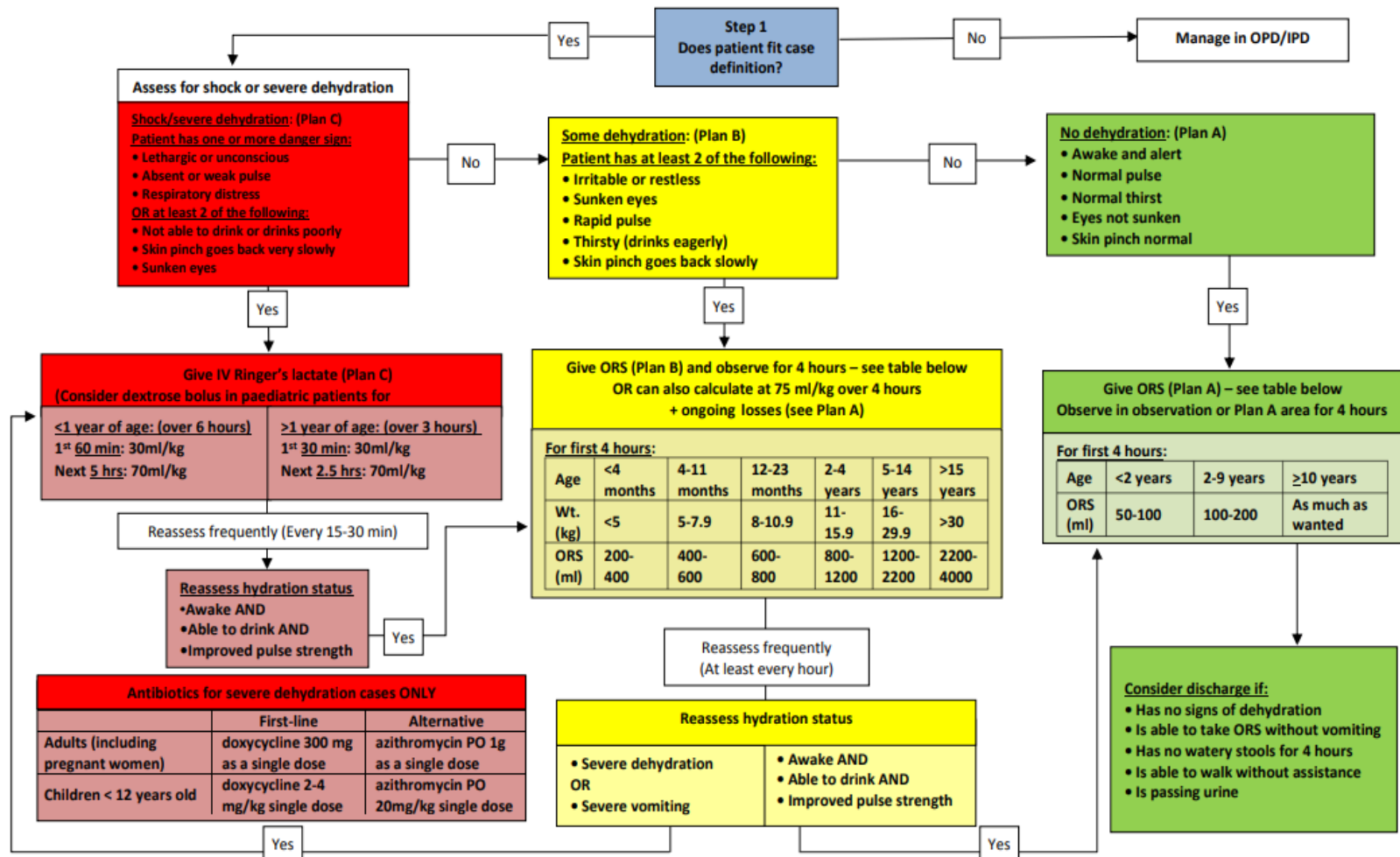
Scheme.MLS	ST
vcholerae	69
vcholerae	75
vcholerae	75
vcholerae	75



Principles of therapy

- The first priority is to correct or prevent dehydration with the appropriate rehydration fluids and maintenance of hydration status.
- Complementary therapies (antibiotic, zinc sulphate) are useful in reducing the duration and severity of diarrhoea but do not replace fluid therapy, which remains indispensable.
- Cholera is associated with some degree of, anorexia and malabsorption which can all impact nutritional status, especially in children.
- Once the patient is capable of oral intake, feeding should resume (usually 3 to 4 hours after starting rehydration).

