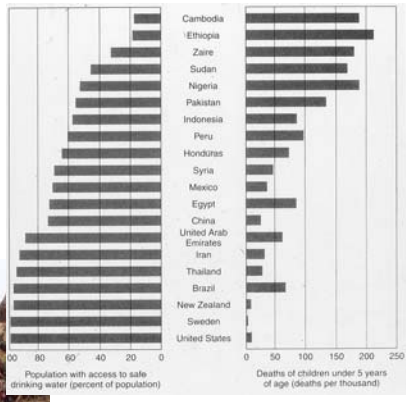
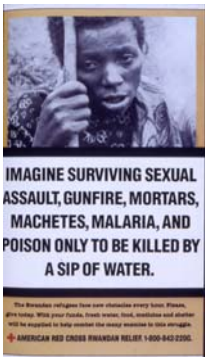
Access to safe drinking water is everyone's right

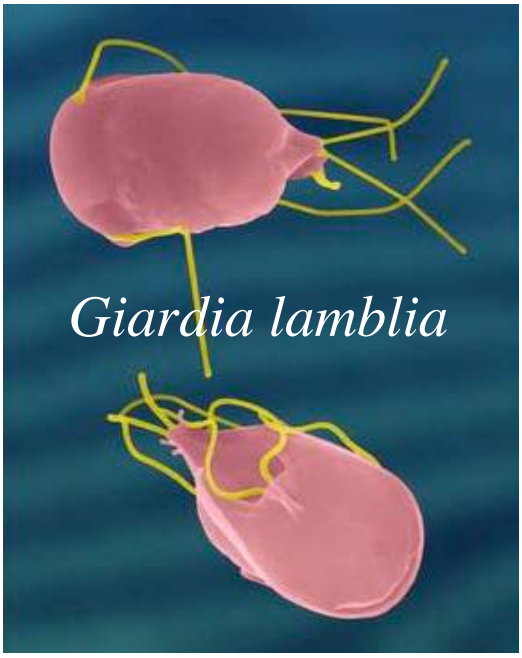




Protozoa:

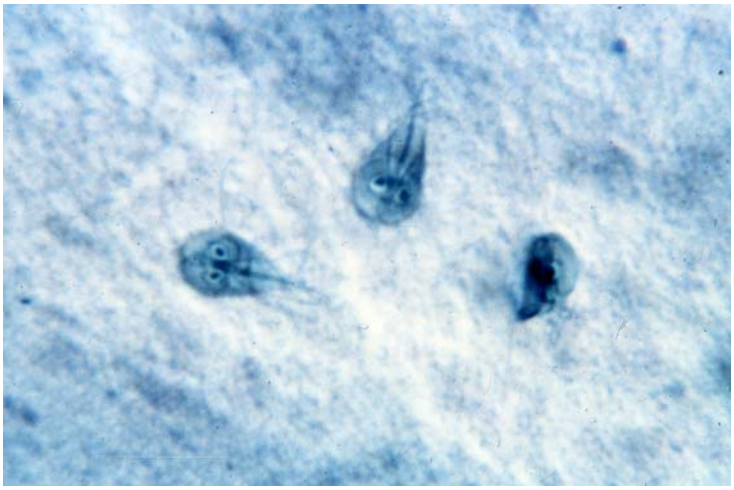
Protozoans that cause diarrheal disease

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

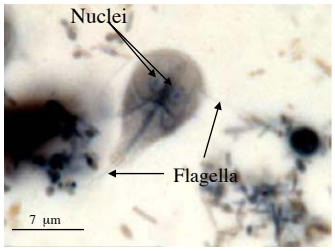


Anton van Leeuwenhoek

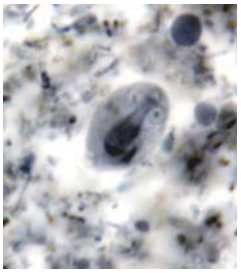
This is what he saw in his own stool sample!



