



## Infectious Diarrhoea

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#### Why do we care about infectious diarrhoea?

- Diarrhoea kills 2,195 children every day—more than AIDS, malaria, and measles combined
- Diarrhoeal diseases account for 1 in 9 child deaths worldwide, making diarrhea the second leading cause of death among children under the age of 5.
- About 88% of diarrhoea-associated deaths are attributable to unsafe water, inadequate sanitation, and insufficient hygiene

#### Death rate from diarrheal diseases, 2017

The annual number of deaths from diarrheal diseases per 100,000 people.



Source: IHME, Global Burden of Disease (GBD)

Note: To allow comparisons between countries and over time this metric is age-standardized.

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Deaths from diarrheal diseases, by age, World, 1990 to 2017 Annual deaths from diarrheal diseases, differentiated by age categories.



#### **← Change country** □ Relative



Source: IHME, Global Burden of Disease (GBD)



#### History

- Bloody Vs Non-Bloody
- Acute (Bacterial/Viral) Vs. Chronic (parasites/not infections)
- Food history Where/What/When/Who else ate it?
- Recent Abx use? (Cdiff)
- Travel (Where/When/What did they eat)
- Weight loss/wasting/malnourishment (suggests a longer process)
- Immunosuppression
- Always send Stool sample to the lab (PCR and OCP depending on history)

### Causes (pretty much any infection)

- Viral
- Rotavirus
- Norovirus (Norwalk virus)
- Enteroviruses
- Adenoviruses
- CMV (Immunocompromised)
- Hepatitis A, E
- Protozoal
- Entaemoeba histolytica
- Giardia duodenalis
- Cryptosporidium
- Cyclospora/Isospora

- Bacterial
- E. coli (Traveller's Diarrheoa)
- Salmonella (Typhoid)
- Vibrio (Cholera)
- Yersinia
- Campylobacter
- Shigella
- Clostridioides difficile
- Bacillus cereus
- Staph aureus
- Helminths
- > (all of them really)

#### Child deaths from diarrheal diseases by cause

Attributable number of deaths for each pathogen in children under 5 in 2016.



191,820 attributable child deaths in 2016	Rotavirus 128,515 attributable child deaths 27% of diarrhea cases		Norovirus 10,629 attributable child deaths 2% of diarrhea cases Adenovirus 52,613 attributable child deaths 11% of diarrhea cases		Amoebiasis 4,567 child deaths 1% of diarrhea cases Cryptosporidium 48,301 child deaths 10% of diarrhea cases	
230,627 attributable child deaths in 2016	<b>Cholera</b> 52,232 attributable child deaths 11% of diarrhea cases	Enterotoxigeni E.coli 18,669 child deaths 4% of diarrhea case	ic **	Enteropathogenic E.coli 9.459 deaths 2% of cases	vphoidal	
	Shigella 63,713 attributable child deaths 13% of diarrhea cases	40,854 attributable cl 9% of diarrhea cases	acter hild deaths	Salmonella 37,410 attributable child deaths 8% of diarrhea cases		

Data source: Troeger et al., 2018.

This is a visualization from OurWorldinData.org, where you find data and research on how the world is changing. Licensed under CC-BY by the author Bernadeta Dadonaite. Protists



12:13 PM - 10 Jan 2019

#### Norovirus

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Follow

One hell of a time on **#OasisoftheSeas** I took a week off from work to sail on a boat for 6 days. **@RoyalCaribbean** this is NOT the trip we purchased. **#completechaos** 



#### Norovirus (Norwalk Virus)

- Member of the Calcivirus Family
- Non-enveloped Single Stranded Positive Sense Virus.
- Transmission of norovirus occurs mainly via the fecal-oral route, but fomite and aerosolization in vomitus have been reported.
- It has an incubation period of 24 to 48 hours
- Very low infectious dose(around 10 particles), hence causes outbreaks in instituionalised setting (Care homes, Hospitals etc.) often seen on cruise ships)
- Treatment is supportive
- Diagnosis can be confirmed with PCR on Stool.
- Healthcare workers who have symptoms consistent with norovirus should be excluded from work until 48 to 72 hours after symptom resolution

