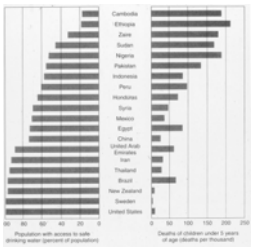
Access to safe drinking water is everyone's right



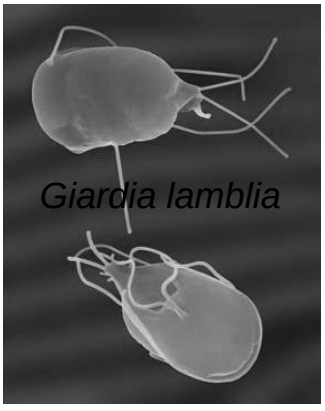
Anton van Leeuwenhoek

Protozoa:

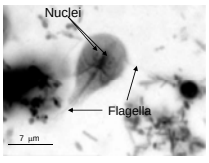
Protozoans that cause diarrheal disease

1. *Giardia lamblia*
2. *Entameba histolytica*
3. *Cryptosporidium parvum*
4. *Cyclospora cayetanensis*

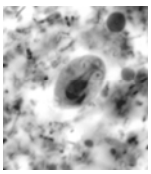
This is what he saw in his own stool sample



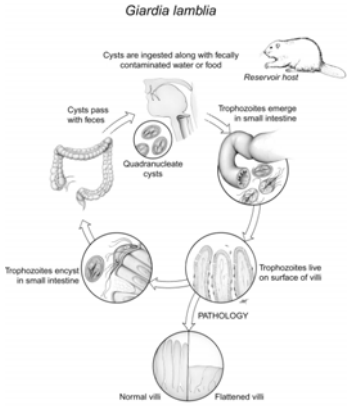
Morphology



Trophozoite

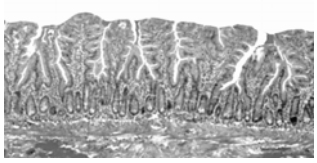


Cyst



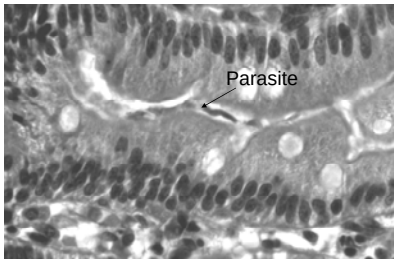
Pathogenesis:

Trophozoite stage induces malabsorption of fats. Mechanism(s) unknown.

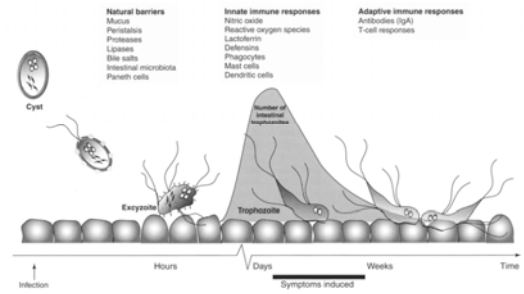


Histopathological correlate: Flattened villi

Biopsy of small intestine positive for *Giardia lamblia*



Giardia and Immune Mechanisms



SEM of *Giardia lamblia* in situ

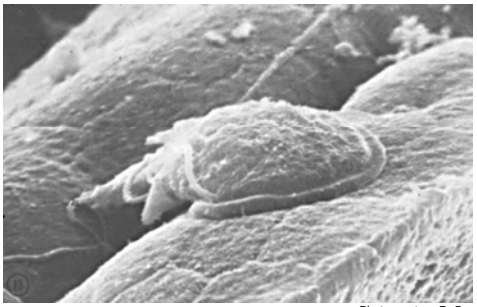


Photo courtesy R. Owen

Clinical Disease:

Diarrhea (steatorrhea)

Weight loss

Constipation

Fatigue

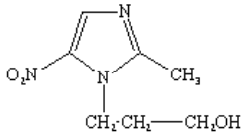
Diagnosis:

1. Identify trophozoites and cysts by microscopic examination of stool

Trophozoite

Cyst

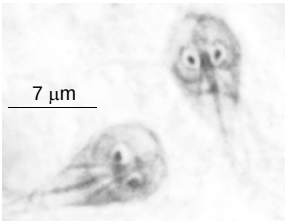
Drug of choice: Metronidazole



Mode of Action:
Inhibits anaerobic metabolism by interfering with oxidoreductase, a protozoan-specific enzyme.

