

Waterborne Diarrheal diseases



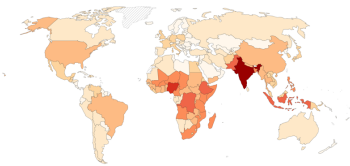
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Epidemiology

Diarrheal disease deaths, 2021

Estimated annual number of deaths from diarrheal diseases¹

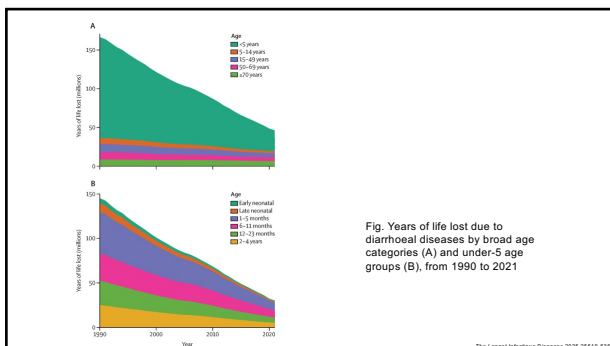


No data 0 300 1,000 3,000 10,000 30,000 100,000 300,000 1 million

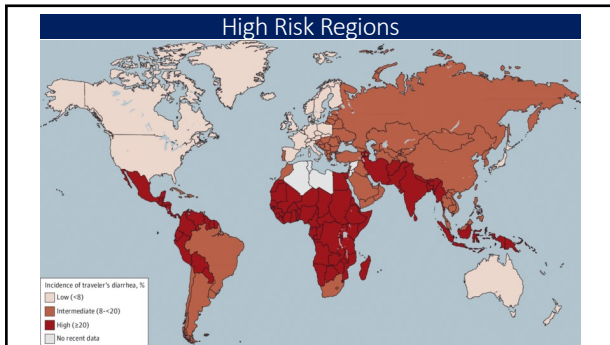
Data source: World Health Organization (2024) [Global burden of diarrhoeal diseases | CC BY](#)

1. Diarrhoeal diseases Diarrhoeal diseases are a group of illnesses that are usually caused by viral, bacterial, or protozoan infections. They tend to be spread through contaminated food or drinking water, or between people through the fecal-oral route or direct contact. There are many public health measures that can prevent diarrhoeal diseases, including sanitation, clean drinking water, pasteurization, food safety, and hand washing with soap.

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Definition of diarrhea

- Passage of loose or watery stools
- At least 3 times in a 24-hour period
- Reflects increased water content of stool, due to:
 - impaired water absorption
 - active water secretion by the bowel

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Classification according to duration of symptoms:


Acute diarrhea

- 14 days or fewer


Persistent diarrhea

- 14- 30 days


Chronic diarrhea

- More than 30 days

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Dysentery / Invasive diarrhea

- Diarrhea with visible blood or mucus
- Associated with fever and abdominal pain

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Etiology

- Bacteria:
 - *Campylobacter*
 - *Non-typhoidal Salmonella*
 - *Shigella*
 - *Enterotoxigenic Escherichia coli*
 - *Vibrio cholerae*

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Viruses

- *Norovirus*
- *Rotavirus*
- *Adenovirus*
- *Astrovirus*

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Protozoa

- *Giardia*
- *Cyclospora*
- *Entamoeba histolytica*
- *Cryptosporidium*

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Key Transmission Routes

- Fecal-oral
- contaminated water
- person-to-person



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Traveler's Diarrhea (TD)

- The **most predictable** travel related illness
- 40-70% of travelers to the developing world get it
- Airport survey in Nepal among departing tourists with stay <3 months, 68% had diarrhea*

*Rajh R, et al. Epidemiology of diarrhea among expatriate residents living in a highly endemic environment. JAMA. 1995 Feb 21;275(7):533-8.

