ENVIRONMENTAL SANITATION AND WATER BORNE DISEASES

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COMPONENTS OF ENVIRNOMENTAL SANITATION

- WATER SANITATION
- FOOD AND MILK SANITATION
- EXCRETA DISPOSAL
- SEWAGE DISPOSAL
- REFUSE DISPOSAL
- VECTOR AND VERMIN CONTROL
- HOUSING
- AIR SANITATION

WATER SANITATION

WATER ANALYSIS CONSISTS OF:

- PHYSICAL
- CHEMICAL
- RADIOLOGICAL
- BIOLOGICAL
- BACTERIOLOGICAL

WATER SANITATION

- **PUBLIC WATER SUPPLY MUST BE-**
  - SAFE
  - REASONABLY SOFT
  - PLENTIFUL
  - CHEAP

WATER SANITATION

- **HOUSEHOLD TREATMENT OF WATER**
  - BOILING, i.e., beyond 2 minutes
  - CHLORINATION- 1-5ppm
  - IODINE TREATMENT- 10 drops per gallon
  - FILTRATION
  - AERATION

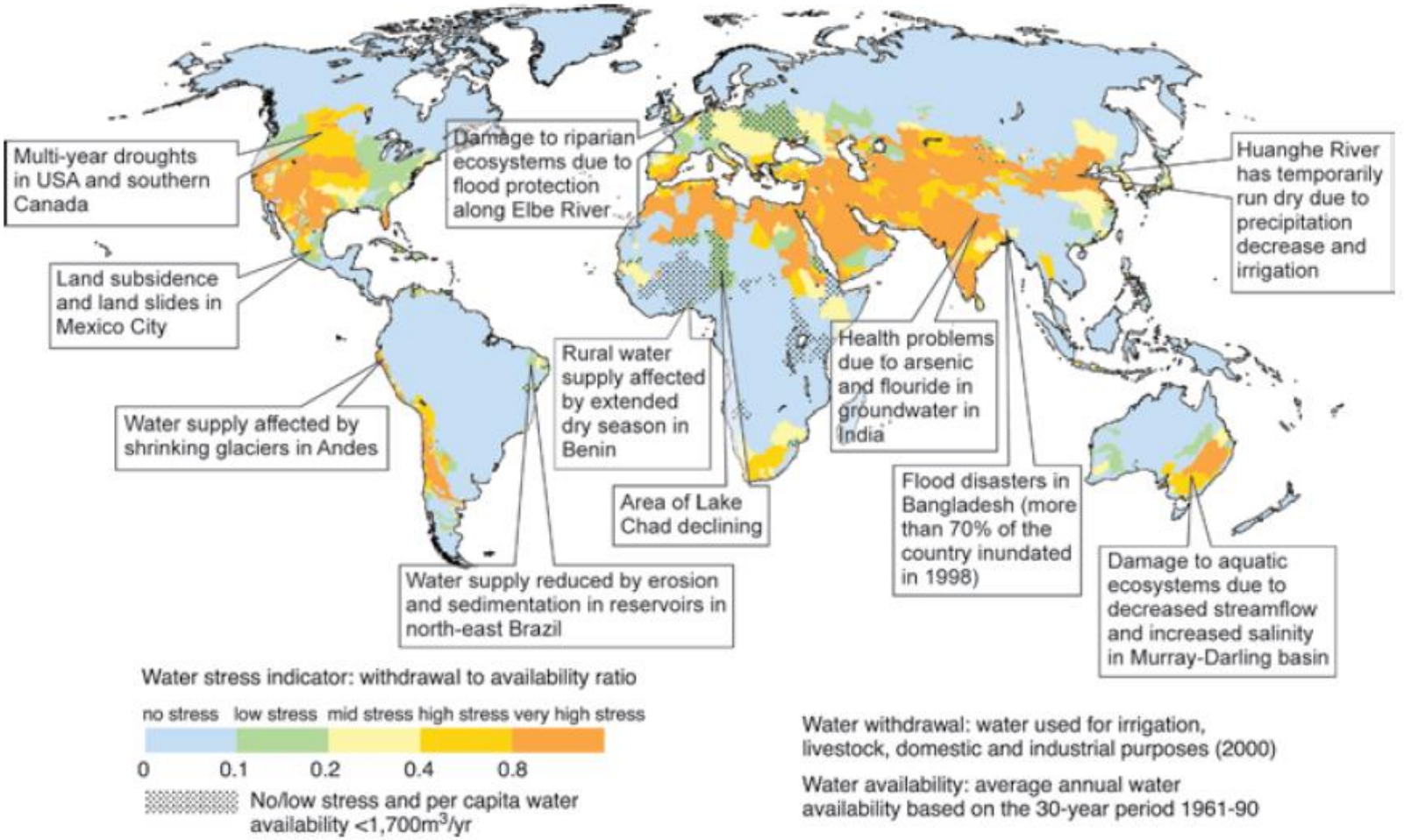
What is a Water-Borne Disease?

- “Pathogenic microbes that can be directly spread through contaminated water.” -CDC
- Humans contract waterborne infections by contact with contaminated water or food.
- May result from human actions, such as improper disposal of sewage wastes, or extreme weather events like storms and hurricanes.

Climate Change Promotes Water-borne Disease

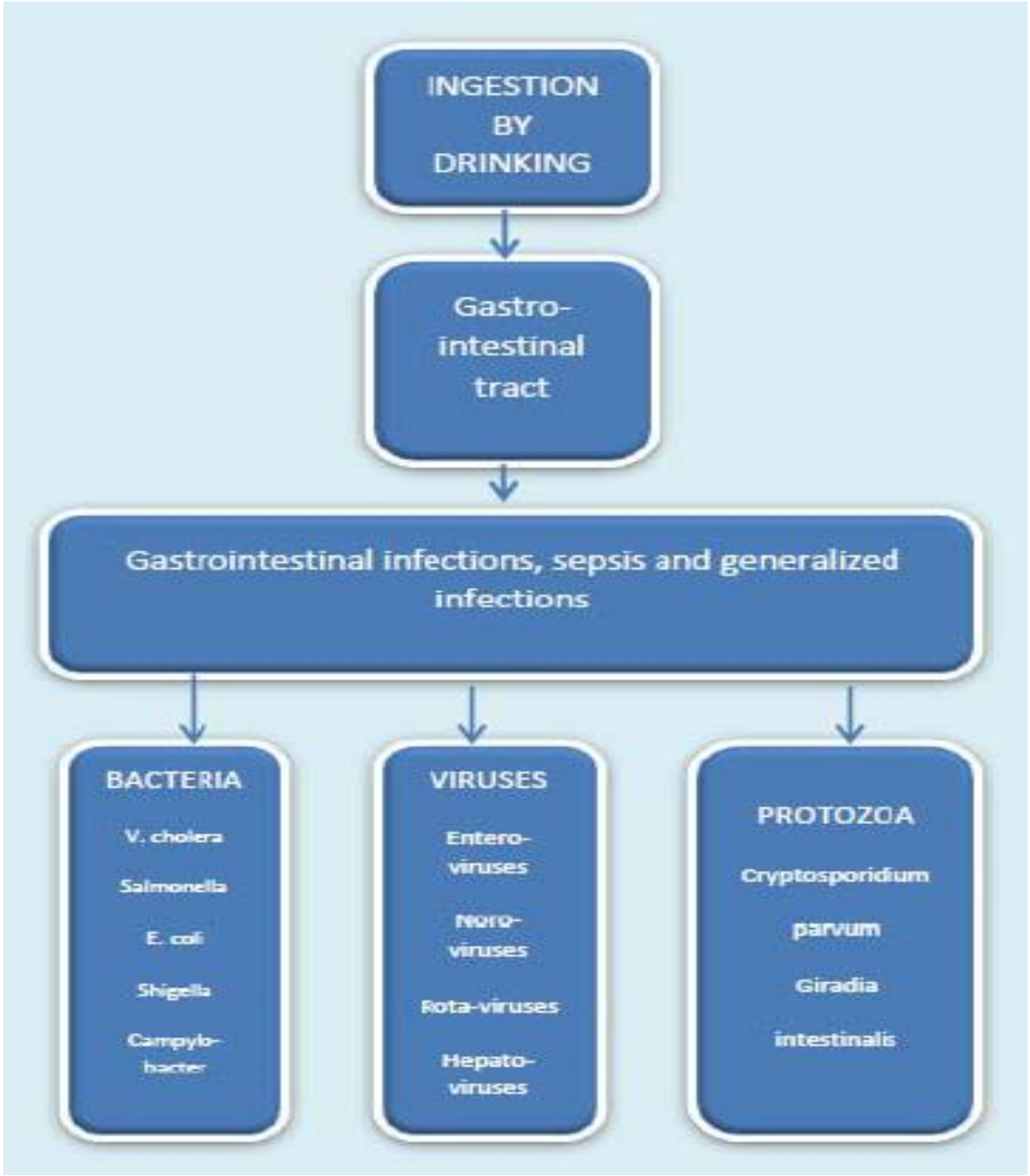
- Rainfall: transport and disseminates infectious agents
- Flooding: sewage treatment plants overflow; water sources contaminated
- Sea level rise: enhances risk of severe flooding
- Higher temperatures: Increases growth and prolongs survival rates of infectious agents
- Drought: increases concentrations of pathogens, impedes hygiene

Water Quantity and Quality Issues



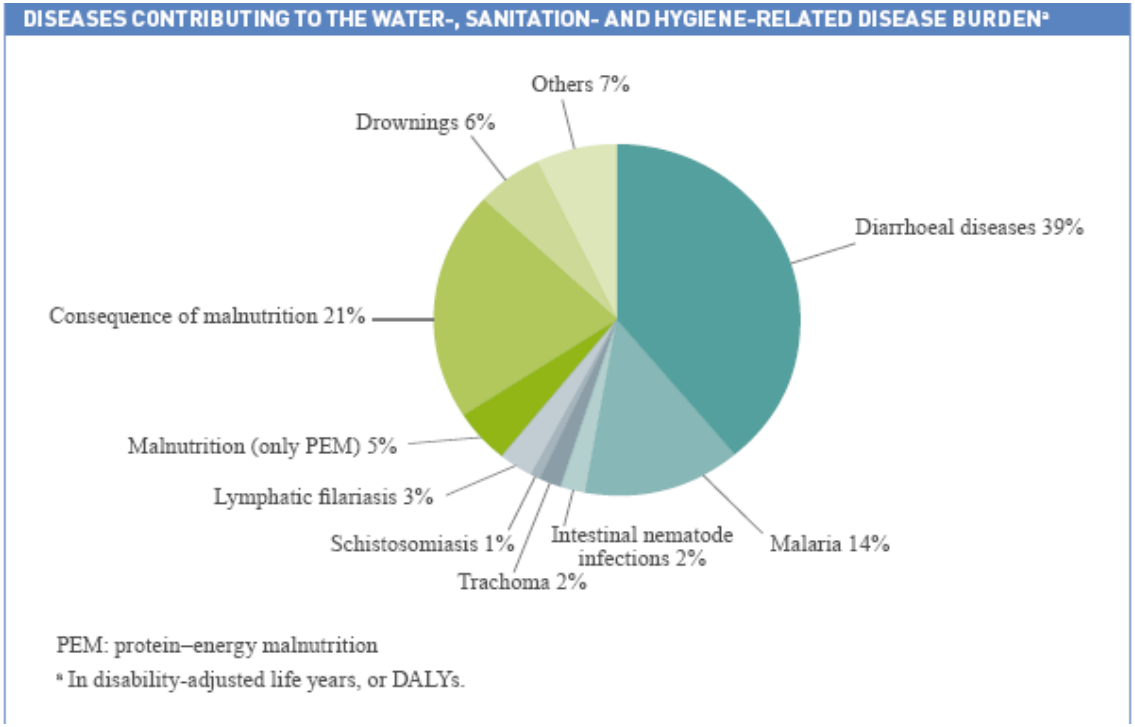
IPCC, 2007a

Figure 1.1: *Examples of current vulnerabilities of freshwater resources and their management; in the background, a water stress map based on WaterGAP (Alcamo et al., 2003a). See text for relation to climate change. [WGII Figure 3.2]*


INGESTION BY DRINKING
Gastro-intestinal tract
Gastrointestinal infections, sepsis and generalized infections
BACTERIA
V. cholera
Salmonella
E. coli
Shigella
Campylo-bacter
VIRUSES
Entero-viruses
Noro-viruses
Rota-viruses
Hepato-viruses
PROTOZOA
Cryptosporidium
parvum
Giradia
intestinalis

Burden of Waterborne Disease

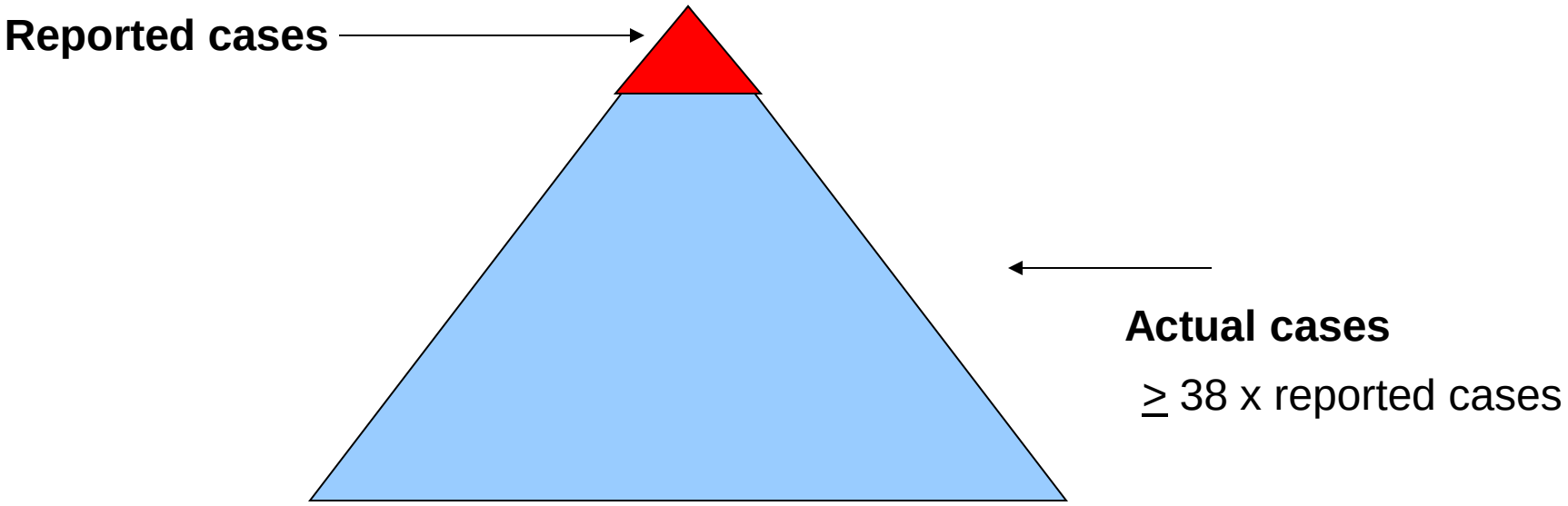
- 1.8 million deaths (4 million cases) in 2004 due to gastroenteritis (WHO)
  - 88% due to unsafe water and poor sanitation