S. aureus	223	23	10.3%	NS
Hepatitis virus	150	6	4.0%	0.002
Pseudomonas spp.	130	10	7.7%	NS
Klebsiella spp.	115	10	8.7%	NS
Acinetobacter spp.	105	24	22.9%	0.02
Serratia spp.	94	14	14.9%	NS
Enterococci	67	8	11.9%	NS
Enterobacter spp.	66	10	15.2%	NS
Streptococci	63	18	28.6%	0.001
Salmonella spp.	56	4	7.1%	NS
Legionella spp.	48	2	4.2%	NS
Norovirus	34	15	44.1%	0.001
Clostridium spp.	34	4	11.8%	NS
Aspergillus spp.	25	5	20.0%	NS
Influenza/parainfluenza virus	26	10	38.5%	< 0.001
Citrobacter spp.	12	3	25.0%	NS
Adenovirus	11	3	27.3%	NS
Shigella spp.	11	4	36.4%	0.04
Rotavirus	27	7	25.9%	0.05
SARS coronavirus	12	4	33.3%	NS
Total	1561	194	12.4%	_

## It's estimated to cost the NHS £100 million pounds per annum in years of high incidence.

#### Rotavirus

- Historically been the most common worldwide cause of severe gastroenteritis in children <5 years of age however, in countries that successfully immunize a large fraction of infants against rotavirus, rotavirus gastroenteritis has decreased substantially (including UK)
- It is a Reovirus which is a non enveloped DS RNA Virus.
- Spread via Faecao-oral route
- Symptoms among children with rotavirus infection include vomiting, nonbloody diarrhea, and fever. In severe cases, dehydration, seizures, and death can occur
- Treatment again is supportive

Table 11.1 Schedule for the UK's routine immunisation programme (excluding catchup campaigns)

Age due		Vaccine given	How it is given <sup>1</sup>	
	Eight weeks old	Diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type b (Hib) and hepatitis B (DTaP/IPV/Hib/HepB) Meningococcal B (MenB)	One injection	
		Rotavirus	One oral application	
	Twelve weeks old	Diphtheria, tetanus, pertussis, polio, Hib and hepatitis B (DTaP/IPV/Hib/HepB) Rotavirus Pneumococcal conjugate vaccine (PCV13)	One injection One oral application One injection	
	Sixteen weeks old	Diphtheria, tetanus, pertussis, polio, Hib and hepatitis B (DTaP/IPV/Hib/HepB) Meningococcal B (MenB)	One injection One injection	
	One year old (on or after the child's first birthday)	Hib/MenC Pneumococcal conjugate vaccine (PCV13) Meningococcal B (MenB) Measles, mumps and rubella (MMR)	One injection <sup>2</sup> One injection <sup>2</sup> One injection <sup>2</sup> One injection <sup>2</sup>	
	Primary school age children (school years reception to six) <u>Chapter 19</u> )	Live attenuated influenza vaccine (LAIV)	Nasal spray, single application in each nostril (if LAIV is contraindicated and child is in a clinical risk group, give inactivated flu vaccine; see <u>Chapter 19</u> )	
	Three years four months old or soon after	Diphtheria, tetanus, pertussis and polio (dTaP/IPV) Measles, mumps and rubella (MMR)	One injection One injection	
	Twelve to thirteen years old	Human papillomavirus (HPV)	Course of two injections at least six months apart	
	Fourteen years old (school year 9)	Tetanus, diphtheria and polio (Td/IPV) Meningococcal ACWY conjugate (MenACWY)	One injection One injection	
	65 years old	Pneumococcal polysaccharide vaccine (PPV)	One injection	
	65 years of age and older	Inactivated influenza vaccine	One injection annually	
	70 years old	Shingles vaccine	One injection	

1 Where two or more injections are required at the same time, these should ideally be given in different limbs. Where this is not possible, injections in the same limb should be given at least 2.5cm apart.

2 Where injections can only be given in two limbs, it is recommended that the MMR, as the vaccine least likely to cause local reactions, is given in the same limb as the MenB with the PCV13 and Hib/MenC doses given into the other limb

#### Adenoviruses

- Non Enveloped DS DNA Virus
- Multiple Serotypes, all associated with different clinical syndromes
- Ubiqutous, causes 5 to 10 percent of acute diarrheal illnesses in young children
- Also a common cause of URTI, Keratoconjunctivitis, Otitis Media,
- Generally self disease but severe disseminated disease can occur (mainly in immunocompromised)
- Diagnosed with PCR
- Often spread amongst people living in close quarters (eg military) hence Military recruits often vaccinated against adenovirus
- Disseminated disease can be treated with Cidofovir.