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Etiology of travelers' diarrhea

- Bacterial – 70-80%
Campylobacter, *E. coli* mainly *ETEC*, *Shigella*, non-typhoidal *Salmonella*,
Other bacteria: *Plesiomonas*, *Yersinia*, *Vibrio parahaemolyticus*, *Vibrio cholerae* (in outbreaks)
 - Viral – 10-20%
Norovirus, Rotavirus, Sapovirus, Astrovirus
 - Parasitic - 10%
Giardia, *Cyclospora*, *Cryptosporidium*, *D. Fragilis*
- Mixed infections are common

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Bacterial Diarrhea

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Campylobacter jejuni - Transmission

- mostly transmitted to humans via raw or undercooked food products
- direct contact with infected animals
- contaminated undercooked poultry
- raw milk
- **untreated water**
- contaminated seafood
- contact with infected household pets
- travel to developing countries
- oral-anal sexual contact

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Campylobacter

- motile
- non-spore forming
- curved
- Gram negative rods



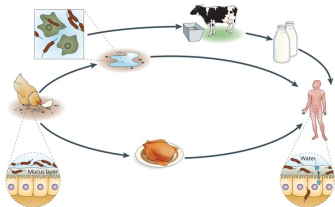
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Campylobacter jejuni

- Incubation period: 2 - 4 days (range 1 – 7 days)
- Hosts in developing countries with multiple prior infections may be partially immune.
- Sites of tissue injury: jejunum, ileum, colon

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Sources and outcomes of *Campylobacter jejuni* infection



Young et. al. Nature Reviews Microbiology. 2007

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Complications of *Campylobacter jejuni*

- Reactive arthritis (2.5%)
 - several weeks after infection
 - HLA-B27 phenotype
 - most commonly knees but other joints too like ankles, wrists, small joints of hands
- Guillain Barre' Syndrome or Miller Fisher variant
 - 1/1000-2000 cases
 - if O19 serotype: 1/100-200 cases
- In immunocompromised patients: osteomyelitis, erysipelas- like rash or cellulitis, cholecystitis, pancreatitis, cystitis, meningitis, endocarditis, peritonitis, septic abortion
- immunoproliferative small intestinal disease (alpha chain disease)

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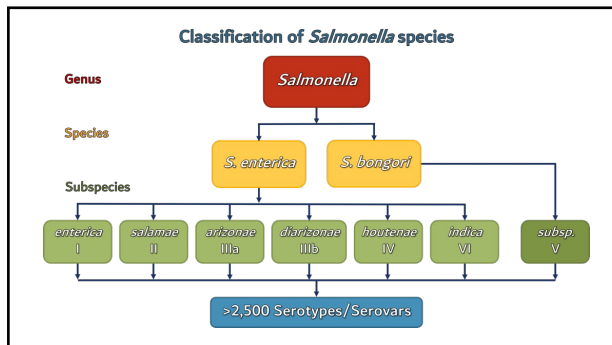
Non-typhoidal *Salmonella*

- Many serotypes, named after the city where they were identified
- Gram negative, non-spore-forming, facultatively anaerobic bacilli
- Measure 2-3 μm x 0.4-0.6 μm



Picture credit: CDC

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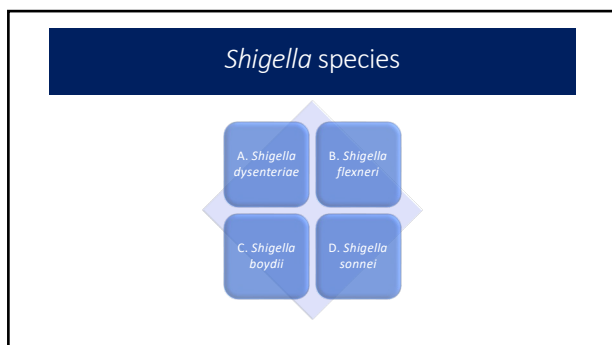