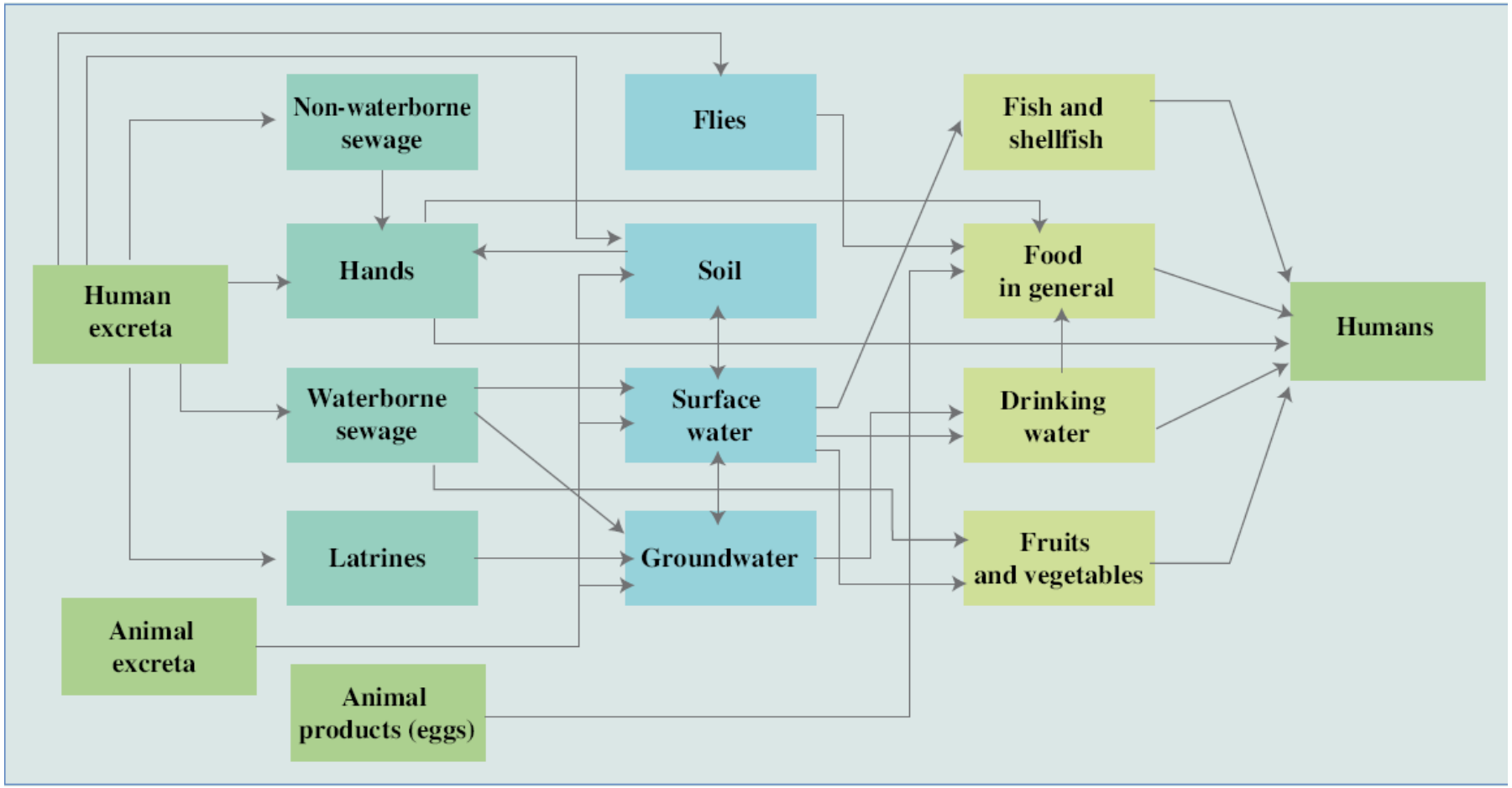
Prüss-Üstün et al., 2008

Burden of Diarrheal Diseases

- Diarrheal diseases are vastly underestimated
  - 211 million cases *estimated* in the US annually (Mead et al., 1999)



Diarrheal Disease Pathways



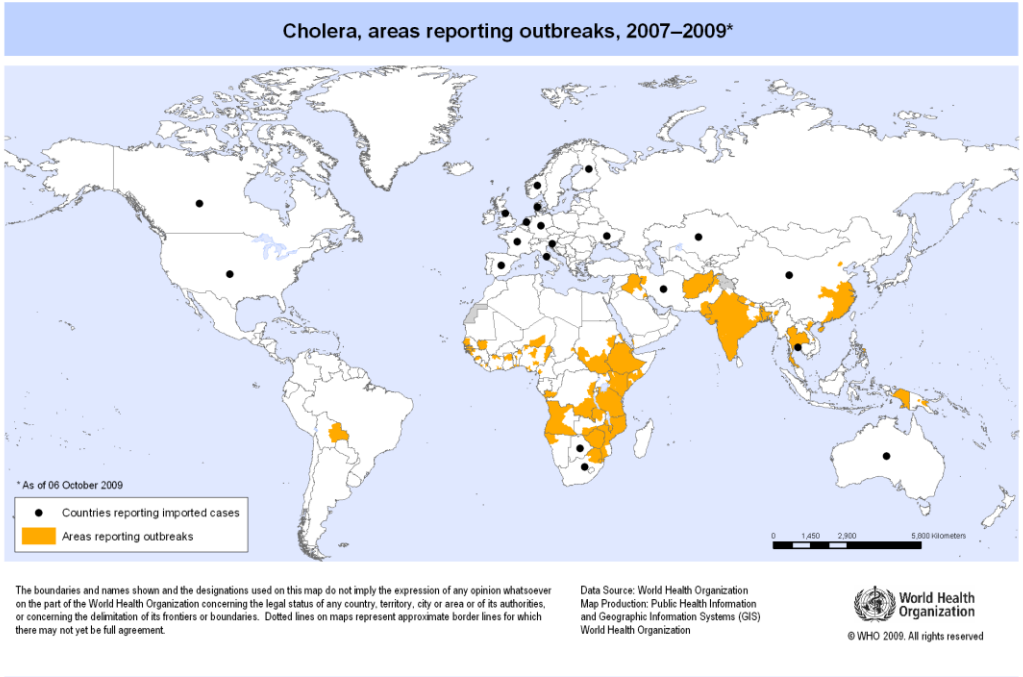
Prüss-Üstün et al., 2008

CHOLERA

Cholera

- Found in water or food sources contaminated by feces from an infected person
- Transmitted by contaminated food, water
- Prevalence increases with increasing temperature and rainfall amounts

Global Prevalence of Cholera (WHO)

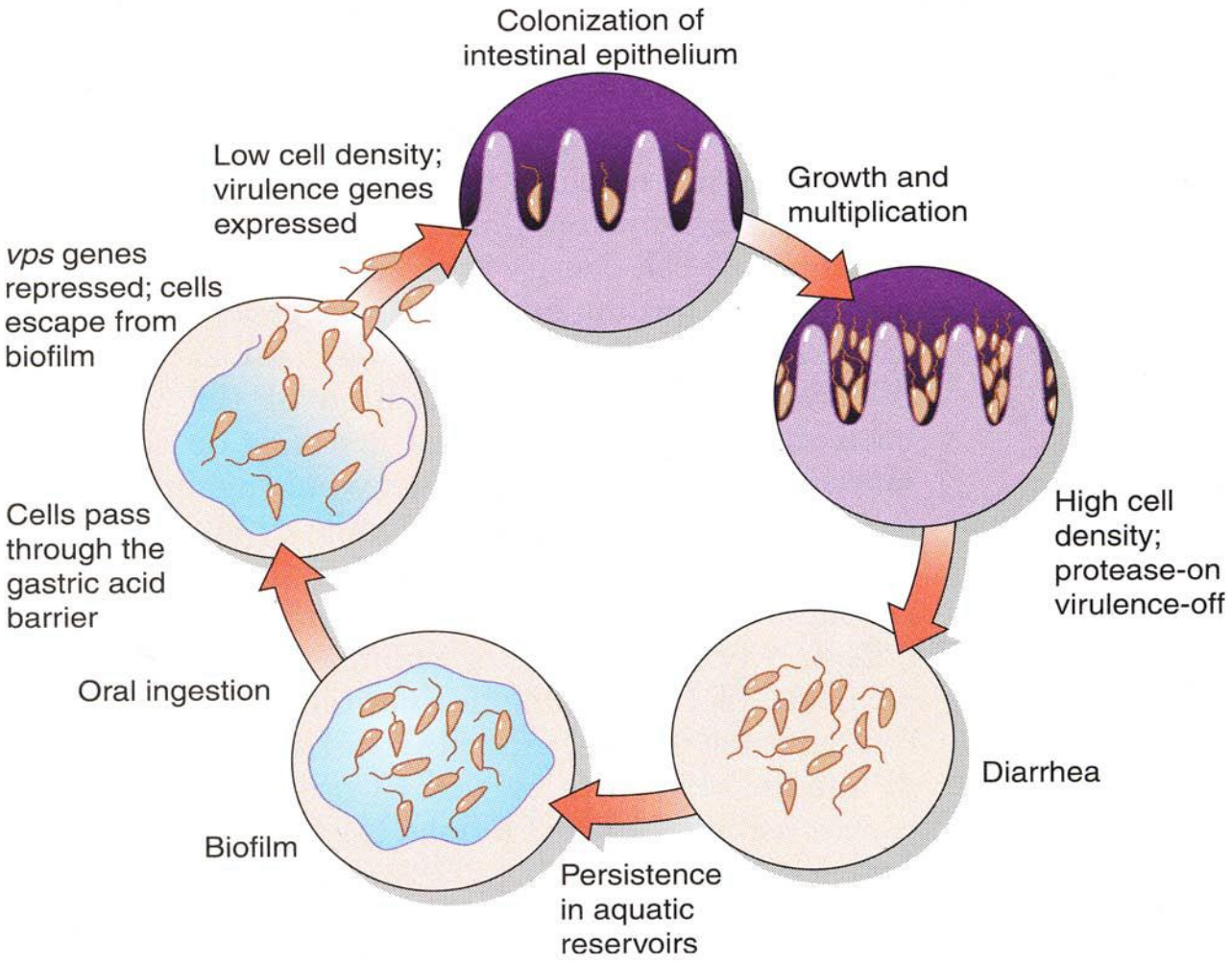


V. CHOLERAE

- The organism is a comma-shaped, gram-negative, aerobic bacillus whose size varies from 1-3 mm in length by 0.5-0.8 mm in diameter.

- Its antigenic structure consists of a flagellar H antigen and a somatic O antigen. It is the differentiation of the latter that allows for separation into pathogenic and nonpathogenic strains.

Mechanisms of Pathogenicity



PATHOGENESIS

- V cholerae cause clinical disease by producing an enterotoxin that promotes the secretion of fluid and electrolytes into the lumen of the gut.

- The result is watery diarrhea with electrolyte concentrations isotonic to those of plasma.

- The enterotoxin acts locally & does not invade the intestinal wall. As a result few WBC & no RBC are found in the stool.

PATHOGENESIS/2

- Fluid loss originates in the duodenum and upper jejunum; the ileum is less affected.

- The colon is usually in a state of absorption because it is relatively insensitive to the toxin.

- The large volume of fluid produced in the upper intestine, however, overwhelms the absorptive capacity of the lower bowel, which results in severe diarrhea.

TRANSMISSION

- Cholera is transmitted by the fecal-oral route through contaminated water & food.

- Person to person infection is rare.

- The infectious dose of bacteria required to cause clinical disease varies with the source. If ingested with water the dose is in the order of 10^3-10^6 organisms. When ingested with food, fewer organisms are required to produce disease, namely 10^2-10^4.

TRANSMISSION/2

- V. cholerae is a saltwater organism & it is primary habitat is the marine ecosystem.

- Cholera has 2 main reservoirs, man & water. Animals do not play a role in transmission of disease.

- V. cholerae is unable to survive in an acid medium. Therefore, any condition that reduces gastric acid production increases the risk of acquisition.

AT RISK GROUPS

- All ages but children & elderly are more severely affected.
- Subjects with blood group “O” are more susceptible; the cause is unknown.
- Subjects with reduced gastric acid.

CLINICAL PICTURE

- Incubation period is 24-48 hours.

- Symptoms begin with sudden onset of watery diarrhea, which may be followed by vomiting. Fever is typically absent.z

- The diarrhea has fishy odor in the beginning, but became less smelly & more watery over time.

CLINICAL PICTURE/2

- The classical textbook “rice water” diarrhea, which describes fluid stool with very little fecal material, appears within 24h from the start of the illness.

- In severe cases stool volume exceeds 250 ml /kg leading to severe dehydration, shock & death if untreated.

Rice-water stools of cholera

The passage of profuse "rice-water" stool is characteristic of severe cholera. The stool is watery with flecks of mucous and has the appearance of water in which rice has been washed.

LAB DIAGNOSIS

- Organism can be seen in stool by direct microscopy after gram stain and dark field illumination is used to demonstrates motility.

- Cholera can be cultured on special alkaline media like triple sugar agar or TCBS agar.

- Serologic tests are available to define strains, but this is needed only during epidemics to trace the source of infection.

TREATMENT

- The primary goal of therapy is to replenish fluid losses caused by diarrhea & vomiting.

- Fluid therapy is accomplished in 2 phases: rehydration and maintenance.

- Rehydration should be completed in 4 hours & maintenance fluids should replace ongoing losses & provide daily requirement.

FLUID THERAPY

- Ringer lactate solution is preferred over normal saline because it corrects the associated metabolic acidosis.

- IV fluids should be restricted to patients who purge >10 ml/kg/h & for those with severe dehydration.

- The oral route is preferred for maintenance & the use of ORS at a rate of 500-1000 ml/h is recommended.