Diagnosis (cont'd):

2. Identify trophozoites on microscopic examination of fluid from string test.



Medical Ecology:

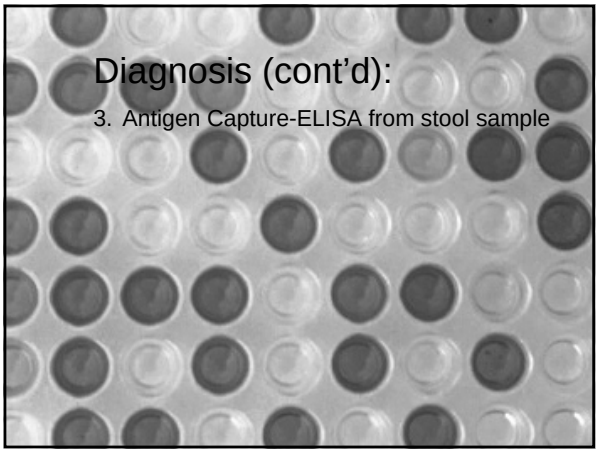
1. Reservoir hosts - beaver, dog

2. Day-care centers are common point sources for outbreaks.

3. Break-downs at filtration plants for drinking water supplies have led to major outbreaks.

Diagnosis (cont'd):

3. Antigen Capture-ELISA from stool sample



Prevention and Control:

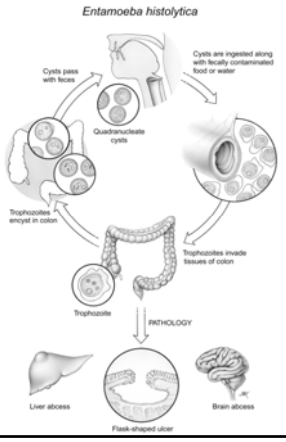
1. Sanitary disposal of feces

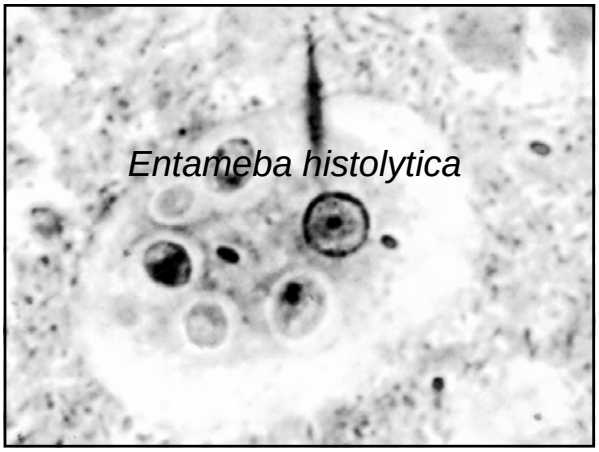
Prevention and Control (cont'd):

2. Safe drinking water supply -maintain watersheds or filter water.

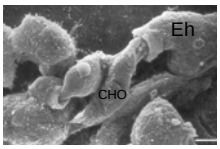
3. Maintain good sanitary practices at day-care facilities - difficult to enforce among small children due to PICA

4. Don't drink unfiltered water from "pristine" rivers and streams while enjoying the great outdoors.

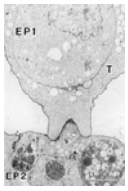




Entameba histolytica in culture with Chinese hamster ovary cells

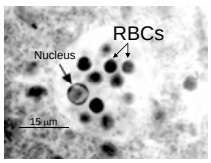


SEM

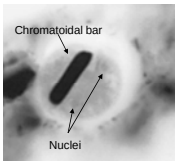


TEM

Morphology



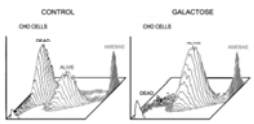
Trophozoite



Cyst

Pathogenesis:

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



From: Ravdin, J.I. (1995) Amebiasis (Review). *Clin. Infect. Dis.* **20**: 1453-1466

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

Clinical Disease:

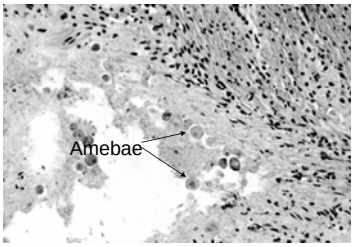
A. Intestinal:

1. Diarrhea
2. Dysentery (bloody diarrhea)

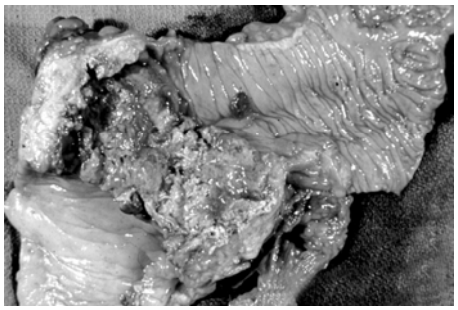
B. Extra-intestinal:

1. Liver abscess (most common site)
2. Lung abscess
3. Brain abscess (usually fatal)

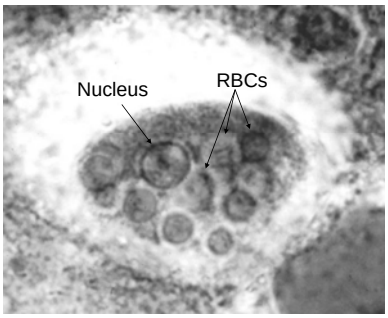
Trophozoites of *Entameba histolytica* in situ in flask-shaped ulcer



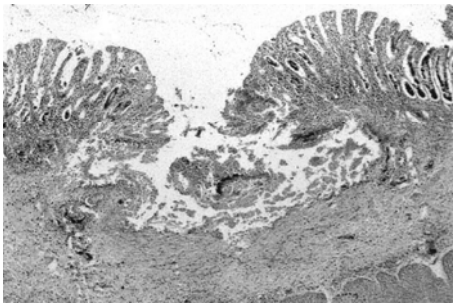
Gross pathology of large intestine due to *Entameba histolytica*



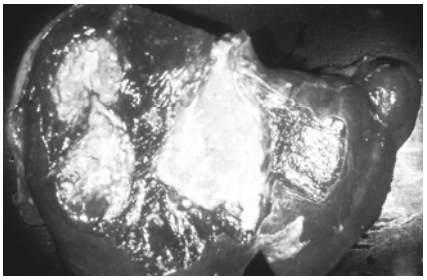
Trophozoite of *Entameba histolytica* with RBCs in cytoplasm



Flask-shaped ulcer due to infection with *Entameba histolytica*



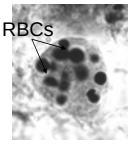
Multiple abscesses in liver from a fatal case of *Entameba histolytica*



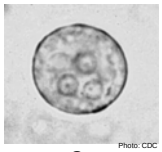
Courtesy WHO

Diagnosis:

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



Trophozoite



Cyst

Prevention and Control:

Sanitary disposal of feces

Diagnosis (cont'd):

2. Antigen Capture ELISA using stool sample

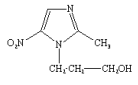
3. PCR

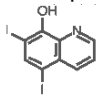
4. IHA serology:
   Intestinal - 95% predictive of active infection
   Extra-intestinal - 100% predictive of active infection

Cryptosporidium hominis

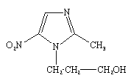
Drugs of Choice:

1. Intestinal:
   Metronidazole and Iodoquinol



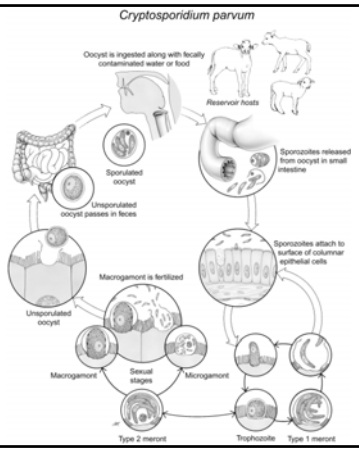


2. Extra-intestinal
   High doses of Metronidazole

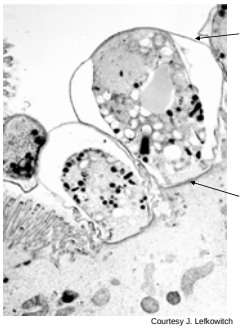


Species of Cryptosporidium capable of infecting humans

- **Long-term Cryptosporidium typing reveals the aetiology and species-specific epidemiology of human cryptosporidiosis in England and Wales, 2000 to 2003.**
- **Chalmers RM**, **Elwin K**, **Thomas AL**, **Guy EC**, **Mason B**.
- UK Cryptosporidium Reference Unit, NPHS Microbiology Swansea, Singleton Hospital, Swansea, United Kingdom. rachel.chalmers@nphs.wales.nhs.uk
- To improve understanding of the aetiology and epidemiology of human cryptosporidiosis, over 8,000 Cryptosporidium isolates were submitted for typing to the species level over a four year period. The majority were either Cryptosporidium parvum (45.9%) or Cryptosporidium hominis (49.2%). Dual infection occurred in 40 (0.5%) cases and six other known Cryptosporidium species or genotypes were found in 67 (0.9%) cases. These were Cryptosporidium meleagridis, Cryptosporidium felis, Cryptosporidium canis, and the Cryptosporidium cervine, horse and skunk genotypes. The remaining 3.5% were not typable. Epidemiology differed between infecting species. C. parvum cases were younger, although C. hominis was more prevalent in infants under one year and in females aged 15 to 44 years. Spring peaks in cases reported to national surveillance were due to C. parvum, while C. hominis was more prevalent during the late summer and early autumn as well as in patients reporting recent foreign travel. Temporal and geographical differences were observed and a decline in C. parvum cases persisted from 2001. Typing of isolates allowed outbreaks to be more clearly delineated, and demonstrated anthroponotic spread of C. parvum as well as C. hominis. Our findings suggest that national surveillance for Cryptosporidium should be conducted at the species level.

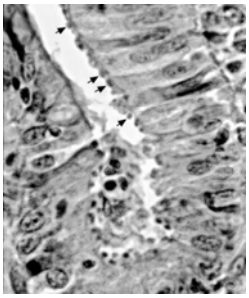


TEM of *Cryptosporidium hominis*



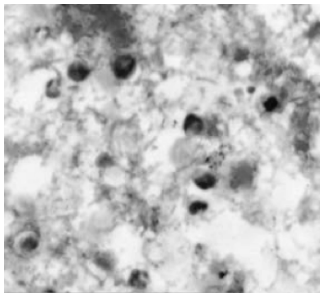
Courtesy J. Lefkowitch

Histologic section of small intestine of patient suffering from HIV/AIDS, infected with *Cryptosporidium hominis*.



Courtesy J. Lefkowitch

Oocysts of *Cryptosporidium hominis*



Pathogenesis:

Secretory diarrhea. May produce up to 10 liters of watery stool per day! Mechanism unknown.

Clinical Disease:

Secretory diarrhea. In HIV(+) patients, this infection was often fatal. There are no drugs that are effective against it.

HAART therapy has essentially eliminated *C. hominis* from HIV/AIDS patients in USA