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Shigella

- isolated by the Japanese microbiologist Kiyoshi Shiga in 1897
- non-spore forming
- Gram negative
- nonmotile
- does not produce gas from sugars, decarboxylate lysine or hydrolyze arginin

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Complications of *Shigella*

- Dehydration
- Seizures
- Rectal prolapse
- Toxic megacolon
- Reactive arthritis
- Hemolytic uremic syndrome



Figure. Toxic megacolon following *Shigella flexneri* infection
Iluoma et. al. BMJ. 2021

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Diarrheagenic <i>E. coli</i>			
<i>E. coli</i> strain	Site of action	Clinical Features	Pathogenesis
Enterotoxigenic (ETEC)	Small intestine	Watery diarrhea, cramps, nausea, low grade fever in travelers and infants	Enterotoxins promote increased cAMP or cGMP, leading to fluid and electrolyte loss
Enteraggregative (EAEC)	Small intestine	Persistent infant diarrhea, sometimes with gross blood, low-grade fever	Aggregative adherence to mucosa prevents fluid absorption
Enteropathogenic (EPEC)	Small intestine	Copious watery diarrhea with fever, nausea, vomiting, and nonbloody, mucus filled stools	Adherence and destruction of epithelial cells
Enteroinvasive (EIEC)	Large intestine	Fever, cramping, watery diarrhea followed by development of dysentery with scant, bloody stools	Invasion and destruction of epithelial cells lining the colon
Enterohemorrhagic (EHEC)	Large intestine	Severe abdominal cramps, initial watery diarrhea followed by grossly bloody diarrhea, little or no fever (hemorrhagic colitis); hemolytic-uremic syndrome associated with strain O157:H7	Cytotoxic verotoxin (Shiga toxin) inhibits protein synthesis

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Clinical Features

- Symptoms
 - loose stools, may contain mucus and/or blood
 - fever
 - abdominal cramps
 - nausea/vomiting
 - decreased urine
 - dizziness
 - headache
 - Rarely, syncope and seizures



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Signs

- Signs of dehydration:
 - decreased skin turgor
 - sunken eyes
 - dry skin
 - may have signs of hypovolemia: such as low blood pressure, increased pulse
 - Abdominal examination: abdominal tenderness, increased bowel sounds

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Stool microscopy (at CIWEC)

- A fresh sample of stool is put on a slide and looked at under the microscope.
- Secondly, an equal volume of formalin ether is mixed with the stool and spun in a centrifuge.
- This method allows for digestion of fecal material and makes viewing of parasites easier.
- Look for pus cells, mucus, RBCs or parasites.



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Stool PCR



Stool PCR	
Sample ID	123456
Sample Type	Stool
Test Name	Stool PCR
Test Result	Positive
Test Date	2025-09-25
Test Time	10:00 AM
Test Location	CIWEC
Test Operator	Dr. Smith
Test Reviewer	Dr. Jones
Test Status	Completed
Test Notes	Sample received from patient with symptoms of gastroenteritis. PCR results show positive for [pathogen].

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Stool Culture

- **Campylobacter**
 - needs *Campylobacter* selective culture media such as
 - **CampyBAP** (Campylobacter Blood Agar Plate),
 - **CCDA** (Charcoal Cefoperazone Deoxycholate Agar),
 - **Skirrow's medium**, and
 - **Butzler's medium**
- Stool culture yield varies from lab to lab

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Treatment of Acute Onset Diarrhea

- Fluid replacement (ORS)
- Paracetamol for fevers
- Anti-nausea medicine (ondansetron, promethazine) if needed
- Loperamide for symptom relief
- May take antibiotic for moderate to severe symptoms (Azithromycin)
- Do not take Loperamide alone if blood in the stools or fever present

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Management

Providers should consider the following in counseling the traveler:

- (1) Definitions of travelers' diarrhea and severity classification
- (2) Importance of oral rehydration through fluid and salt intake for all travelers' diarrhea
- (3) Information on effectiveness of treatments for travelers' diarrhea and the risk of travel, travelers' diarrhea, and antibiotic use with the acquisition of multidrug resistance bacteria
- (4) Provision of empiric treatment medications as indicated by itinerary and provider-traveler determination
- (5) Pre- and post-travel illness follow-up recommendations