Estimated electrolyte content of cholera stool and therapeutic fluids for cholera

	Millimoles/liter					Comment
	Na+	K+	Cl−	HCO3−	Carbohydrate	
Electrolyte losses in stools						
Cholera stool, adult	130	20	100	45	--	Stool sodium losses in cholera are higher than in other diarrheal illnesses.
Cholera stool, child	100	30	90	30	--	
Non-cholera stool, child (ETEC)	50	35	25	20	--	
Intravenous therapy						
Lactated Ringer's solution	130	4	109	28	--	Lactated Ringer's (LR) solution is preferred over normal saline because it contains potassium and bicarbonate. 'Dhaka solution' contains more potassium and bicarbonate than LR, and also contains dextrose.
Normal saline	154	0	154	0	--	
Cholera saline (Dhaka solution)	133	13	154	48	140	
Oral rehydration therapy						
ORS (WHO 2002)	75	20	65	10 (citrate)	75 (glucose)	WHO ORS utilizes glucose as a carbohydrate source. Rice based ORS formulation have been found in randomized trials to reduce the duration of diarrhea and stool losses in severe cholera. A homemade preparation of ORS could be used in an emergency scenario.
Rice based ORS (eg, CeraORS 75®)	75	20	65	10 (citrate)	27 grams rice syrup solids	
Homemade ORS: ▪ Half (1/2) teaspoon salt ▪ Six (6) teaspoons sugar ▪ 1 liter of clean water	~75	0	~75	0	~75	

DRUG THERAPY

- The goals of drug therapy are to eradicate infection, reduce morbidity and prevent complications.

- The drugs used for adults include tetracycline, doxycycline, cotrimoxazole & ciprofloxacin.

- For children erythromycin, cotrimoxazole and furazolidone are the drugs of choice.

DRUG THERAPY/2

- Drug therapy reduces volume of stool & shortens period of hospitalization. It is only needed for few days (3-5 days).

- Drug resistance has been described in some areas & the choice of antibiotic should be guided by the local resistance patterns .

- Antibiotic should be started when cholera is suspected without waiting for lab confirmation.

Oral antibiotics for suspected cholera

Class	Antibiotic	Typical pediatric dose*	Adult dose	Comment(s)
Tetracyclines	Doxycycline	4-6 mg/kg (single dose)	300 mg (single dose)	Antibiotic resistance to all tetracyclines is common[1]. Empiric use is appropriate in epidemics caused by documented susceptible isolates. Not recommended for pregnant women and children less than 8 years.
	Tetracycline	50 mg/kg/day in four equally divided doses, for three days	500 mg four times per day for three days	
Macrolides	Azithromycin	20 mg/kg (single dose)	1 g (single dose)	Single dose azithromycin is preferred therapy[2]. Rare reports of macrolide resistance.
	Erythromycin	40 mg/kg/day in four equally divided doses, for three days	500 mg four times per day for three days	
Fluoroquinolones	Ciprofloxacin	20 mg/kg (single dose)	1 g (single dose)	Reduced susceptibility to fluoroquinolones has been reported in Asia and Africa[2,3]. Not recommended for pregnant women and children less than 8 years.

* Not to exceed maximum dose.

References:

1. *Yamamoto T, Nair GB, Albert MJ, et al. Survey of in vitro susceptibilities of Vibrio cholerae O1 and O139 to antimicrobial agents. Antimicrob Agents Chemother 1995; 39:241.*
2. *Saha D, Karim MM, Khan WA, et al. Single-dose azithromycin for the treatment of cholera in adults. N Engl J Med 2006; 354:2452.*
3. *Islam MS, Midzi SM, Charimari L, et al. Susceptibility to fluoroquinolones of Vibrio cholerae O1 isolated from diarrheal patients in Zimbabwe. JAMA 2009; 302:2321.*

COMPLICATIONS

- If dehydration is not corrected adequately & promptly it can lead to hypovolemic shock, acute renal failure & death.

- Electrolyte imbalance is common.

- Hypoglycemia occurs in children.

- Complications of therapy like over hydration & side effects of drug therapy are rare.

PUBLIC HEALTH ASPECTS

- Isolation & barrier nursing is indicated
- Notification of the case to local authorities & WHO.
- Trace source of infection.
- Resume feeding with normal diet when vomiting has stopped & continue breastfeeding infants & young children.

PREVENTION

- Education on hygiene practices.
- Provision of safe, uncontaminated, drinking water to the people.
- Antibiotic prophylaxis to house-hold contacts of index cases.
- Vaccination against cholera to travellers to endemic countries & during public gatherings.

CHOLERA VACCINES

- The old killed injectable vaccine is obsolete now because it is not effective.

- Two new oral vaccines became available in 1997. A Killed & a live attenuated types.

- Both provoke a local immune response in the gut & a blood immune response.

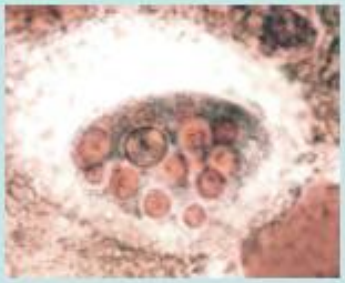
- Cholera vaccination is no more required for international travellers because risk is small.

Water Borne Infectious Diseases:

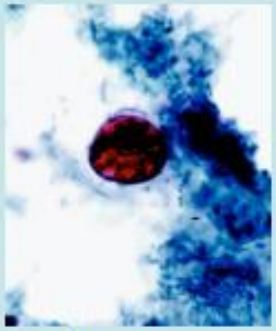
Protozoa

Giardia lamblia

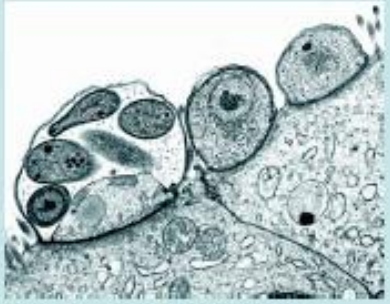
Giardia lamblia
Entameba histolytica
Cryptosporidium parvum
Cyclospora cayetanensis
Balantidium coli



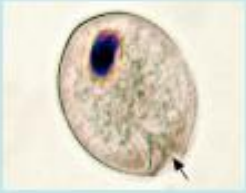
Entameba histolytica



Cyclospora cayetanensis



Cryptosporidium parvum

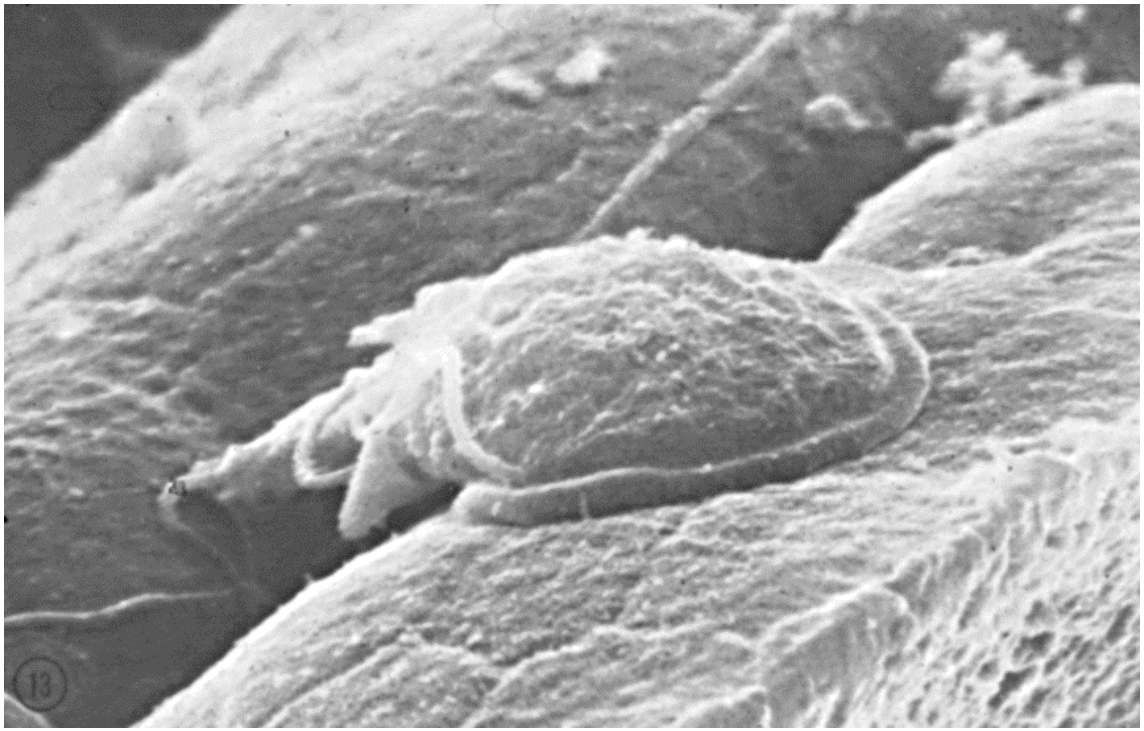


Balantidium coli

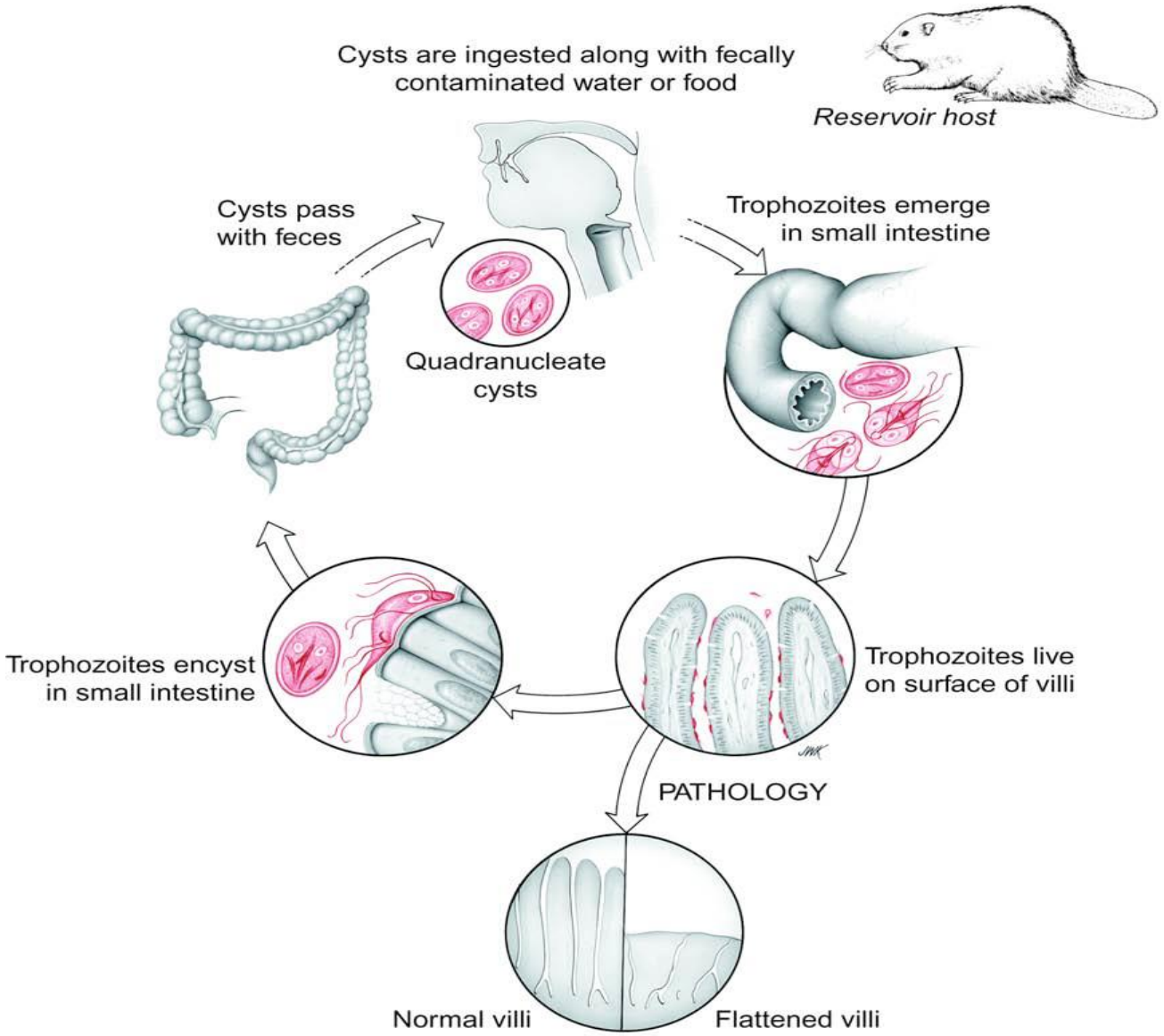
Giardiasis

Giardia lamblia

- SEM of Giardia lamblia in situ



Giardia lamblia



Clinical Disease

- 1. Diarrhea (steatorrhea)
- 2. Weight loss
- 3. Constipation
- 4. Fatigue

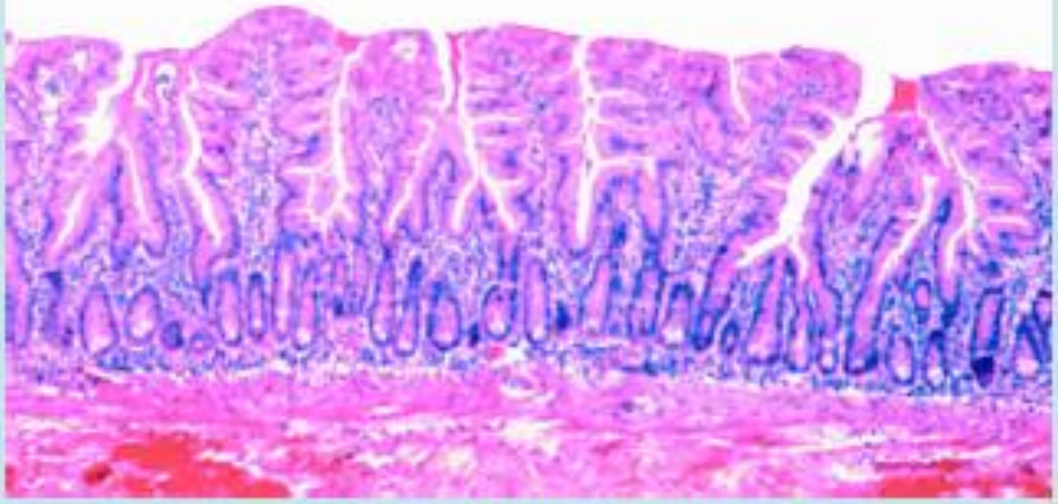
COMPLICATIONS

- Rarely giardia can spread from the duodenum to the biliary and pancreatic ducts, leading to cholecystitis, cholangitis or granulomatous hepatitis.

- Impaired exocrine pancreatic function with diminished secretion of trypsin and lipase has also been described.