Morphology

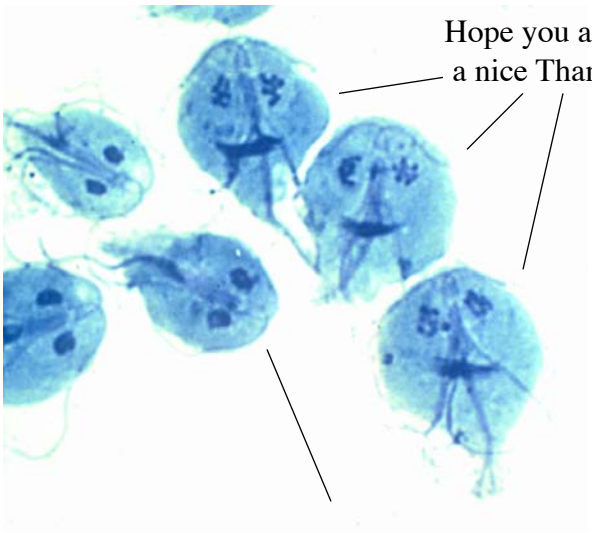


Trophozoite



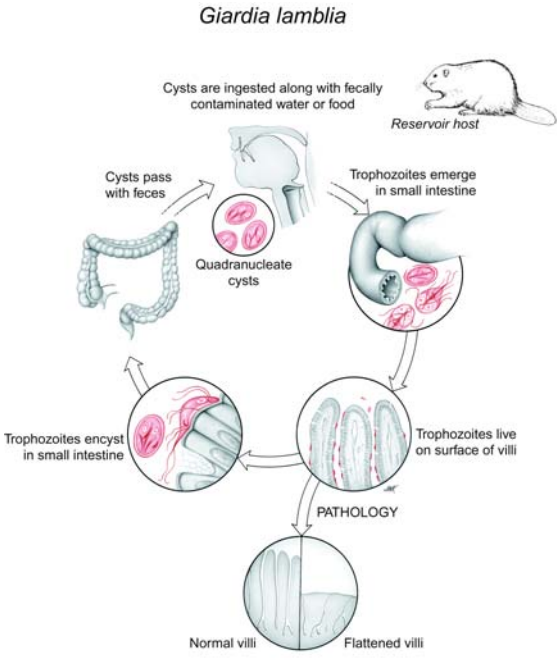
Cyst

Trophozoites of *Giardia lamblia*



Hope you all have
a nice Thanksgiving!

Yeh! You eat well, we eat well!



Biopsy of small intestine positive for *Giardia lamblia*

SEM of *Giardia lamblia* in situ

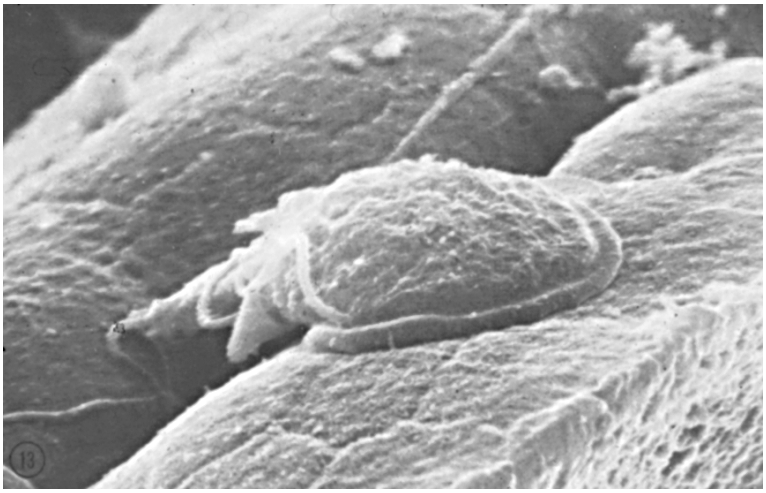
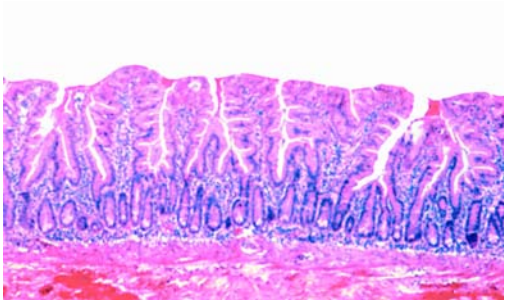