Suspected cholera case
 In areas where a cholera outbreak has not been declared: any patient ≥ 2 years presenting with acute watery diarrhea and severe dehydration or dying from acute watery diarrhea
 In areas where a cholera outbreak is declared: any person presenting with or dying from acute watery diarrhea





Dehydrated patients

- Treatment consists of two phases: a rehydration phase and a maintenance phase.
- Rehydration phase:
 - is aimed at correcting the estimated initial fluid deficit over a defined time period.
 - **Severe dehydration:** a volume of Ringer's lactate corresponding to 10% of the patient's body weight (i.e. 100 ml/kg), is administered by IV route. This corresponds to **"Treatment Plan C"**
 - **Some dehydration:** the patient receives a volume of oral rehydration solution (ORS) corresponding to 5-9% of their body weight. By convention, 7.5% is used (i.e. 75ml/kg). This corresponds to **"Treatment Plan B"**

- 
- During the oral or IV rehydration phase, fluid losses will continue due to significant ongoing diarrhoea. If these losses are not compensated by an additional volume of ORS or RL, dehydration will persist, even if the volume initially required has been administered.
 - Once dehydration has been corrected, i.e. when there are no longer signs of dehydration, the patient enters the maintenance phase.
 - Maintenance phase:
 - is aimed at preventing a relapse of dehydration. It is directed at continuing the systematic oral replacement of ongoing fluid losses as they occur until diarrhoea ceases. This corresponds to "Treatment Plan A"



Complementary therapy

Antibiotic therapy

- Antibiotics can reduce the volume and duration of diarrhoea and decrease the period of shedding. Antibiotics are specifically indicated for:
 - cholera patients hospitalised with severe dehydration
 - patients with high purging (at least one stool per hour during the first 4 hours of treatment) or treatment failure (the patient is still dehydrated after completing the initial 4 hours of rehydration therapy), regardless of the degree of dehydration;
 - patients with co-existing conditions (including pregnancy) or co-morbidities (HIV, SAM), regardless of dehydration
- The choice of antibiotic should be based on the antimicrobial susceptibility results of the circulating strain of *V. cholerae* from cultures performed early in the outbreak.
- While awaiting results of antimicrobial susceptibility testing, patients can be given **ciprofloxacin**.



Ciprofloxacin PO		
Adults	1g single dose	
Children	20 mg/kg single dose	Maximum dose: 750mg



Complementary therapy

Zinc supplementation

- In children diarrhoea causes a significant loss of zinc which must be replaced.
- Zinc is indicated for children aged 6 months to 5-years of age presenting with diarrhoea, regardless of dehydration status.
- It can be given when the child is able to tolerate oral intake (usually on the first day).

In all children who are able to take oral medication:

- Zinc (elemental), oral 10 mg/day for 14 days (lower doses of zinc have been associated with less vomiting in children presenting with acute diarrhoea)



Caution

!! Dextrose 5% should not be used for fluid replacement in patients with cholera as it does not contain electrolytes, which are required to ensure adequate fluid resuscitation!!



Case definitions

- **Suspected case definition**

- In an area where the disease is not known to be present, a suspected case is defined as a patient, irrespective of age, with severe dehydration or death from acute watery diarrhoea
- In an area where there is a cholera outbreak, a suspected case is defined as a patient who develops acute watery diarrhoea, with or without vomiting.

- **Probable case definition**

- A suspected case with an epidemiologic link to a confirmed cholera case.

- **Confirmed case definition**

- A case of cholera is confirmed when toxigenic *Vibrio cholerae* O1 or O139 is isolated from any patient with diarrhoea.

Active case Finding

- Among individuals at risk of exposure (e.g., household members and close neighbours living in proximity to a suspected cholera case or using the same water source).
- Ask the sick person about family, shared meals, and visitors.
- Check symptoms: Look for fast watery diarrhoea or vomiting for up to 5 days.
- Test environment: Inspect local drinking water and sanitation.
- Provide Education: Give clean water tablets and early care





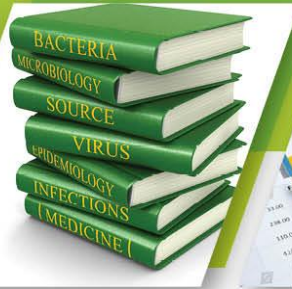
Prevention and Control

- Preventing and controlling cholera involves a combination of
 - strengthening **surveillance**,
 - improving water, sanitation and hygiene, (**WASH**)
 - increasing **risk communication** and **community engagement**,
 - improving access to quality **treatment** and
 - Implementing oral cholera vaccine (**OCV**) campaigns



Water, Sanitation, and Hygiene

- Water, sanitation, and hygiene (WaSH) are of the utmost importance for the prevention and control of cholera and other enteric infections.
- WASH interventions help prevent many waterborne illnesses, including cholera, and contribute to the Sustainable Development Goals.
- During outbreaks, implementing WASH activities can reduce cholera transmission.
- These activities include improving WASH in healthcare facilities, conducting water quality monitoring, distributing WASH kits to communities and promoting protective hygiene practices



Thank you



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