Pathogenesis:

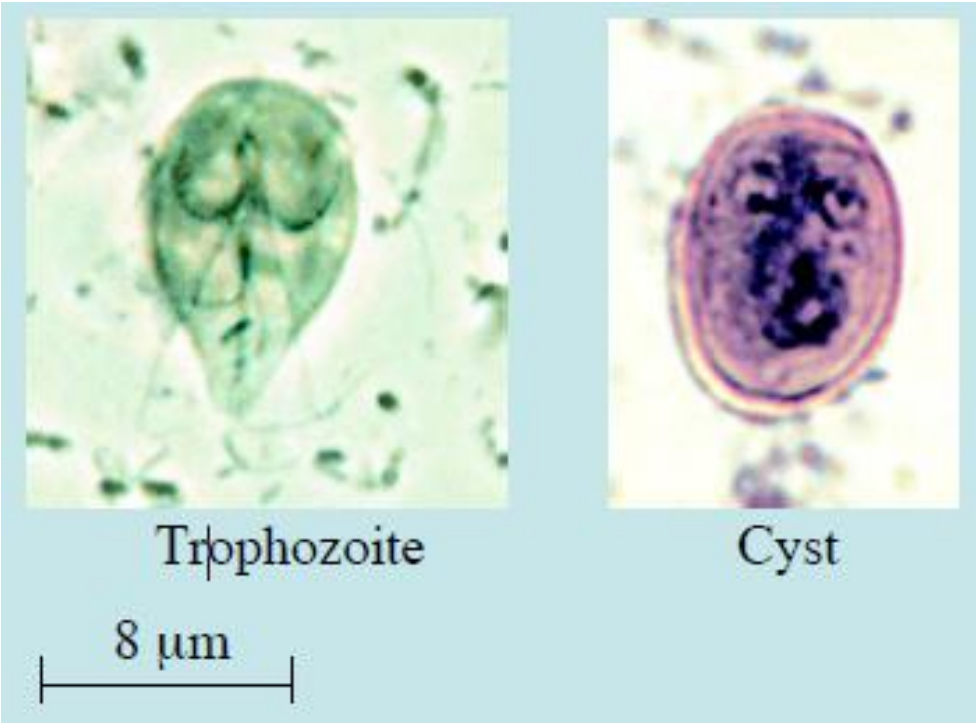
- Trophozoites induce malabsorption of fats.
- Mechanism(s) unknown.



Histopathological correlate: Flattened villi

Diagnosis:

1. Identify trophozoites and cysts by microscopic examination of stool



Diagnosis

2. Antigen Capture ELISA using stool sample
3. PCR
4. IHA serology:
   - Intestinal - 95% predictive of active infection
   - Extra-intestinal - 100% predictive of active infection

Treatment

- Supportive measures for the treatment of children with symptomatic giardiasis include correction of fluid and electrolyte abnormalities.

- We recommend antimicrobial therapy for symptomatic patients with giardiasis (**Grade 1A**).

Treatment

- Treatment is not indicated for most patients with Giardia who are asymptomatic.

- To prevent the spread of infection, however, we suggest treatment of asymptomatic carriers who are food handlers, household contacts of pregnant women or immunocompromised individuals, or children in a day care or other setting who might transmit infection to others

Treatment

- We suggest metronidazole, tinidazole, or nitazoxanide as the drugs of choice for initial therapy (**Grade 2A**).

- Alternative- albendazole, mebendazole, paromomycin, furazolidone, and quinacrine.

- Patients should be counseled to avoid lactose-containing foods for one month after therapy

Treatment of giardiasis

Drug	Dosage	
	Adults	Children
Drugs of choice		
Tinidazole	2 grams orally, single dose	50 mg/kg orally, single dose (maximum dose 2 grams)
Metronidazole	500 mg orally twice daily, OR 250 mg orally three times per day; duration 5 to 7 days	5 to 10 mg/kg orally three times per day for 7 days (maximum 250 mg per dose)
Nitazoxanide	500 mg orally two times per day for three days	Age 1-3 years: 100 mg orally two times per day for 3 days Age 4-11 years: 200 mg orally two times per day for 3 days Age over 11 years: Same as adult dose
Alternative agents		
Albendazole	400 mg orally once daily for 5 days	10 to 15 mg/kg orally once daily for 5 days (maximum 400 mg per dose)
Mebendazole	200 mg orally three times per day for 5 days	200 mg orally three times per day for 5 days
Paromomycin*	10 mg/kg orally three times per day for 5 to 10 days	10 mg/kg orally three times per day for 5 to 10 days
Furazolidone¶	100 mg orally four times per day for 7 to 10 days	1.5 mg/kg orally four times per day for 7 to 10 days (maximum 100 mg per dose)
Quinacrine	100 mg orally three times per day for 5 days	2 mg/kg orally three times per day for 5 days (maximum 100 mg per dose)

Refer to text for additional information regarding choice of therapy, approach to recurrent infection, and availability.

* Poor intestinal absorption; may be useful for treatment of giardiasis in pregnancy.
¶ Potentially significant drug and food interactions with use greater than 5 days due to monoamine oxidase inhibition. For additional information (see "Furazolidone: Drug information" section 'Drug Interactions').

Follow up

- There is no need to repeat the stool examination for parasite clearance in patients whose symptoms resolve.

- Patients with recurrent diarrhea should undergo reevaluation of the stool for parasites before empiric retreatment since the diarrhea may be related to lactose intolerance rather than recurrent Giardia

Relapse

- The optimal approach to relapse after treatment is uncertain.

- We suggest treatment with a drug from a different class (**Grade 2C**).

- Alternative approaches include treatment with a second course of the original agent, treatment with a longer course or higher dose of the original agent, or treatment with a combination of drugs

PREVENTION

- Person-to-person spread of giardiasis can be prevented through strict handwashing, care with diaper disposal, and treatment of symptomatic patients.

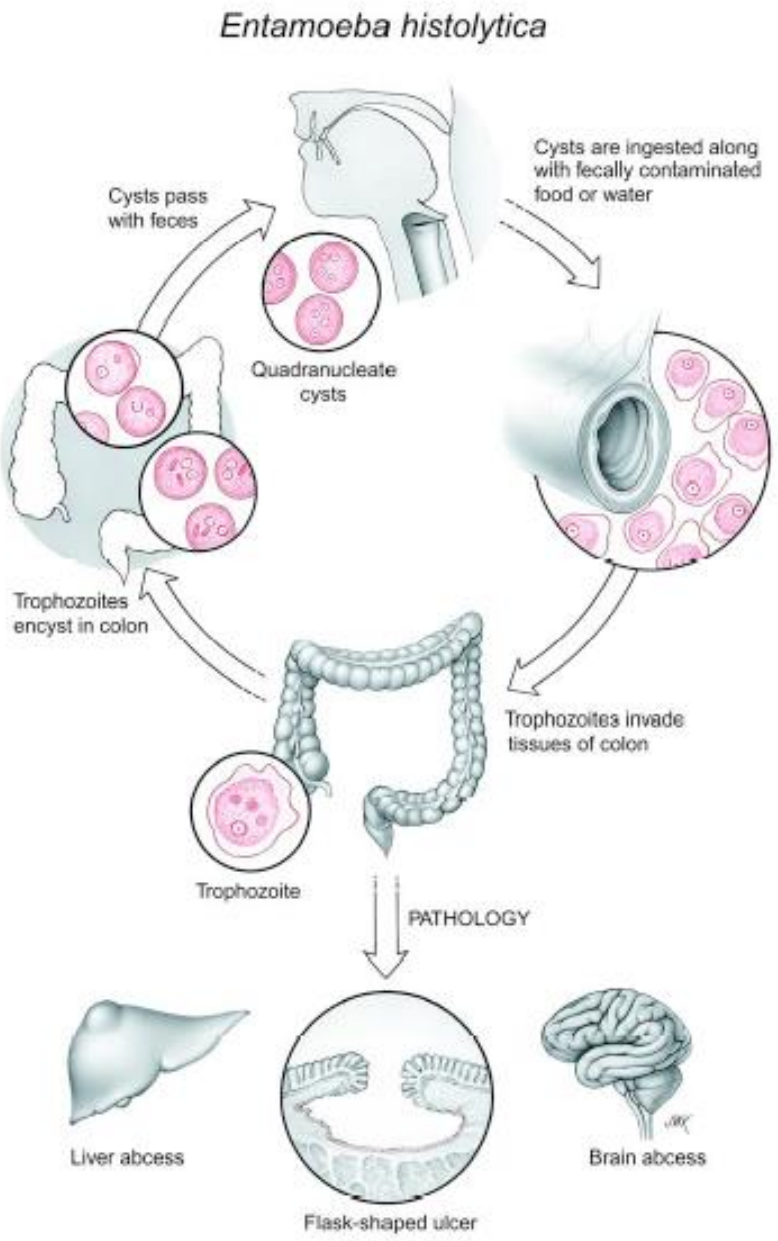
- The local health department should be contacted when an outbreak of giardiasis is suspected.

- Waterborne Giardia infection can be prevented through effective treatment of drinking water.

- Individuals with giardiasis should refrain from using recreational water venues until they have been asymptomatic for two weeks

E.Histolytica

Entameba histolytica



Pathogenesis

- Attachment of amebae to target cells mediated by galactose, then pore-forming protein disrupts target cell membrane:

- Cell-cell contact induces synthesis of lysosomal enzymes in amebae at interface with target cells.

- Cell death ensues.

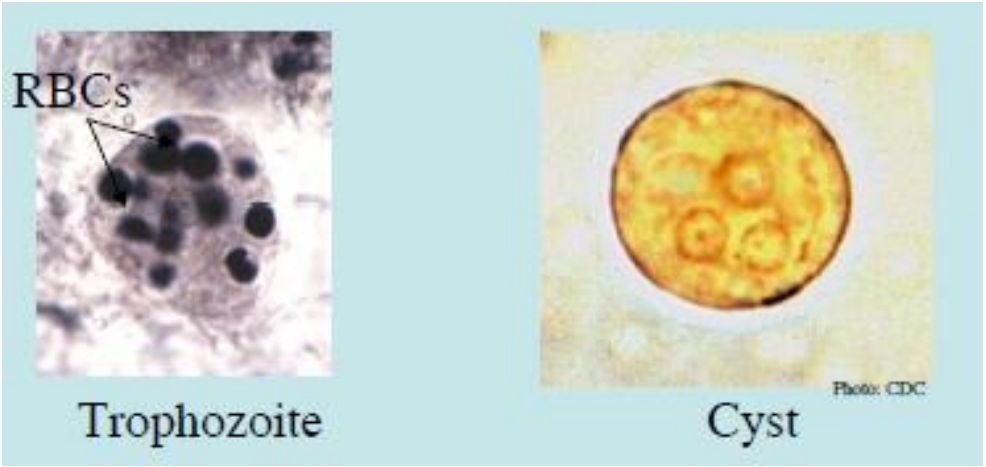
Clinical symptoms

- Intestinal:
  - Diarrhea
  - Dysentery (bloody diarrhea)

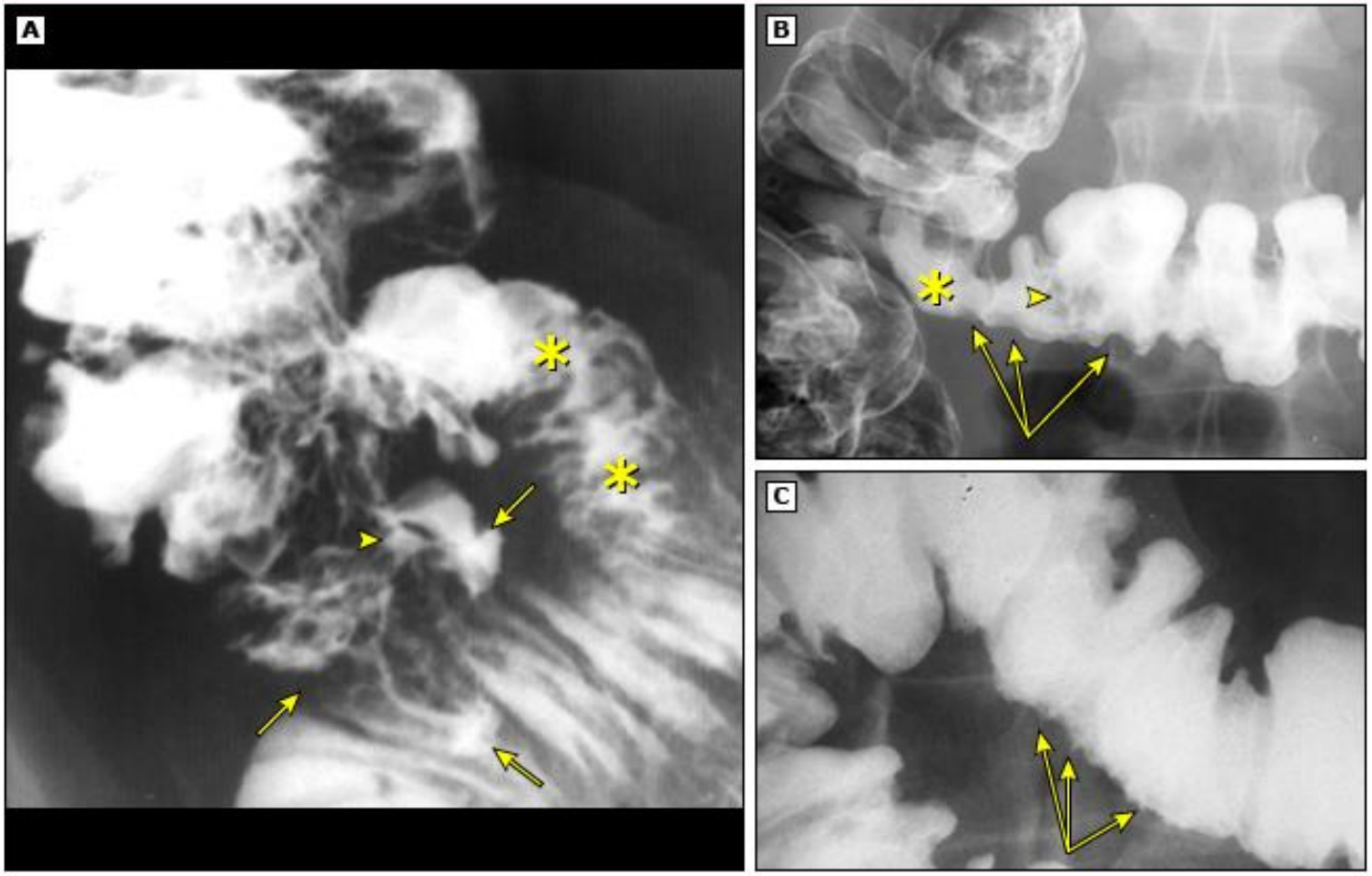
- B. Extra-intestinal:
  - Liver abscess (most common site)
  - Lung abscess
  - Brain abscess (usually fatal)

Diagnosis

- Identify trophozoites and/or cysts in feces. Cannot distinguish E. histolytica from E. dispar by morphology unless cytoplasm contains RBCs.