Photo courtesy R. Owen

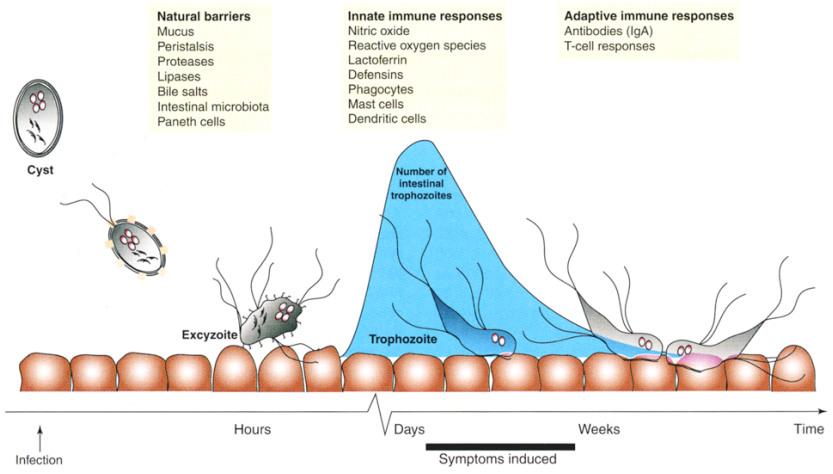
Pathogenesis:

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



Histopathological correlate: Flattened villi

Giardia and Immune Mechanisms



Clinical Disease:

Diarrhea (steatorrhea)

Weight loss

Constipation

Fatigue

Diagnosis:

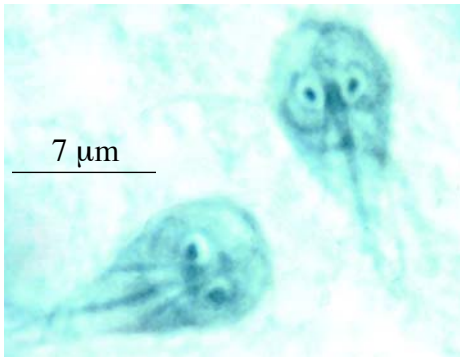
1. Identify trophozoites and cysts by microscopic examination of stool

Trophozoite

Cyst

Diagnosis (cont'd):

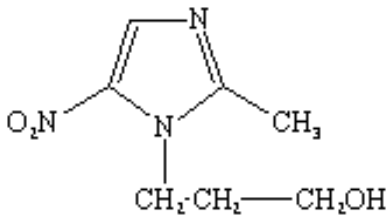
2. Identify trophozoites on microscopic examination of fluid from string test.



Diagnosis (cont'd):

3. Antigen Capture-ELISA from stool sample

Drug of choice: Metronidazole



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

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.

Prevention and Control:

1. Sanitary disposal of feces

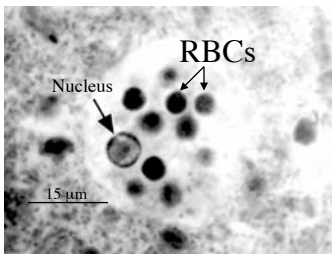
Prevention and Control (cont'd):

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

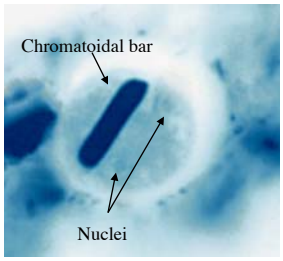
3. Maintain good sanitary practices at day-care facilities - difficult to enforce among small children due to PICA