#### Hepatitis A & E

- Hepatitis A is a Pico Virus and Hep E is a Calcivirus (like Norovirus)
- Both are SS Non-enveloped (see the pattern) positive sense RNA Viruses.
- Both associated with faecal/Oral Transmission.
- Hep A classically seen in sewage workers
- Hep E transmitted mainly in areas with poor sanitation (but growing numbers in the UK felt to be related to pork)
- Foreign travel is the biggest risk factor for both
- Hep A treatment Supportive/Vaccine/HNIG for immunouprressed contacts and those >60 – Normally a self limited illness.
- Hep E causes fulminant hepatic failure in pregancy, Ribavirin can be ussed for treatment.



#### E. coli (Traveller's Diarrhoea)

- Travelers' diarrhea is the most common illness in persons traveling from resource-rich to resource-limited regions of the world.
- Among travelers to such areas, 40 to 60 percent develop diarrhea
- Episodes of travelers' diarrhea are nearly always benign and selflimited
- Classically produces malaise, anorexia, and abdominal cramps followed by the sudden onset of watery diarrhea within 10 days of returning from an affected area.



**Risk Level** 



#### Types of diarrhoea caused by E. coli

- ETEC Enterotoxigenic E. coli
- Releases exotoxins which inhibit the aborption of Na+ Cl and secrete Cl- and HCO3- leading to profuse diarrhoea.
- EHEC Enterohaemorrhagic E. coli
- Secretes Shiga like Toxin which causes bloody diarrhoea and abdominal cramps known as haemmorhagic colitis.
- EIEC Enteroinvasive E. coli
- Actually invades the epithelial cells of the colon resulting in fever, bloody diarrhoea and systemic symptoms.

### (Typical) Haemolytic Uraemic Syndrome

- This is a triad of
- ➢Acute Kidney Injury
- ➤Thrombocytopaenia
- Microangiopathic Haemolytic Anaemia
- associated with Shiga toxin producing ECOLI 0157 (a form of EHEC)
- Mainly affects Children
- Typically have a prodromal illness with abdominal pain, vomiting, and diarrhea that generally precedes the development of HUS by 5 to 10 days

#### (Typical) Haemolytic Uraemic Syndrome

- Treatment is mainly Supportive
- Ecluzimab (a C5 monoclonal Ab)
- DO NOT give Abx (as can worsen symptoms)
- Mortality typically occurs acutely during the initial hospitalization with reported rates of about 3 to 4 percent.
- Approximately 60 to 70 percent of patients recover completely from the acute phase of HUS
- Long term complications include CKD/HTN/Proteinuria

### Shigella

- Gram Negative rod, multiple species (Flexneri, dysenteriae, Boydii, Sonnei)
- Humans are the only host
- Produces bloody diarrhoea as produces Shiga toxin
- Can cause disseminated symptoms as invades the intestine.
- Spread by faecal oral route via contaminated water (also there has been multiple recent outbreaks amongst MSM
- Diagnosed via PCR.
- Should be treated with Antibiotics (depending on species/resistance in the area)

#### Vibrio Cholerae (Cholera)

- Curved Gram Negative Rod
- Transmitted by faecal oral route, particularly in faecally contaminated water. (Causes epidemics)
- Mainly affects children and travellers ass adults in endemic areas develop immunity.
- Classically produces rice water stool (due to it's toxin Choleragen, which is similar in action to ETEC)
- Fever is uncommon.
- Treatment is supportive and death can occur rapidly without rehydration (can loose up to 1litre of fluid an hour)
- Antibiotics have been shown to shorten the duration of symptoms



#### Typhoid fever

- Caused by Salmonella Typhi which is a Gram Negative Rod.
- Humans are the only reservoir for S. Typhi (unlike non typhoidal salmonella which colonises the guts of many animals)
- Presents 1-3 weeks after exposure with fevers, severe abdominal pain (often in RLQ), diarrhoea and rose spots on the belly.
- Causes severe illness and needs to be treated with Abx (usually a 3rd generation Cephalosporin eg Ceftriaxone, but depends on resistance pattern where acquired)
- Diagnosed on culture (Blood/Stool)
- Can cause an asymptomatic chronic carrier state, where it resides in the gallbladder and is constantly excreting the bacteria (eg Typhoid Mary)