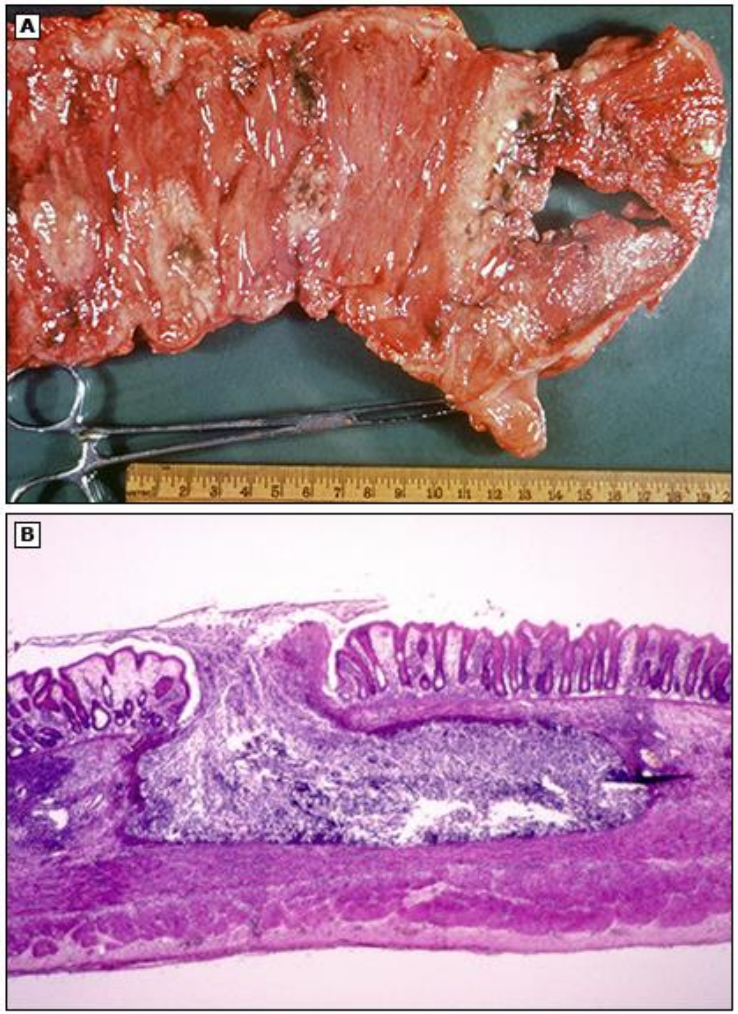


Amebic colitis on barium enema



A barium enema (A) shows a cone-shaped spastic cecum (between arrows), a deep ulcer (arrowhead) with surrounding halo of edema, and an incompetent ileocecal valve allowing for opacification of a normal appearing terminal ileum (asterisks). Image B shows a punctate ulcer (arrowhead) with surrounding halo of edema, spasm and narrowing of the proximal transverse colon (asterisk), and thumb printing (arrows) indicating submucosal edema. Image C shows spiculation (arrows) indicating fine ulceration of the mucosa.

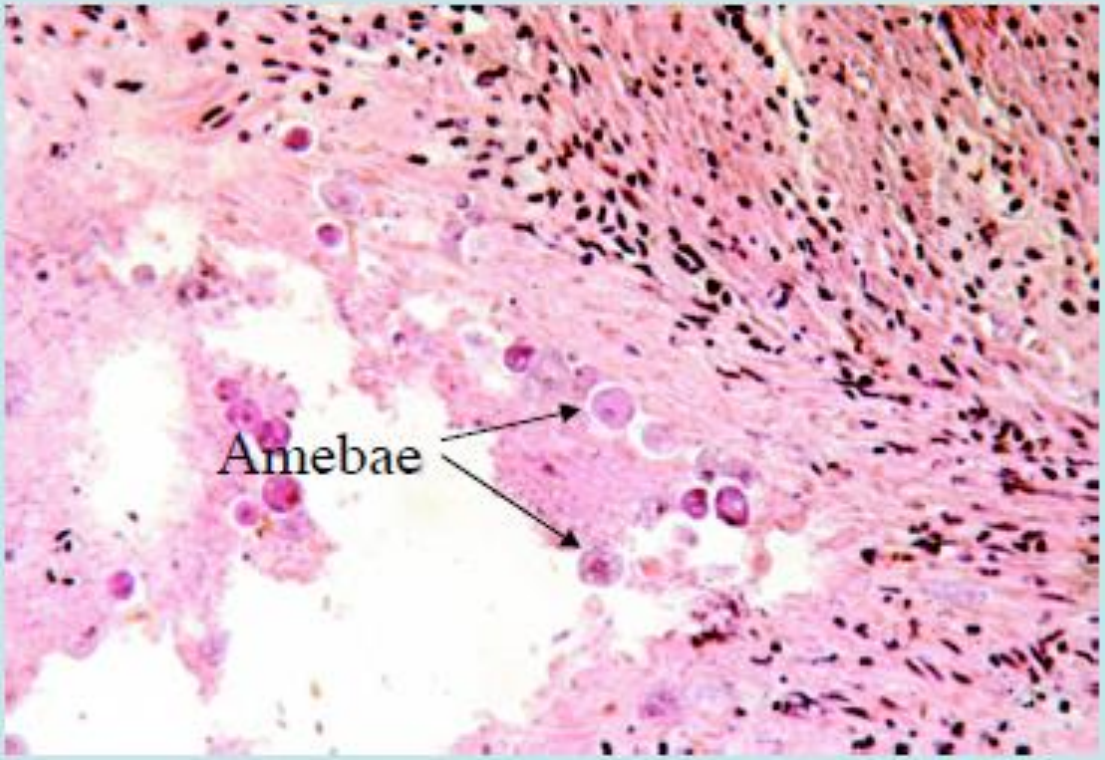
Ulceration in amebic colitis



(A) Gross pathology of amebic colitis showing multiple ulcer formation.
(B) Classic flask-shaped ulcer of amebiasis. Mucosal ulceration with widespread submucosal invasion shown.

Reproduced from: the Centers for Disease Control and Prevention and Drs. Mae Melvin and E West.

Trophozoites of *Entameba histolytica* in situ in flask-shaped ulcer



Treatment

- All *E. histolytica* infections should be treated, even in the absence of symptoms, given the potential risk of developing invasive disease and the risk of spread to family members.

- The goals of antibiotic therapy of intestinal amebiasis are to eliminate the invading trophozoites and to eradicate intestinal carriage of the organism.

- We suggest treatment of invasive colitis with metronidazole or tinidazole (**Grade 2B**).
- We suggest subsequent treatment with paromomycin to eliminate intraluminal cysts (**Grade 2C**).

Treatment – Invasive Colitis

- Metronidazole (alternative therapies include tinidazole, ornidazole, and nitazoxanide),
- followed by a luminal agent (such as paromomycin, diiodohydroxyquin, or diloxanide furoate) to eliminate intraluminal cysts.
- A 10-day course of metronidazole eliminates intraluminal infection in many cases, but a second agent is still warranted
- Asymptomatic patients with *E. histolytica* (and not *E. dispar* or *E. moshkovskii*) should be treated with an intraluminal agent alone.

Metronidazole Dosing

- 500 to 750 mg by mouth three times daily for 7 to 10 days in adults and
- 35 to 50 mg/kg per day in three divided doses for 7 to 10 days in children.
- Shorter duration of metronidazole is generally not recommended
- Metronidazole is well absorbed from the gastrointestinal tract; intravenous therapy offers no significant advantage as long as the patient can take oral medications and has no major defect in small bowel absorption.

Tinidazole

- Tinidazole and ornidazole

- Tinidazole (2 g by mouth daily for three days) has a cure rate of 90 to 93 percent

- Tinidazole resulted in greater resolution of clinical symptoms compared with metronidazole, but there was inconclusive evidence of its advantage in eradication of *E. histolytica* in the stools

- Tinidazole is also better tolerated than metronidazole.

Nitazoxanide

- Nitazoxanide has been proposed as an alternative agent;

- it is likely to be effective at reducing clinical treatment failure

Intraluminal Infection

- Paromomycin (25 to 30 mg/kgper day orally in three divided doses for 7 days), OR

- Diiodohydroxyquin (650 mg orally three times daily for 20 days for adults and 30 to 40 mg/kg per day in three divided doses for 20 days for children), or

- Diloxanide furoate (500 mg orally three times daily for 10 days for adults and 20 mg/kg per day in three divided doses for 10 days for children).

PREVENTION

- Prevention of amebic infection in travelers to endemic areas involves avoidance of untreated water in endemic areas and uncooked food, such as fruit and vegetables, that may have been washed in local water.

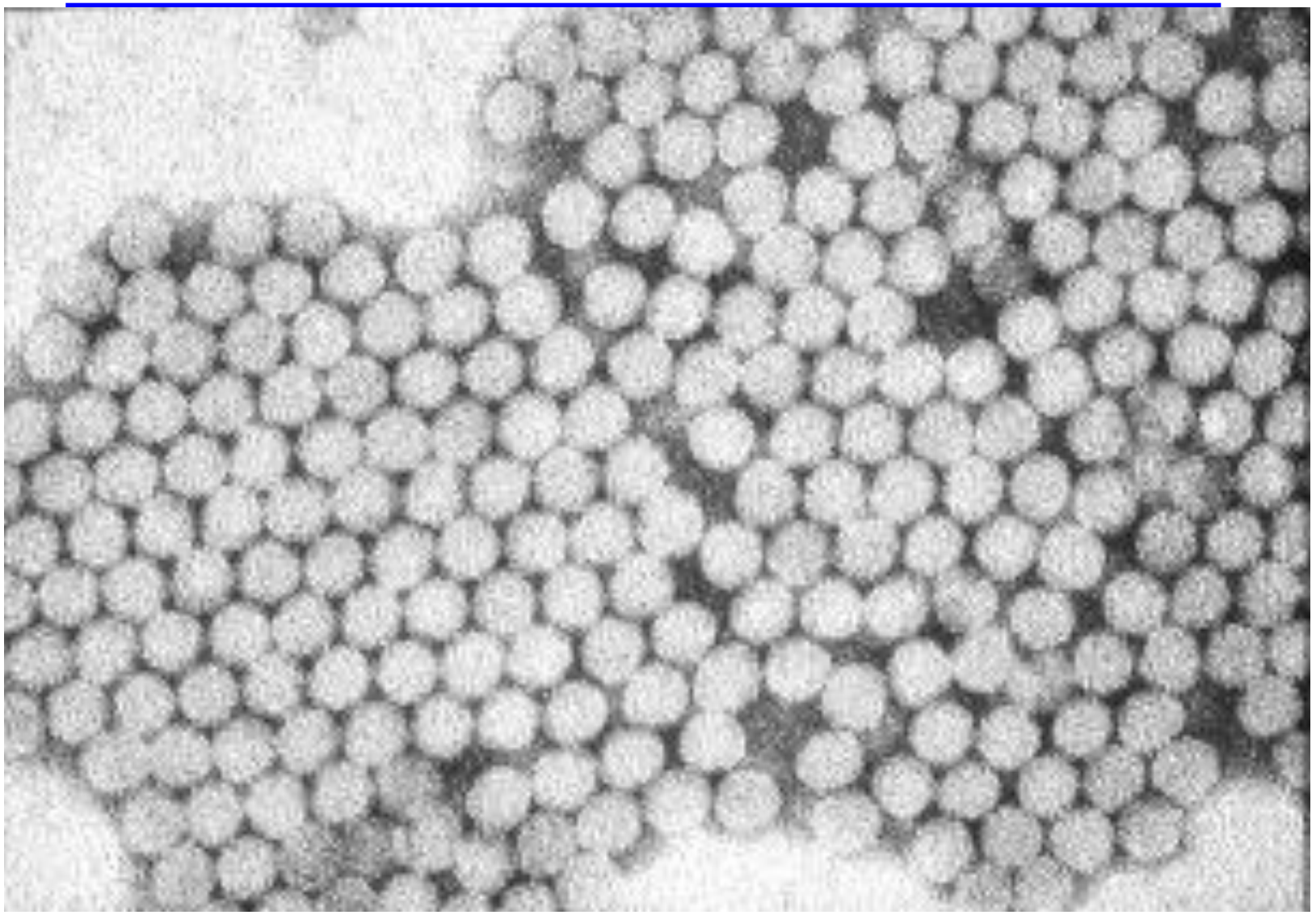
- Amebic cysts are resistant to chlorine at the levels used in water supplies, but disinfection with iodine may be effective.