	Self-determination of Illness Severity		
	Mild	Moderate	Severe
During Travel	Diarrhea that is idiopathic, is not distressing, and does not interfere with planned activities	Diarrhea that is distressing or interferes with planned activities	Diarrhea that is incapacitating or prevents planned activities
	May use loperamide or bismuth subsalicylates	May use loperamide alone or as an adjunct to antibiotics	May use loperamide as adjunct to antibiotics
Post-travel	May use antibiotic (Table 2)		Should use antibiotic (Table 2)

Acute travelers' diarrhea should be treated empirically as above.

Microbiologic testing is recommended in returning travelers with severe or persistent symptoms or in those who fail empiric therapy.

Multiplex molecular diagnostics are preferred in patients with persistent or chronic symptoms.

Riddle et al. JTM, 2017

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Antibiotic regimens for travelers' diarrhea

Antibiotic ^{a, c, d}	Dose	Treatment duration
Azithromycin ^{c, d}	1000 mg by mouth or	Single or 1-day divided ^b
	500 mg by mouth	3 day course
Levofloxacin	500 mg by mouth	Single dose ^b or 3 day course
Ciprofloxacin	750 mg by mouth or	Single dose ^b
	500 mg by mouth	3 day course
Ofloxacin	400 mg by mouth	Single dose ^b or 3 day course
Rifaximin ^a	200 mg by mouth three times daily	3 days

Riddle et. al. JTM. 2017

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Mild diarrhea

- Tolerable, not distressing, does not interfere with planned activities
- Antibiotic treatment not recommended
- Consider treatment with bismuth subsalicylate or loperamide

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Moderate diarrhea

- Distressing or interferes with planned activities
- Antibiotics can be used:
 - Azithromycin
 - Fluoroquinolones
 - Rifaximin (for moderate, noninvasive diarrhea)
- Consider loperamide for use as monotherapy or as adjunctive therapy

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Severe diarrhea

- Incapacitating or completely prevents planned activities (all dysentery is considered severe)
- Antibiotic treatment is advised (single-dose regimens may be used):
 - Azithromycin is preferred
 - Fluoroquinolones or rifaximin can be used for severe, non-dysenteric diarrhea
- Consider loperamide for use as adjunctive therapy (not recommended as monotherapy for patients with bloody diarrhea or diarrhea and fever)

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Cholera

- caused by *Vibrio cholerae* bacteria
- *Vibrio* species are highly motile, facultatively anaerobic, curved Gram-negative rods with one or more flagella.
- Reside in tidal rivers and bays under conditions of moderate salinity.
- Proliferate in summer months when water temperature exceeds 20°C
- was first isolated by Koch (1883) from cholera patients in Egypt



Figure. Darting motility of *Vibrio cholerae* in "fish in stream" appearance.

Figure credit: MMCH Laboratory YouTube channel

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Cholera ... continued

- can result in profound, rapidly progressive dehydration and death.
- Diarrhea caused by *V. cholerae* serogroup O1 or O139
- Rice-water stools
- Hypovolemic shock



Figure. Rice water stool in cholera

Figure courtesy: Faruque, ICDDR, Dhaka

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Stool Culture

thiosulfate-citrate-bile-salts-sucrose (TCBS) agar or taurocholate-tellurite-gelatin (TTG) agar
high specificity (up to 97.4%)
low sensitivity (up to 33.3%)