Excellent Review of Diarrheal Diseases

- **1:** Gastroenterology. 2009 May;136(6):1874-86. Epub 2009 May 7. Links
- **Diagnosis and treatment of acute or persistent diarrhea.**
- **Pawlowski SW**, **Warren CA**, **Guerrant R**.
- Division of Infectious Disease and International Health, Center for Global Health, University of Virginia School of Medicine, Charlottesville, Virginia 22908, USA.
- Studies of microbial pathogens and the toxins they produce are important for determining the mechanisms by which they cause disease and spread throughout a population. Some bacteria produce secretory enterotoxins (such as cholera toxin or the heat-labile or stable enterotoxins produced by Escherichia coli) that invade cells directly. Others invade cells or produce cytotoxins (such as those produced by Shigella, enteroinvasive E coli, or Clostridium difficile) that damage cells or trigger host responses that cause small or large bowel diseases (such as enteroaggregative or enteropathogenic E coli or Salmonella). Viruses (such as noroviruses and rotaviruses) and protozoa (such as Cryptosporidium, Giardia, or Entamoeba histolytica) disrupt cell functions and cause short- or long-term disease. Much epidemiologic data about these pathogens have been collected from community- and hospital-acquired settings, as well as from patients with traveler's or persistent diarrhea. These studies have led to practical approaches for prevention, diagnosis, and treatment.

New Treatment for Giardia and Cryptosporidium

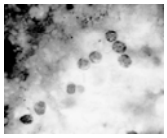
- Exp Parasitol. 2009 Jul 24.
- **Cryptosporidium and Giardia: Treatment options and prospects for new drugs.**
- **Rossignol JF**.
- Division of Gastroenterology & Hepatology, Department of Medicine, Stanford University School of Medicine, Pasteur Drive MC: 5187, Room 3115A, Stanford, CA 94305-5187, USA; The Romark Institute for Medical Research, Tampa, FL 33607, USA.
- Cryptosporidium species and Giardia intestinalis are the most common enteric protozoan pathogens affecting humans worldwide. In recent years, nitazoxanide has been licensed in the United States for the treatment of cryptosporidiosis in non-immunodeficient children and adults, becoming the first drug approved for treating this disease. There is a need for a highly effective treatment for cryptosporidiosis in immunodeficient patients, but the quest for such a drug has proven to be elusive. While not effective against Cryptosporidium, nitroimidazoles such as metronidazole or tinidazole are effective treatments for giardiasis and can be administered as a single dose. Albendazole and nitazoxanide are effective against giardiasis but require multiple doses. Nitazoxanide is the first new drug developed for treating giardiasis in more than 20years. New potentially promising drug targets in Cryptosporidium and Giardia have been

identified, but there appears to be little activity toward clinical development of new drugs.

Diagnosis:

Identify oocysts on microscopic examination.

A. acid fast-stain



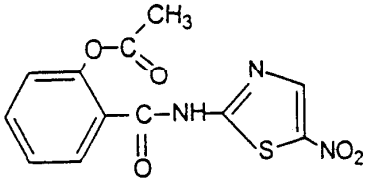
B. Indirect Fluorescent Antibody test

Complete Genome Sequence of the Apicomplexan, *Cryptosporidium parvum*

Mitchell S. Abrahamsen,[1,2*†] Thomas J. Templeton,[3†] Shinichiro Enomoto,[1] Juan E. Abrahante,[1] Guan Zhu,[4] Cheryl A. Lancto,[1] Mingqi Deng,[1] Chang Liu,[1‡] Giovanni Widmer,[5] Saul Tzipori,[5] Gregory A. Buck,[6] Ping Xu,[6] Alan T. Bankier,[7] Paul H. Dear,[7] Bernard A. Konfortov,[7] Helen F. Spriggs,[7] Lakshminarayan Iyer,[8] Vivek Anantharaman,[8] L. Aravind,[8] Vivek Kapur[2,9]

Science: 304:441-445. 2004

*Nitazoxanide is the only approved drug for treating infections with Cryptosporidium**



* Effective in non-HIV/AIDS patients only

Medical Ecology

1. *Cryptosporidium sp.* infect a wide variety of animals (birds and mammals), many of which can also infect humans.

2. Suckling farm animals (calves, kids, lambs) are potential sources of infection for urban centers that get their drinking water from reservoirs that are surrounded by farmland (e.g., NYC).

Prevention and Control:

1. Sanitary disposal of feces

Prevention and Control (cont'd):

2. Protect public drinking water supplies from contamination with animal feces by creating buffer zones between the reservoir an and the watershed.

Pepacton Reservoir