Hepatitis A and E

Type of Hepatitis

	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre/post-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

Hepatitis A Virus



Hepatitis A Virus

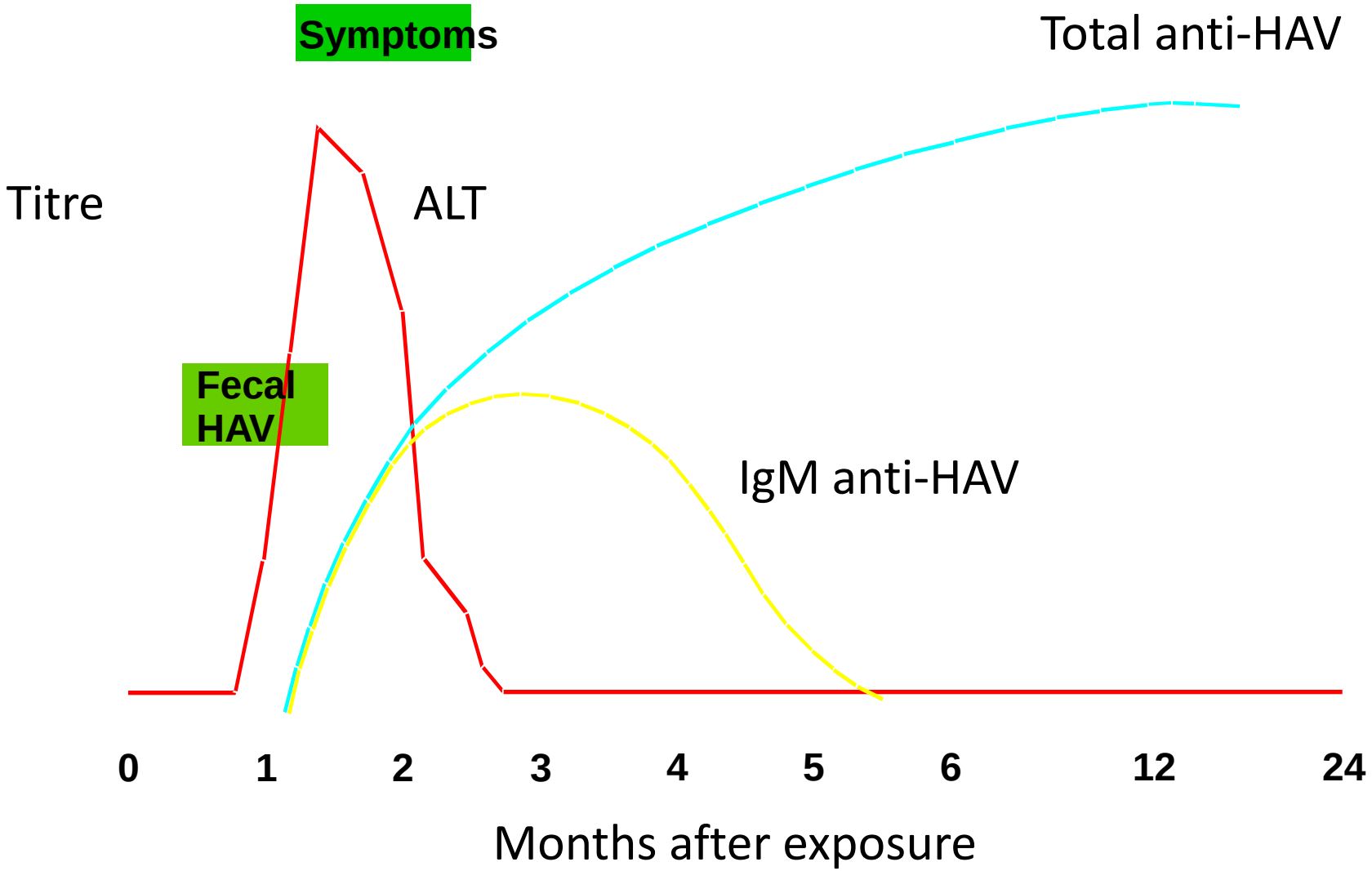
- Naked RNA virus
- Related to enteroviruses, formerly known as enterovirus 72, now put in its own family: heptovirus
- One stable serotype only
- Difficult to grow in cell culture: primary marmoset cell culture and also in vivo in chimpanzees and marmosets
- 4 genotypes exist, but in practice most of them are group 1

Hepatitis A - Clinical Features

- Incubation period: Average 30 days
  Range 15-50 days
- Jaundice by age group: <6 yrs, <10%
  6-14 yrs, 40%-50%
  >14 yrs, 70%-80%
- Complications: Fulminant hepatitis
  Cholestatic hepatitis
  Relapsing hepatitis
- Chronic sequelae: None

Hepatitis A Infection

Typical Serological Course



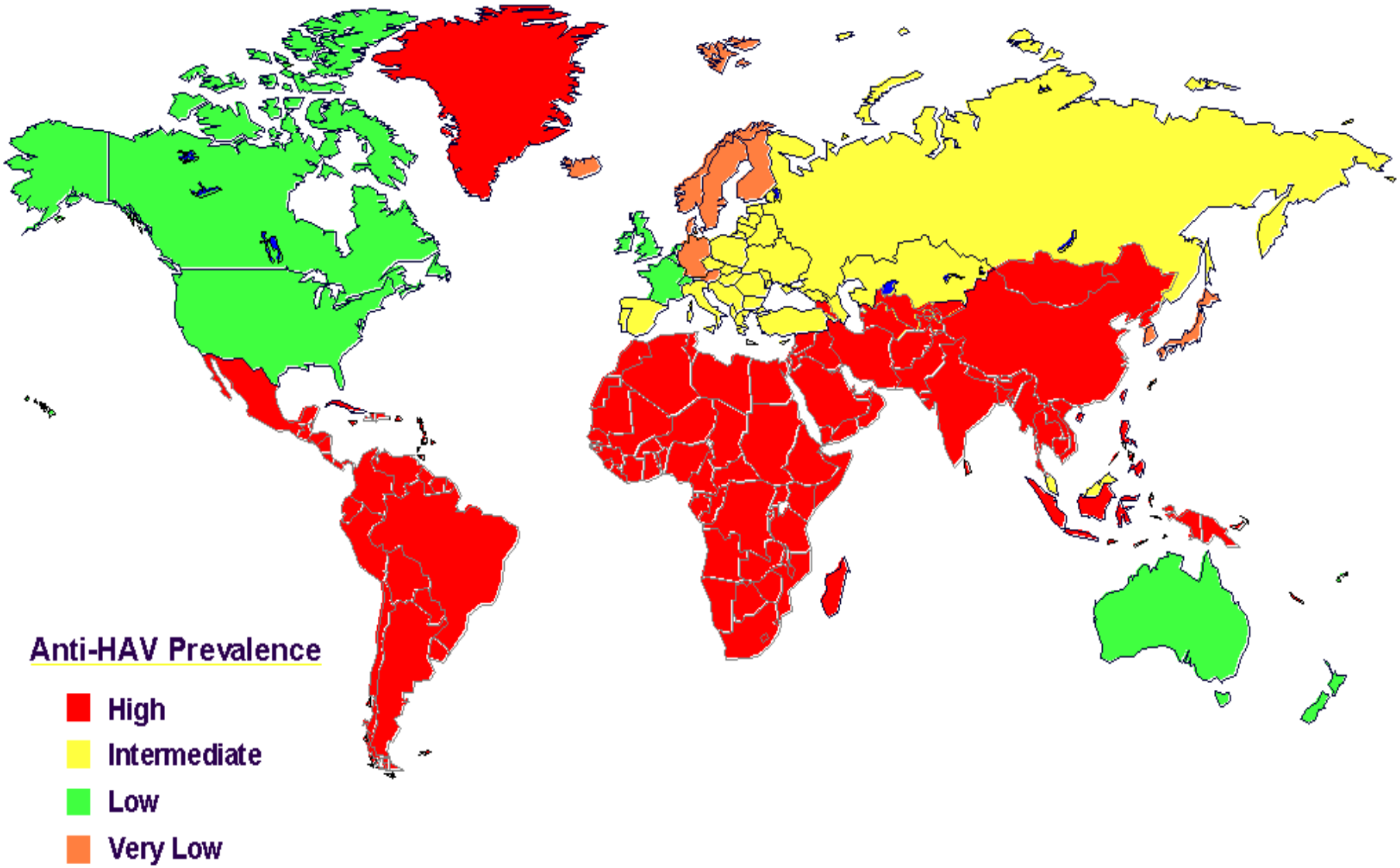
Hepatitis A Virus Transmission

- Close personal contact
  (e.g., household contact, sex contact, child day care centers)
- Contaminated food, water
  (e.g., infected food handlers, raw shellfish)
- Blood exposure (rare)
  (e.g., injecting drug use, transfusion)

Global Patterns of Hepatitis A Virus Transmission

Endemicity	Disease Rate	Peak Age of Infection	Transmission Patterns
High	High	Early childhood	Person to person; outbreaks uncommon
Moderate	High	Late childhood/ young adults	Person to person; food and waterborne outbreaks
Low	Low	Young adults	Person to person; food and waterborne outbreaks
Very low	Very low	Adults	Travelers; outbreaks uncommon

Geographic Distribution of HAV Infection



Laboratory Diagnosis

- Acute infection is diagnosed by the detection of HAV-IgM in serum by EIA.
- Past Infection i.e. immunity is determined by the detection of HAV-IgG by EIA.
- Cell culture – difficult and take up to 4 weeks, not routinely performed
- Direct Detection – EM, RT-PCR of faeces. Can detect illness earlier than serology but rarely performed.

Hepatitis A Vaccination Strategies
Epidemiologic Considerations

- Many cases occur in community-wide outbreaks
  - no risk factor identified for most cases
  - highest attack rates in 5-14 year olds
  - children serve as reservoir of infection
- Persons at increased risk of infection
  - travelers
  - homosexual men
  - injecting drug users

Hepatitis A Prevention - Immune Globulin

- Pre-exposure
  - travelers to intermediate and high HAV-endemic regions
- Post-exposure (within 14 days)

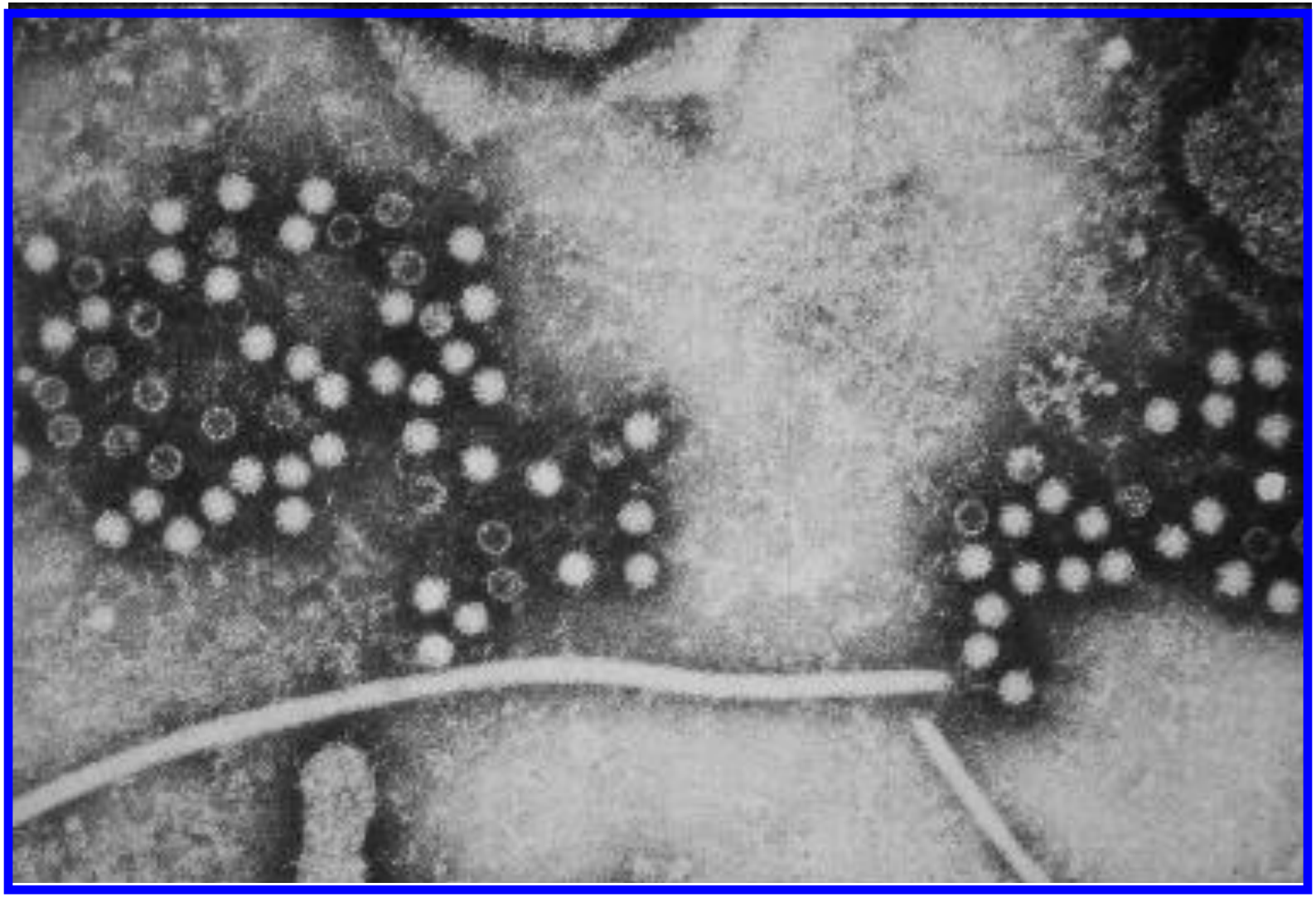
  Routine
  - household and other intimate contacts

  Selected situations
  - institutions (e.g., day care centers)
  - common source exposure (e.g., food prepared by infected food handler)

Hepatitis A Vaccine

- Hepatitis A vaccine is an inactivated (killed) vaccine.
- 2 Doses are needed that are given at least 6 months apart.
- It can be considered for
  - those traveling to countries where hepatitis A is common,
  - Homosexuals
  - Drug Abusers
  - have a chronic liver disease such as hepatitis B or hepatitis C
  - are being treated with clotting-factor concentrates

Hepatitis E Virus



Hepatitis E Virus

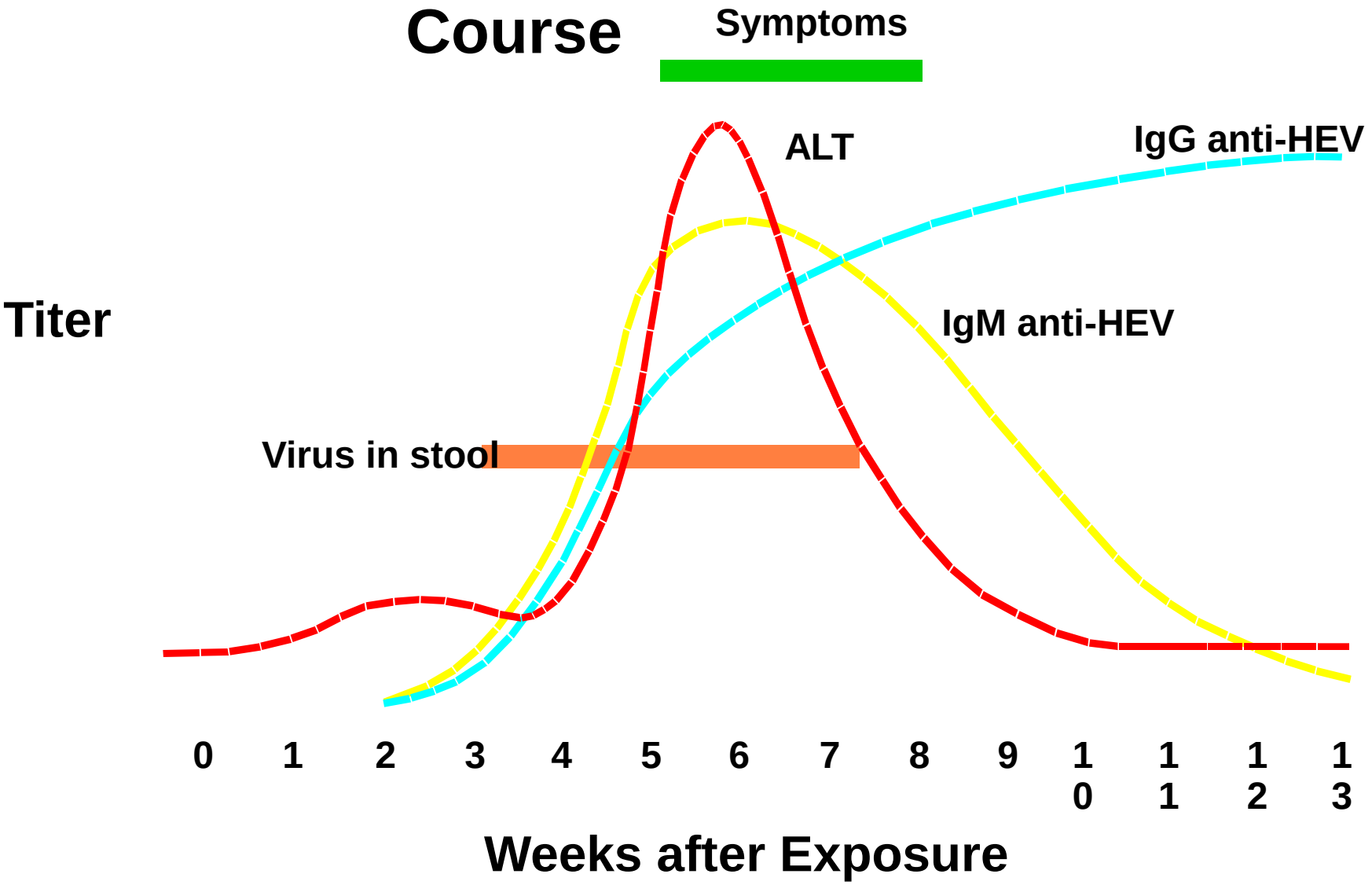
- now classified as a member of the genus Orthohepevirus in the Hepeviridae family
- unenveloped RNA virus, 32-34nm in diameter
- +ve stranded RNA genome, 7.6 kb in size.
- 4 genotypes: genotype 1 (Asia), genotype 2 (Africa and Mexico), genotype 3 (Europe and North America) and **genotype 4 (Asia)**
- very labile and sensitive
- Can only be cultured recently