#### Campylobacter Jejuni

- Gram Negative curved rod.
- Common cause of bloody diarrhoea here in Wales.
- Associated with undercooked meat (esp chicken) See lots during the summer (BBQs)
- Diaagnosed with stool PCR
- Again normally self limiting, but if severe symptoms/immunocompromised etc can treatment with Abx (Azithromycin first line)
- Asssociated with Guillan Barre syndrome (a few weeks after the acute illness)
- About 1 in every 1,000 reported Campylobacter illnesses leads to GBS (CDC)

#### Bacillus cereus

- Common cause of food poisoning
- Able to survive at extreme temperatures and able to form biofilms and spores, so persists in food processing environments.
- Classsically occurss with re-heated rice.

#### Staph aureus

- Associated with Exotoxin produced by staph aureus in the food (similar to B. cereus)
- Causes abrupt onset of symptoms and abrupt improvement
- Normally Staph aureus associated with much more severe infections (bacteraemia/Endocarditis/Discitis/Osteomyelitis etc)

#### Clostridioides difficile

- Spore-forming, toxin-producing, gram-positive anaerobic bacterium that causes antibiotic-associated colitis.
- It colonizes the human intestinal tract after the normal gut flora has been disrupted (frequently in association with antibiotic therapy).
- One of the most common health care-associated infections and a significant cause of morbidity and mortality, especially among older adult hospitalized patients
- Big Problem in SBUHB

#### Management

- Prevention (ideally) Minimise innapropriate Abx usage
- Isolation of cases, Barrier Nursing, environmental cleaning.
- Wash your hand with Water and Soap.
- Stop PPIs
- Antibiotic management includes PO Vancomycin and Fidaxomycin (Metronidazole no longer recommend due to Resistance)
- Recurrent infection can be treated with Faecal Microbiota transplantation (FMT) – improve colonic microbial diversity.

#### Amoebiasis (Entamoeba Histolytica)

- Intestinal amebiasis is caused by the protozoan *Entamoeba histolytica*.
- Most infection is asymptomatic; clinical manifestations include amebic dysentery and extraintestinal disease eg amoebic liver abscess and more rare manifestations such as pulmonary, cardiac, and brain involvement
- Worldwide, approximately 50 million people develop colitis or extraintestinal disease, with over 100,000 deaths annually
- It is most common in Low and Middle Income countries.

#### Amebiasis life cycle



Cysts and trophozoites are passed in feces (1). Cysts are typically found in formed stool, whereas trophozoites are typically found in diarrheal stool. Infection by Entamoeba histolytica occurs by ingestion of mature cysts (2) in fecally contaminated food, water, or hands. Excystation (3) occurs in the small intestine and trophozoites (4) are released, which migrate to the large intestine. The trophozoites multiply by binary fission and produce cysts (5), and both stages are passed in the feces (1). Because of the protection conferred by their walls, the cysts can survive days to weeks in the external environment and are responsible for transmission. Trophozoites passed in the stool are rapidly destroyed once outside the body, and if ingested would not survive exposure to the gastric environment. In many cases, the trophozoites remain confined to the intestinal lumen (A: noninvasive infection) of individuals who are asymptomatic carriers, passing cysts in their stool. In some patients the trophozoites invade the intestinal mucosa (B: intestinal disease), or, through the bloodstream, extraintestinal sites such as the liver, brain, and lungs (C: extraintestinal disease), with resultant pathologic manifestations. It has been established that the invasive and noninvasive forms represent two separate species, respectively E. histolytica and E. dispar. These two species are morphologically indistinguishable unless E. histolytica is observed with ingested red blood cells (erythrophagocystosis). Transmission can also occur through exposure to fecal matter during sexual contact (in which case not only cysts, but also trophozoites could prove infective).