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

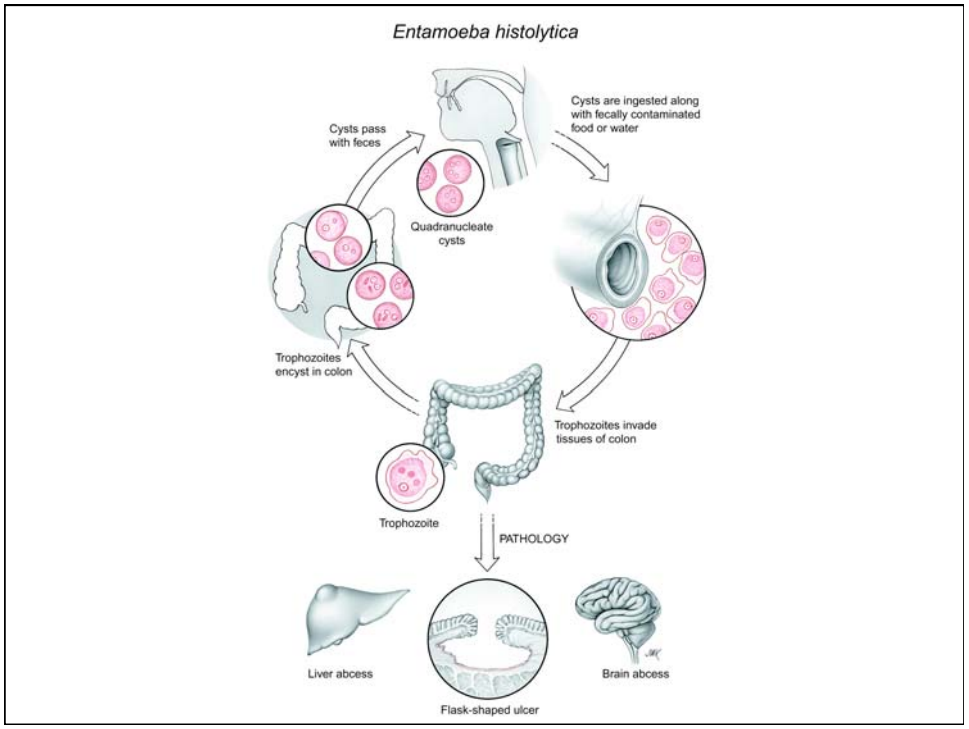
Morphology



Trophozoite

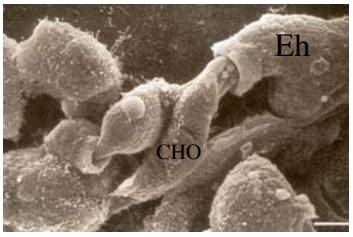


Cyst

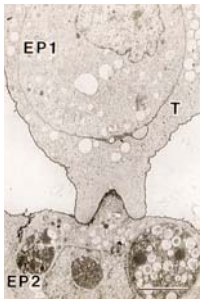


Entameba histolytica in culture

with Chinese hamster ovary cells



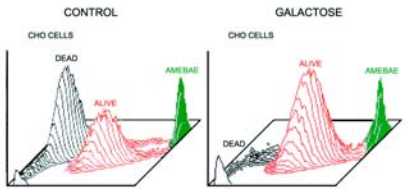
SEM



TEM

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:

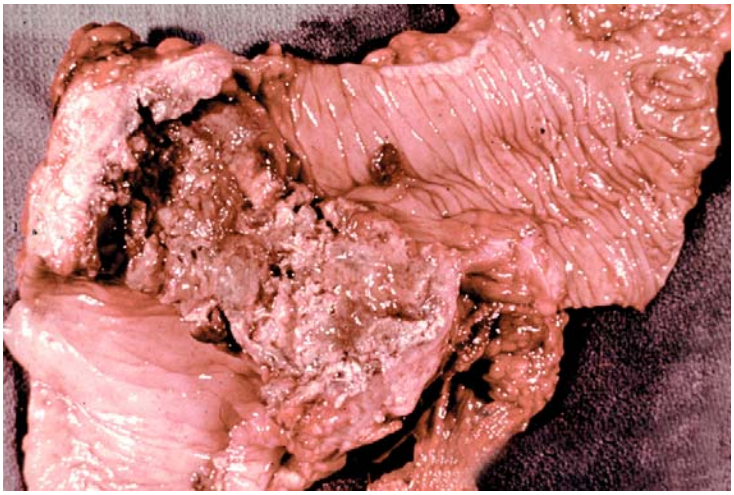
A. Intestinal:

1. Diarrhea
2. Dysentery (bloody diarrhea)

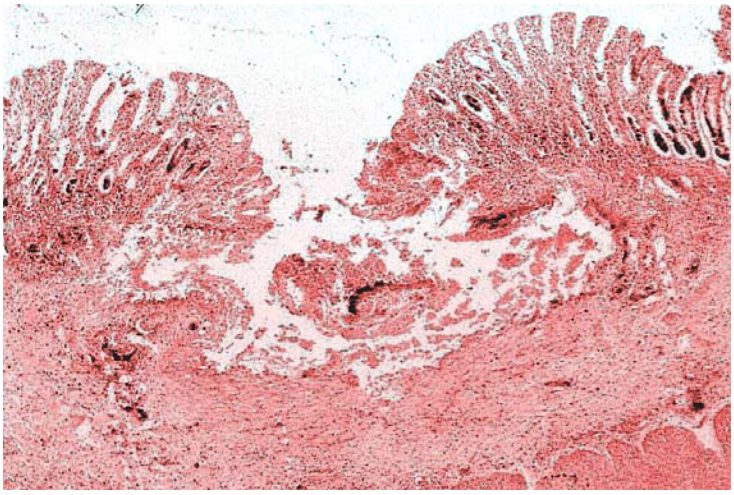
B. Extra-intestinal:

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

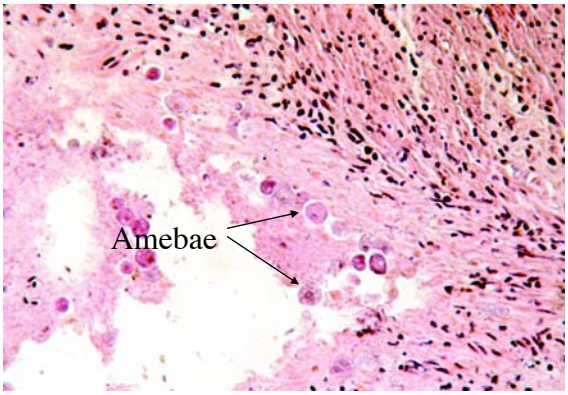
Gross pathology of large intestine due to *Entameba histolytica*



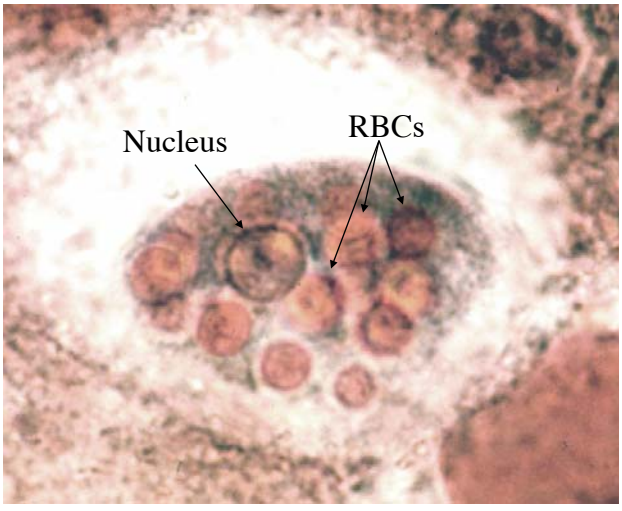
Flask-shaped ulcer due to infection with *Entameba histolytica*