Hepatitis E - Clinical Features

- Incubation period: Average 40 days
Range 15-60 days
- Case-fatality rate: Overall, 1%-3%
Pregnant women, 15%-25%
- Illness severity: Increased with age
- Chronic sequelae: None identified

Hepatitis E Virus Infection

Typical Serologic Course

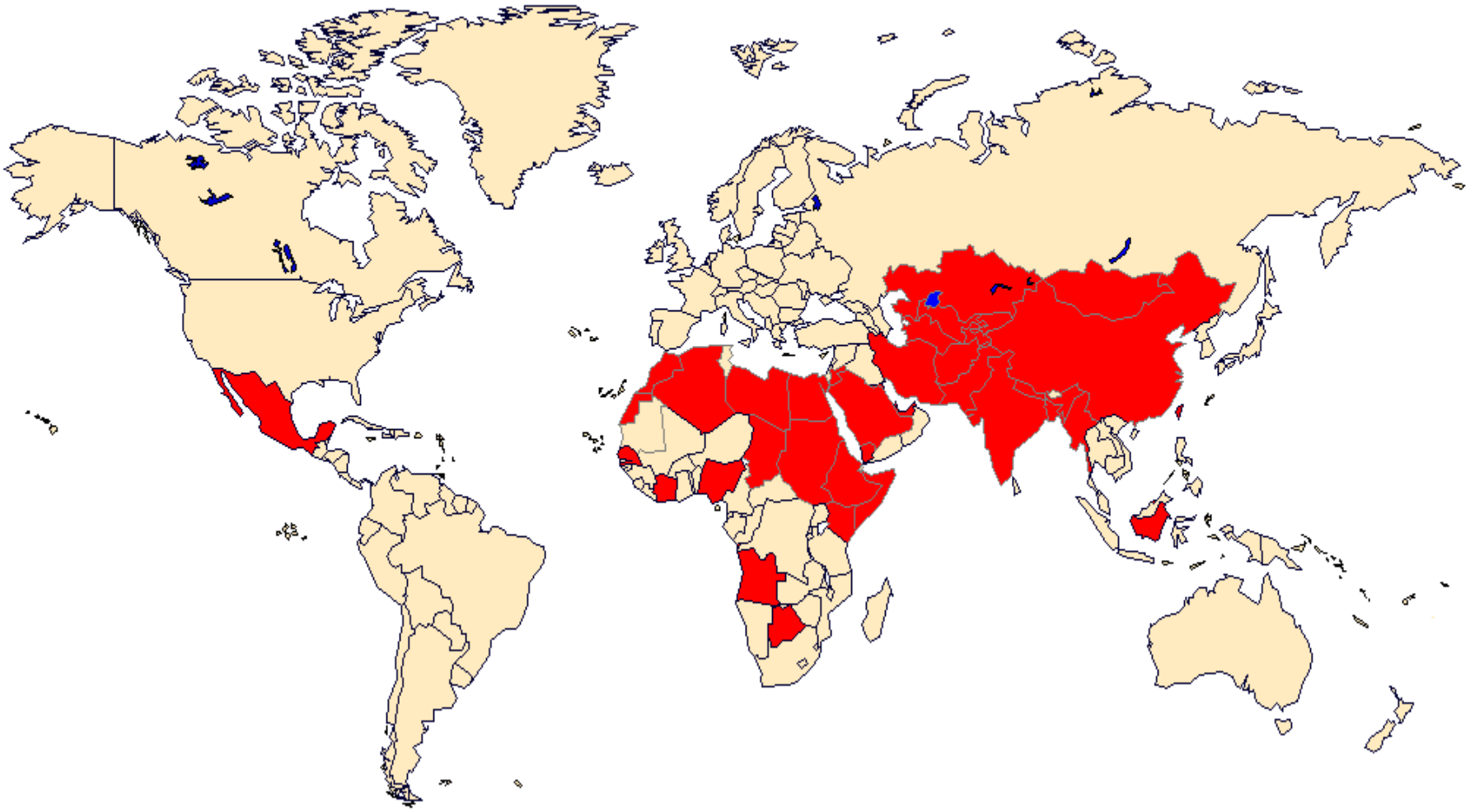


Hepatitis E - Epidemiologic Features

- Most outbreaks associated with faecally contaminated drinking water.
- Several large epidemics have occurred since in the Indian subcontinent and the USSR, China, Africa and Mexico.
- In the United States and other nonendemic areas, a low prevalence of anti-HEV (<2%) has been found in healthy populations. The source of infection for these persons is unknown.
- Minimal person-to-person transmission.

Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis



Prevention and Control Measures for Travelers to HEV-Endemic Regions

- Avoid drinking water (and beverages with ice) of unknown purity, uncooked shellfish, and uncooked fruit/vegetables not peeled or prepared by traveler.
- IG prepared from donors in Western countries does not prevent infection.
- Unknown efficacy of IG prepared from donors in endemic areas.
- . A recombinant vaccine called HEV 239 has been developed and is licensed for use in China.

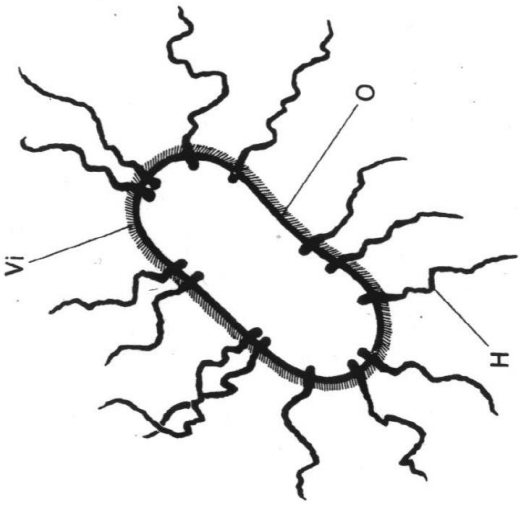
Enteric Fever

Etiology :

- Typhoid fever is caused by a virulent bacterium called Salmonella typhi thriving in conditions of poor sanitation and crowding. G-ve bacilli in family Enterobacteriaceae

- Antigens: located in the cell capsule

  - ❖ H (flagellar antigen).
  - ❖ Vi (polysaccharide virulence Ag).
  - ❖ O (Somatic Ag)



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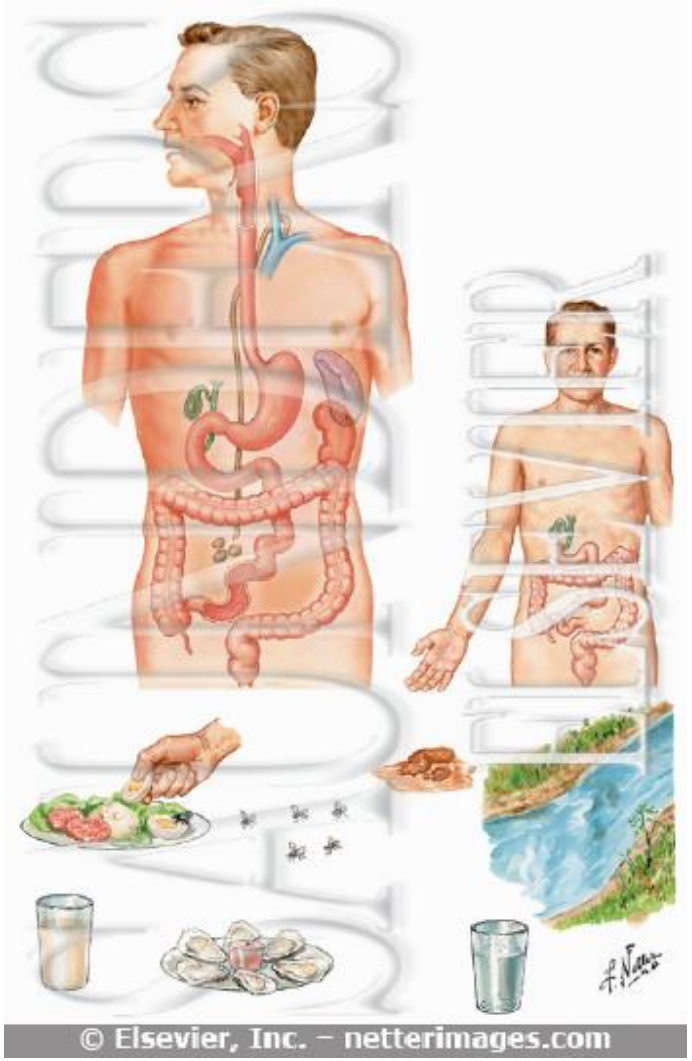
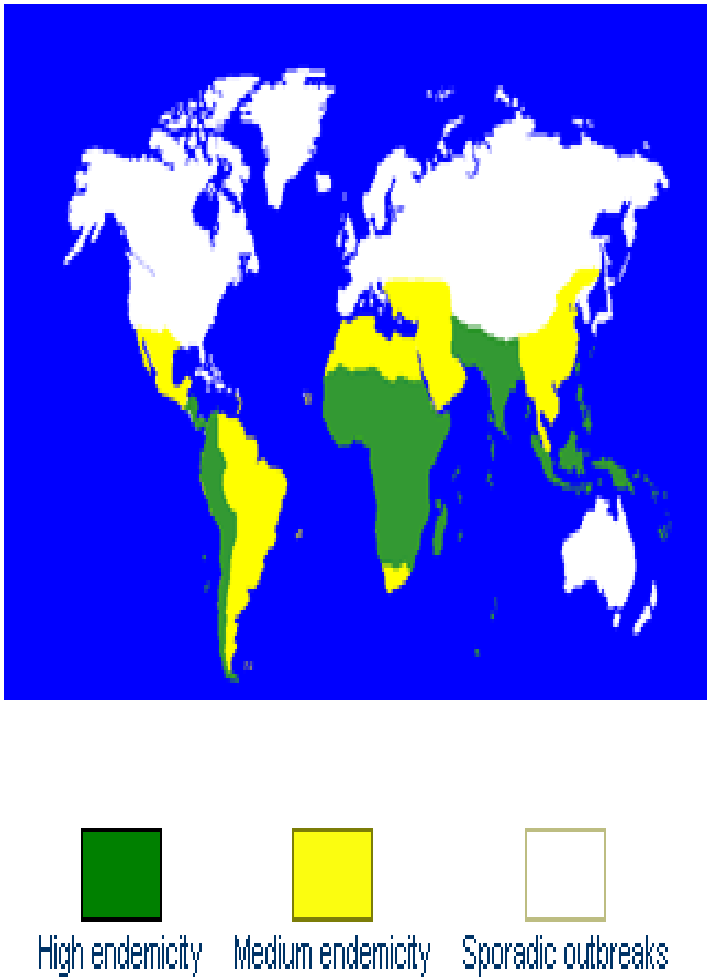
Transmission

- *S typhi* has no nonhuman vectors.
  - ❖ via food handled by an individual who chronically sheds the bacteria through stool or, less commonly, urine
  - ❖ Hand-to-mouth transmission after using a contaminated toilet and neglecting hand hygiene
  - ❖ Oral transmission via sewage-contaminated water or shellfish



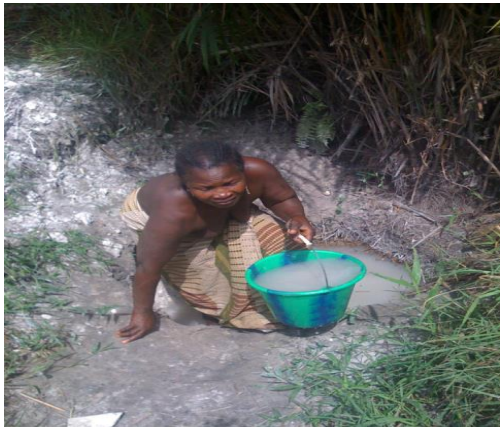
Epidemiology

- Typhoid fever occurs worldwide, primarily in developing nations whose sanitary conditions are poor.
- Typhoid fever is endemic in Asia, Africa, Latin America, the Caribbean, and Oceania.
- Typhoid fever infects roughly 21.6 million people and kills an estimated 200,000 people every year.



Risk factors

- Worldwide, children are at greatest risk of getting the disease
- Work in or travel to endemic area
- Have close contact with someone who is infected or has recently been infected with typhoid fever
- Weak immune system such as use of corticosteroids or diseases such as HIV/AIDS
- Drinking water contaminated by sewage that contains S. typhi



Pathogenesis

- The organisms penetrate ileal mucosa reach mesentric lymph nodes via Lymphatics , Multiply,
- Invade Blood stream via thoracic duct
- In 7 – 10 days through blood stream infect
- Liver, Gall Bladder,, spleen, Kidney, Bone marrow.
- After multiplication, bacilli pass into blood causing secondary and heavier bacteremia

Pathology

Essential lesion:

- proliferation of RES
- specific changes in lymphoid tissues
- and mesenteric lymph nodes.