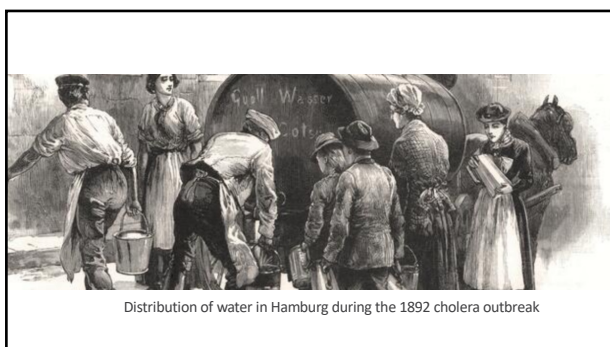
Polymerase Chain Reaction

Rapid Antigen Test

	For Crystal Vc Antigen kit	
	<i>V. cholerae</i> O1	<i>V. cholerae</i> O139
Sensitivity	88 - 100%	99%
Specificity	81 - 87.3%	98%

- If delay in sample processing: Carey Blair transport medium or alkaline peptone water (APW) enrichment medium, APW enhances sensitivity and specificity of Ag tests
- Other tests: Hanging drop test, Dark field microscopy
- Confirmation requires stool culture or PCR

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Parasites causing diarrhea

Whipworm

Tapeworm

Roundworm

Giardia

Hookworm

Coccidia

• Treatment:

- **Albendazole**: hookworm, whipworm (trichuris), roundworm (ascariasis)
- **Mebendazole**: also for enterobiasis (pinworm)
- **Praziquantel**: tapeworm

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Chronic Sequelae

- Post-infectious Irritable Bowel Syndrome
- Malnutrition
- Stunting in children

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Viral diarrhea

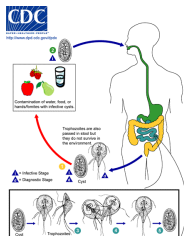
- Most common – Noroviruses
- Distributed worldwide, common cause of acute gastroenteritis in the developed world, has been known to cause outbreaks
- Incubation period – 24-48 hours
- Acute onset, with vomiting and diarrhea, fever in 50%
- Getting identified more as PCR based technologies readily available

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Parasitic diarrhea

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Giardia



- Worldwide distribution
- Most common parasitic cause of TD (10% of travelers to Nepal)
- Incubation period- 1-2 weeks
- Low grade symptoms – diarrhea, fatigue, excess gas/bloating
- Fatigue common, never fever

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Giardiasis

• Diagnosis:

- Stool microscopy (only 50% yield)
- Fecal immunoassays: antigen detection
- Immunofluorescence
- PCR
- Often, classic symptoms and empiric Rx

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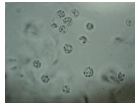
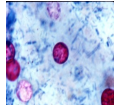
Giardiasis

- Treatment: Tinidazole 2g stat with dinner daily x 2 nights, no alcohol
- Children: Metronidazole 15mg/kg/day divided into 2-3 doses for 5-7 days
- Other therapies:
 - Nitazoxanide 500mgx2x3 days, albendazole
 - Resistant Giardia:** Paromomycin or Quinacrine, combined therapies
 - Look for immunodeficiency states (hypogammaglobulinemia, IgA deficiency) in resistant or refractory giardiasis

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Cyclospora Diarrhea

- Seen in the months of May-August
- Iodine and chlorine do not kill this parasite
- Waxing and waning course.
- Fatigue and weight loss common



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Cyclospora

- Treatment – Bactrim DS 1 tab BDx7 days cures 95% of patients
- If symptoms persist, use a longer course: 10-14 days of Bactrim
- Avoid empiric treatment with Bactrim

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Amebiasis

- Common in locals of endemic countries, but rare in travelers
- Only 1% of diarrhea cases at CIWEC
- Alternating diarrhea with constipation predominating, weight loss, mucus in stools
- Amebic dysentery not common
- Treatment: Metronidazole, Tinidazole followed by luminal agent like diloxanide furuate/paromomycin/iodoquinol

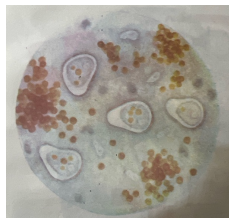
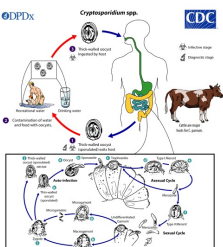