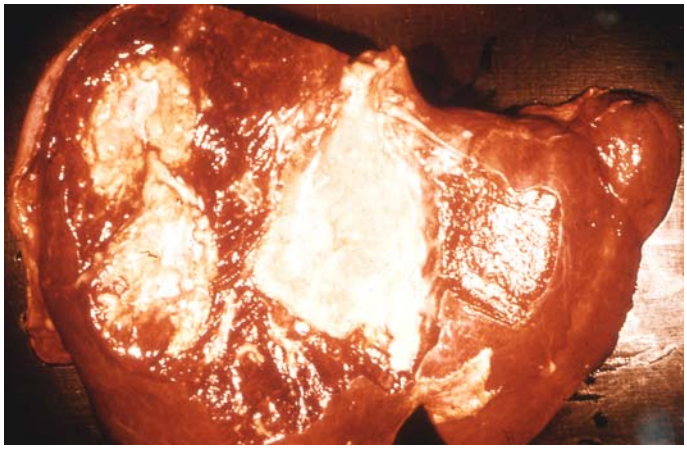
Trophozoites of *Entameba histolytica* in situ in flask-shaped ulcer



Trophozoite of *Entameba histolytica* with RBCs in cytoplasm



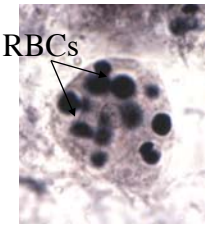
Multiple abscesses in liver from
a fatal case of *Entameba histolytica*



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

Photo: CDC

Cyst

Diagnosis (cont'd):

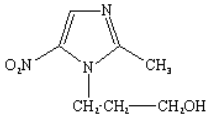
2. Antigen Capture ELISA using stool sample

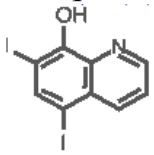
3. PCR

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

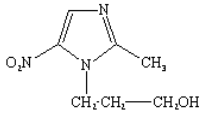
Drugs of Choice:

1. Intestinal:
   Metronidazole and Iodoquinol





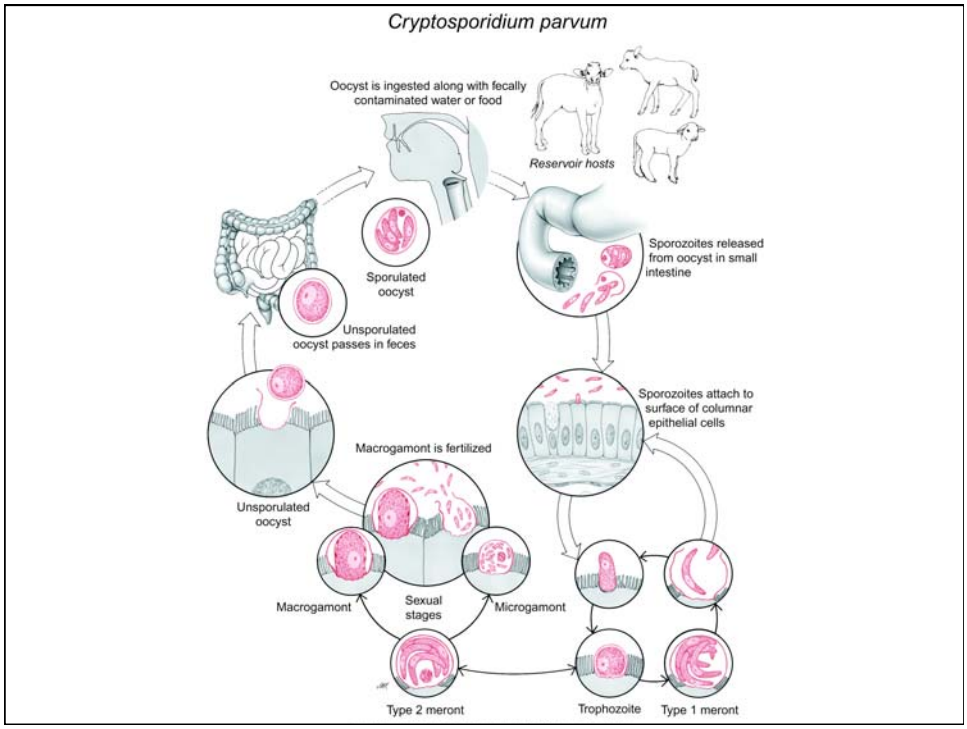
2. Extra-intestinal
   High doses of Metronidazole