"typhoid nodules“

Most characteristic lesion:

- ulceration of mucous membrane in the region of the Peyer’s patches of the small intestine

Clinical presentation

- The incubation period for typhoid fever is 7-14 days (range 3-60 days)

- If not treated, the symptoms develop over four weeks, with new symptoms appearing each week but with treatment, symptoms should quickly improve.

Clinical manifestations

The initial period (early stage due to bacteremia)

- First week: non-specific, insidious onset of fever

Fever up to 39-40^{0}C in 5-7 days, step-ladder (seen in < 12%),

Headache, chills, toxic, tired, sore throat, cough,

abdominal pain

and diarrhea or constipation.

The fastigium stage

- **second and third weeks.**
- **fever reaches a plateau at 39-40. Last 10-14 days.**
- **more toxic and anorexic with significant weight loss. The conjunctivae are injected, and the patient is tachypnoeic with a thredy pulse and crackles over the lung bases. Abdominal distension is severe. Some patients experience foul, green-yellow, liquid diarrohea (pea soup diarrohea).**
- **The(typhoid state) is characterized by apathy, confusion, and even psychosis. Necrotic Payer patches may cause bowel perforation and peritonitis. This complication may be masked by corticosteroids. At this point, overwhelming toxaemia, myocarditis, or intestinal hemorrhage may cause death.**

- **Signs and symptoms:**

relative bradycardia.

- **Splenomegaly, hepatomegaly**

- **rash (rose-spots):30%, maculopapular**

a faint pale color, slightly raised

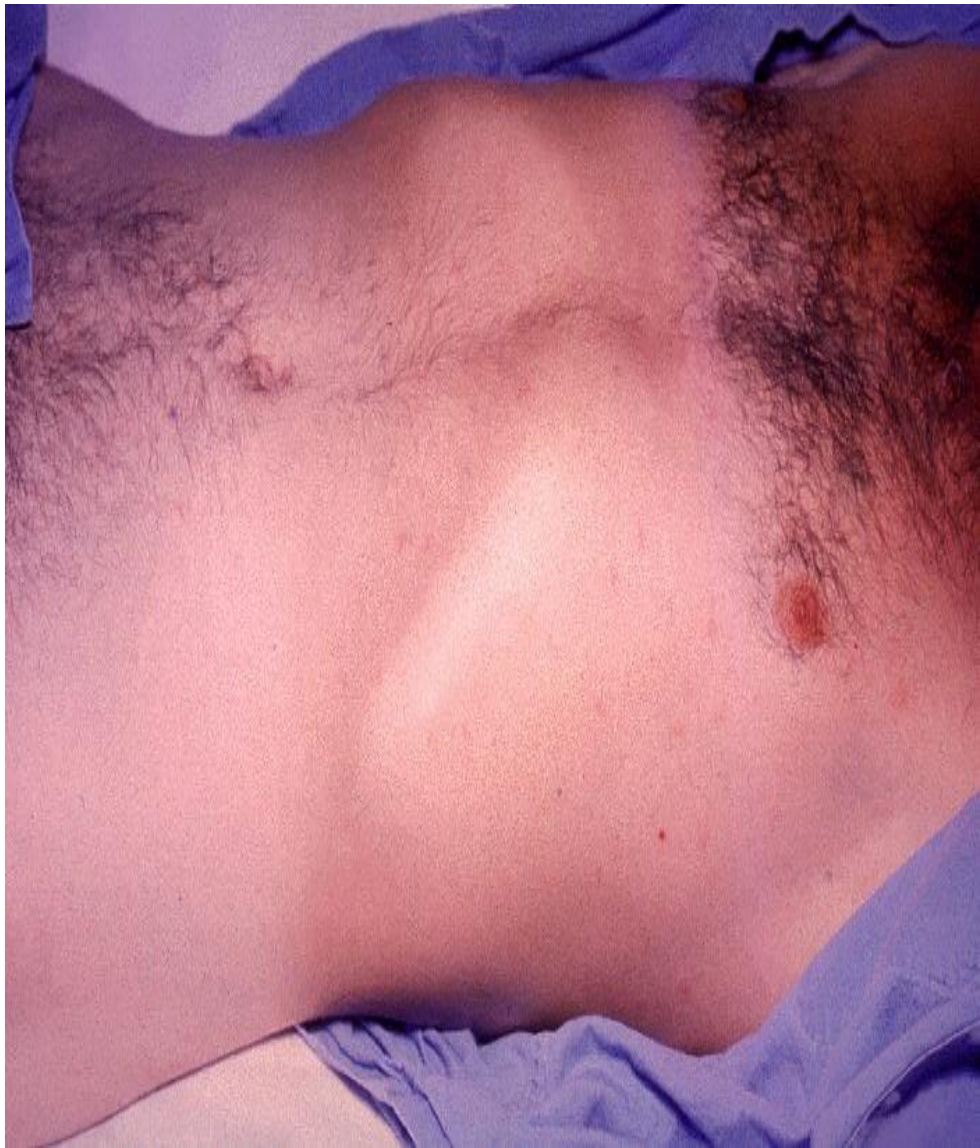
round or lenticular, fade on pressure

2-4 mm in diameter, less than 10 in No.

on the trunk, disappear in 2-3 days.

Rash in Typhoid

- Rose- spots: found in front of chest
- Appear in crops of upto a dozen at a time



defervescence stage

- **By the fourth week of infection:**

  If the individual survives , the fever, mental state, and abdominal distension slowly improve over a few days. Intestinal and neurologic complications may still occur. Weight loss and debilitating weakness last months. Some survivors become asymptomatic carriers and have the potential to transmit the bacteria indefinitely

convalescence stage

- **the fifth week: disappearance of all symptoms, but can relapse**

Atypical manifestations :

- **Mild infection:**

very common seen recently

symptom and signs are mild

good general condition

temperature is 38^0C

short period of disease

recovery expected in 1~3 weeks

seen in early antibiotic users

in young children more common

easy to misdiagnose

- **Persistent infection:**

  disease continue > 5weeks

Ambulatory infection:

mild symptoms, early intestinal bleeding or perforation.

- **Fulminant infection:**

  rapid onset, severe toxemia and septicemia.

  High fever, chill, circulatory failure, shock, delirium, coma, myocarditis, bleeding and other complications, DIC.

- **In the aged**

temperature not high, weakness common.

More complications.

High mortality.

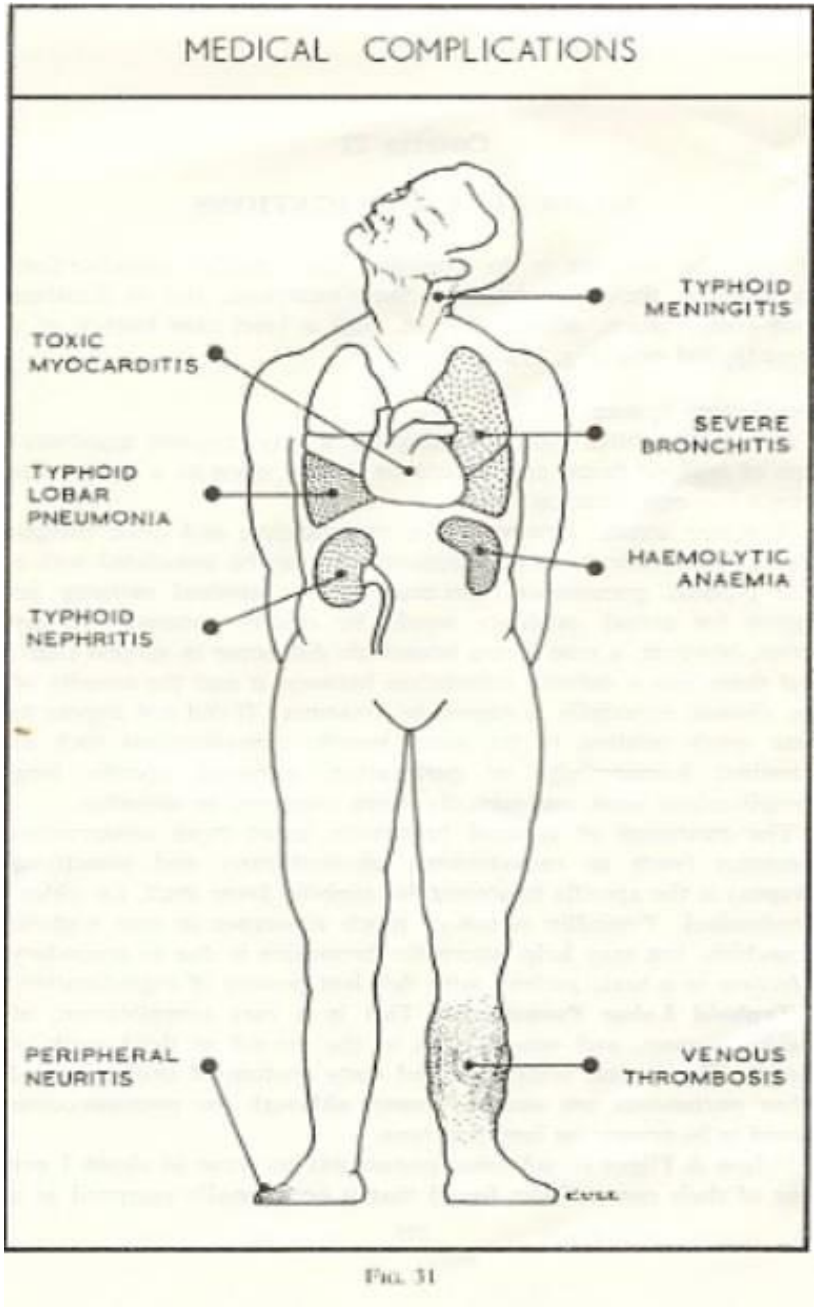
Complications

Intestinal bleeding or perforation

The most serious complication of typhoid fever

Other, less common

- Myocarditis
- Pneumonia
- pancreatitis
- UTI
- Osteomyelitis
- Meningitis
- Psychiatric problems



Complications

Intestinal hemorrhage

Commonly appear during the second-third week

may be mild or severe bleeding

often caused by unsuitable food, and diarrhea

serious bleeding in about 2~8%

clues: sudden drop in temperature, rise in pulse, and signs of shock followed by dark or fresh blood in the stool.

Intestinal perforation:

- more serious. Incidence:1-4%
- Commonly appear during 2nd-3rd week.
- Take place at the lower end of ileum.
- Before perforation, abdominal pain or diarrhea, intestinal bleeding .
- When perforation: ↑ abdominal pain, sweating, drop in temperature, and increase in pulse rate, then rebound tenderness +ve

  reduce or disappear in the dullness of liver, leukocytosis .
- Temperature rise when peritonitis appear.
- free air in abdominal x-ray.

- **Toxic hepatitis:**

  common,1-3 weeks

  hepatomegaly, ALT elevated

  get better with improvement of disease in 2~3 weeks

- **Toxic myocarditis.**

  seen in 2nd-3rd week, usually severe toxemia.

- **Bronchitis, bronchopneumonia.**

  seen in early stage

Blood cultures in Typhoid fever

- In Adults 5-10 ml of Blood is inoculated into 50 – 100 ml of Bile broth (0.5 %).
- Larger volumes 10-30 ml and clot cultures increase sensitivity
- Blood culture is positive as follows:

1st week in 90%

2nd week in 75%

3rd week in 60%

4th week and later in 25%

- **Bone marrow culture**

  the most sensitive test

  even in patients pretreated (up to 5 days) with antibiotics.

- **Urine and stool cultures**

  increase the diagnostic yield

  positive less frequently

  stool culture better in 3rd~4th weeks

- **Duodenal string test to culture bile useful for the diagnosis of carriers.**

Widal test

- Serum agglutinins raise abruptly during the 2nd or 3rd week, it is +ve by 10th day, but max. during 18-23rd day
- The widal test detects antibodies against O and H antigens
- Two serum specimens obtained at intervals of 7 – 10 days to read the rise of antibodies.
- The test is neither sensitive nor specific

TREATMENT

1-General :

- Isolation and rest
- suitable diet include easy digested food or half-liquid food and drinking more water
- IV fluid to maintain water and acid-base and electrolyte balance
- Symptomatic : antipyretic

Drug treatment

- ***Ciprofloxacin***: 15 mg/kg/d for 7 days
- For quinolone-resistant: ***azithromycin*** 10mg/kg/d for 7 days OR ***ceftriaxone*** 75mg/kg/d for 10-14 days

Carrier

Asymptomatic and have positive stool or rectal swab cultures for *S. typhi* a year following recovery from acute illness.

Treatment: **co-trimoxazole** 2 tab twice/d for 6 wk, OR

ciprofloxacin 750 mg twice/d for 4 wk

Carrier

Carriers should be excluded from activities involving food preparation and serving. Food handlers should not resume their duties until they have had three negative stool cultures at least one month apart.

- Vi Ab is used as a screening technique to identify carriers among food handlers and in outbreak investigations. Vi Abs are very high in chronic *S. typhi* carriers

Relapse

- **Apparent recovery can be followed by relapse in 5 – 10 % of untreated patient**
- **culture +ve of S.typhi after 1-3 wks of defervescence**
- **Symptom and signs reappear**
- **the bacilli have not been completely eradicated**
- **Some cases relapse more than once**
- On few occasions relapses can be severe and may be fatal.

Prognosis:

- Case fatality 0.5-1%.
- but high in old ages, infant, and serious complications

- About 3% of patients become fecal carriers .

Vaccines for Typhoid Prevention

- Two types :

1. Oral – A live vaccine (typhoral)

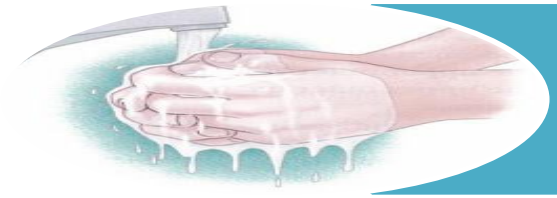
   One capsule given orally taken before food, with a glass of water or milk, on day 1, 3, 5 (three doses)

   No antibiotics should be taken during the period of administration of vaccine

2. The injectable vaccine, (typhim –vi)

   Given as single sc or im injection

Prophylaxis



Wash your hands.

Avoid drinking untreated water.

id raw fruits and vegetables

Choose hot foods.

Prevention: Water-borne Disease

- Improve quality and quantity of drinking water at source, at the tap, or in the storage vessel
- Interrupt routes of transmission by emptying accumulated water sources
- Chlorinate water
- Change hygiene behavior (ex. Hand washing)
- Take care in disposing of waste and human and animal feces
- Proper use of latrines by adults and children
- Proper use and maintenance of water supply, sanitation systems, pumps and wells
- Good food hygiene (ex. protect food from flies)