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#### Clinical Symptoms

- Clinical amebiasis generally has a subacute onset, usually over one to three weeks.
- Symptoms range from mild diarrhea to severe dysentery, producing abdominal pain (12 to 80 percent), diarrhea (94 to 100 percent), and bloody stools (94 to 100 percent), to fulminant amebic colitis.
- Liver abscess symptoms include right upper quadrant pain, fevers, abnormal LFTs, jaundice and characteristic imaging findings

#### Diagnosis

- **Stool Microscopy:** demonstration of cysts or trophozoites in the stool suggests intestinal amebiasis
- Antigen testing : Easy, Quick, good in endemic settings.
- PCR : High Specificity and Sensitivity (almost 100% for both)
- Serology: helpful for exclusion of disease, but positive serology cannot distinguish between acute and previous infection.

#### Treatment

- Metronidazole
- Antiluminal agent (paromomycin)

#### Giardiasis (Giardia duodenalis)

- Important cause of waterborne and foodborne disease, daycare center outbreaks, and illness in international travelers.
- Infection occurs worldwide
- Especially common in areas with poor sanitary conditions and limited water-treatment facilities
- Worldwide, third most common agent of diarrheal disease in children (>300 million cases)
- Risk factors for sporadic giardiasis: international travel, drinking water from a river, lake, stream, or spring, swimming in a natural body of water, male-male sexual behavior

Giardia life cycle



Cysts are resistant forms and are responsible for transmission of giardiasis. Both cysts and trophozoites can be found in the feces (diagnostic stages) (1). The cysts are hardy and can survive several months in cold water. Infection occurs by the ingestion of cysts in contaminated water, food, or by the fecal-oral route (hands or fomites) (2). In the small intestine, excystation releases trophozoites (each cyst produces two trophozoites) (3). Trophozoites multiply by longitudinal binary fission, remaining in the lumen of the proximal small bowel where they can be free or attached to the mucosa by a ventral sucking disk (4). Encystation occurs as the parasites transit toward the colon. The cyst is the stage found most commonly in nondiarrheal feces (5). Because the cysts are infectious when passed in the stool or shortly afterward, person-to-person transmission is possible. While animals are infected with *Giardia*, their importance as a reservoir is unclear.

Reproduced from: Centers for Disease Control and Prevention. DPDx: Giardia. Available at: <u>http://www.cdc.gov/parasites/giardia/biology.html</u> (Accessed on April 13, 2015).

#### Symptoms (Acute Giardiasis)

- Diarrhea 90 percent
- Malaise 86 percent
- Foul-smelling and fatty stools (steatorrhea) 75 percent
- Abdominal cramps and bloating 71 percent
- Flatulence 75 percent
- Nausea 69 percent
- Weight loss 66 percent

### Symptoms (Chronic Giardiasis)

- Loose stools but usually not diarrhea
- Steatorrhea
- Profound weight loss (10 to 20 percent of body weight)
- Malabsorption
- Stunted growth
- Malaise
- Fatigue
- Depression
- Abdominal cramping
- Borborygmi
- Flatulence
- Burping

#### Diagnosis

- Stool Microscopy
- PCR
- Antigen testing

#### Treatments

• Tinidazole or Metronidazole (Tinidazole is one dose so often better tolerated)

#### Cryptosporidium

- UK Reference lab here in Swansea
- Ubiquitous pathogen
- Mainly self limiting diarrhoea in the immunocompetent
- BIG problem in the immunocompromised (HIV etc) Profound watery diarrhoea
- Diagnosed via PCR (need to specifically ask)
- Treatment mainly treat the underlying immunosuppression

#### ORIGINAL ARTICLE

#### A Massive Outbreak in Milwaukee of Cryptosporidium Infection Transmitted through the Public Water Supply

William R. Mac Kenzie, Neil J. Hoxie, Mary E. Proctor, M. Stephen Gradus, Kathleen A. Blair, Dan E. Peterson, James J. Kazmierczak, David G. Addiss, Kim R. Fox, Joan B. Rose, and Jeffrey P. Davis

# Crypto outbreaks linked to swimming have doubled since 2014

Diarrhea caused by parasite is problem for swimming pools and water playgrounds

Press Release Embargoed Until: Thursday, May 18, 2017, 1:00 p.m. ET Contact: Media Relations (404) 639-3286

# Not washing your hands is cool.

# False. Clean hands prevent the spread of disease.

#### Any questions

- Contact me via email with questions or if anyone wants to discuss ID/Micro
- Lorcan.O'Connell@wales.nhs.uk