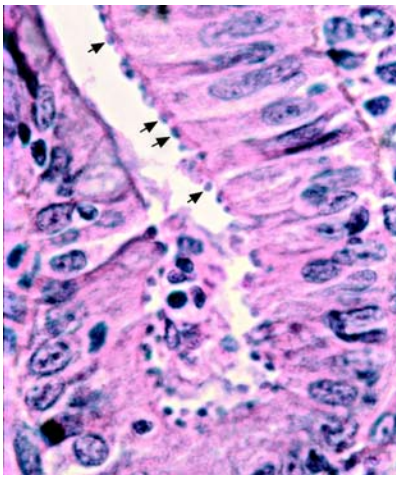
Prevention and Control:

Sanitary disposal of feces

Cryptosporidium parvum



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

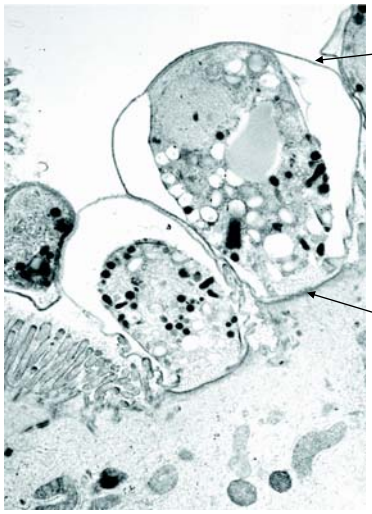


Courtesy J. Lefkowitch

Pathogenesis:

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

TEM of *Cryptosporidium parvum*

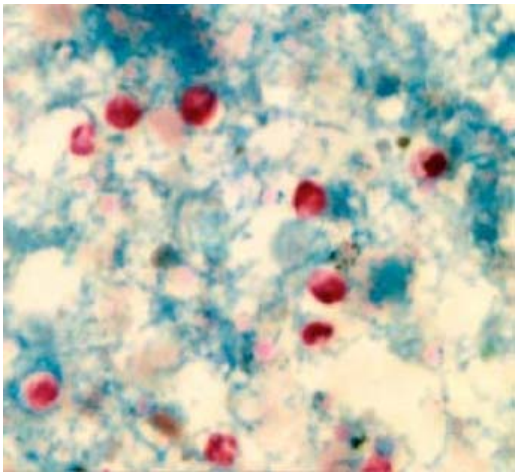


Altered host cell membrane protects parasite from all chemotherapeutic agents tested, so far.

Attachment zone

Courtesy J. Lefkowitch

Oocysts of *Cryptosporidium parvum*



Clinical Disease:

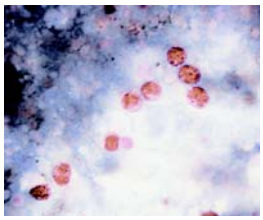
Secretory diarrhea. In HIV(+) patients, this infection was often fatal. There are no drugs that are effective against it.

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

Diagnosis:

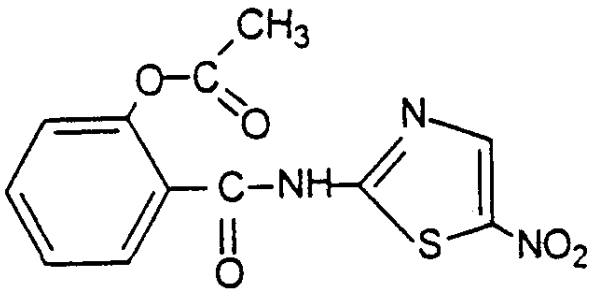
Identify oocysts on microscopic examination.

A. acid fast-stain



B. Indirect Fluorescent Antibody test

There is no approved chemotherapeutic agent for Cryptosporidium



Nitazoxanide may offer some hope

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

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