Figure. Stool in acute amebic dysentery
Source: Chatterjee. Parasitology

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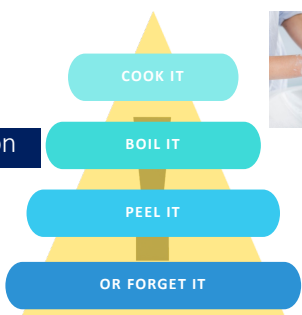
Cryptosporidiosis



- Self limited in immunocompetent hosts (2-3 weeks) but can be severe in immunocompromised hosts (may have chronic and profuse diarrhea)
- Incubation period: average 7 days (range 2-10 days)
- Treatment: Nitazoxanide 500 mg BD for 3 days.

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Prevention







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Cholera vaccines



- **Dukoral:** *V. cholerae* O1 bacteria and recombinant cholera toxin B subunit
- for protection against *V. cholerae* O1 serotype and ETEC diarrhea, useful in areas with high rates of ETEC
- 2 years and older



Vaxchora: (live, oral, single dose)
—licensed in USA. Start 10 days before travel to areas of risk



Evuichol-Plus (whole cell killed)

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Vaccine name (Manufacturer)	Number of doses recommended	Recommended age	How long vaccination is effective
Vaxchora (Emergent BioSolutions)	1 dose	2-64 years	At least 3–6 months
Dukoral (SBL Vaccines)	2 doses, given 1-6 weeks apart (Children ages 2-5 years need 3 doses, given 1-6 weeks apart)	2 years and older	2 years
EuVichol/EuVichol-Plus (EuBiologics) / Shancol (Sanofi)	2 doses, given at least 2 weeks apart	1 year and older	At least 3 years for 2 doses. (One dose provides short-term protection for about one year.)

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Safe drinking water

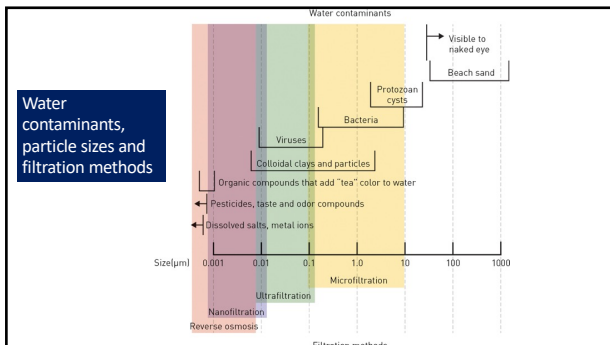
- Bottled water
- Boiled water
- Chemical disinfection with iodine (limit to few weeks of use, avoid in pregnancy, thyroid disease, iodine allergy) or chlorine
- Filtered water with filter pore sizes 0.1- 0.4 micron

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Waterborne pathogens (average sizes) and filter pore size needed for their removal

Waterborne Pathogen	Average Size (µm)	Filter Pore Size Needed (µm)	Filter class
Viruses	0.03	Not specified (optimally ≤0.01)	Ultrafilter
Enteric bacteria (e.g., Escherichia coli)	0.5 × 2–8	≤0.2–0.4	Microfilter
Cryptosporidium oocysts	4–6	≤1	Microfilter
Giardia cysts	8 × 19	≤3.0–5.0	Microfilter
Helminth eggs	30 × 60	Not specified	Any
Schistosome larvae	50 × 100	Not specified	Any

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Conclusion

- Waterborne diarrheal disease are mostly bacterial. Bacteria causing TD are highly resistant to FQ's in South and Southeast Asia
- In this region, emerging resistance to azithromycin among *Campylobacter*
- Azithromycin remains the drug-of-choice for TD in Nepal, South and South east Asia
- Treat moderate to severe symptoms

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Thank you

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