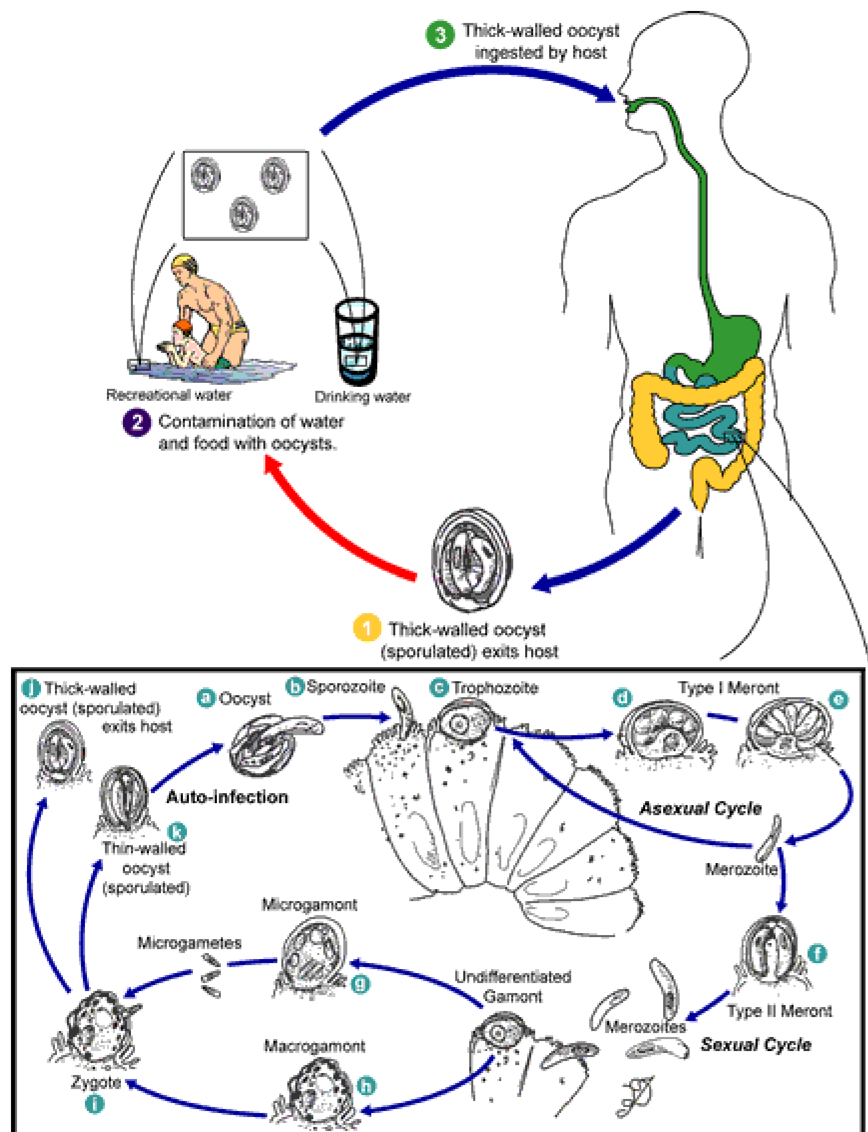
Cryptosporidiosis

Causal Agent:

Many species of *Cryptosporidium* exist that infect humans and a wide range of animals. Although *Cryptosporidium parvum* and *Cryptosporidium hominis* (formerly known as *C. parvum* anthroponotic genotype or genotype 1) are the most prevalent species causing disease in humans, infections by *C. felis*, *C. meleagridis*, *C. canis*, and *C. muris* have also been reported.

Life Cycle:



Sporulated oocysts, containing 4 sporozoites, are excreted by the infected host through feces and possibly other routes such as respiratory secretions 1. Transmission of *Cryptosporidium parvum*

and *C. hominis* occurs mainly through contact with contaminated water (e.g., drinking or recreational water). Occasionally food sources, such as chicken salad, may serve as vehicles for transmission. Many outbreaks in the United States have occurred in waterparks, community swimming pools, and day care centers. Zoonotic and anthroponotic transmission of *C. parvum* and anthroponotic transmission of *C. hominis* occur through exposure to infected animals or exposure to water contaminated by feces of infected animals 2. Following ingestion (and possibly inhalation) by a suitable host 3, excystation a occurs. The sporozoites are released and parasitize epithelial cells (b, c) of the gastrointestinal tract or other tissues such as the respiratory tract. In these cells, the parasites undergo asexual multiplication (schizogony or merogony) (d, e, f) and then sexual multiplication (gametogony) producing microgamonts (male) g and macrogamonts (female) h. Upon fertilization of the macrogamonts by the microgametes (i), oocysts (j, k) develop that sporulate in the infected host. Two different types of oocysts are produced, the thick-walled, which is commonly excreted from the host j, and the thin-walled oocyst k, which is primarily involved in autoinfection. Oocysts are infective upon excretion, thus permitting direct and immediate fecal-oral transmission.

Note that oocysts of *Cyclospora cayetanensis*, another important coccidian parasite, are unsporulated at the time of excretion and do not become infective until sporulation is completed. Refer to the life cycle of *Cyclospora cayentanensis* for further details.

Geographic Distribution:

Since the first reports of human cases in 1976, *Cryptosporidium* has been found worldwide. Outbreaks of cryptosporidiosis have been reported in several countries, the most remarkable being a waterborne outbreak in Milwaukee (Wisconsin) in 1993, that affected more than 400,000 people.

Clinical Features:

Infection with *Cryptosporidium* sp. results in a wide range of manifestations, from asymptomatic infections to severe, life-threatening illness; incubation period is an average of 7 days (but can range from 2 to 10 days). Watery diarrhea is the most frequent symptom, and can be accompanied by dehydration, weight loss, abdominal pain, fever, nausea and vomiting. In immunocompetent persons, symptoms are usually short lived (1 to 2 weeks); they can be chronic and more severe in immunocompromised patients, especially those with CD4 counts <200/µl. While the small intestine is the site most commonly affected, symptomatic *Cryptosporidium* infections have also been found in other organs including other digestive tract organs, the lungs, and possibly conjunctiva.

Laboratory Diagnosis:

Acid-fast staining methods, with or without stool concentration, are most frequently used in clinical laboratories. For greatest sensitivity and specificity, immunofluorescence microscopy is the method of choice (followed closely by enzyme immunoassays). Molecular methods are mainly a research tool.

Safety

Oocysts in stool specimens (fresh or in storage media) remain infective for extended periods. Thus stool specimens should be preserved in 10% buffered formalin or sodium acetate-acetic acid-formalin (SAF) to render oocysts nonviable. (Contact time with formalin necessary to kill oocysts is not clear; we suggest at least 18 to 24 hours). In addition, the usual safety measures for handling potentially infectious material should be adopted.

Specimen processing

Stool specimens may be submitted fresh, preserved in 10% buffered formalin (see above,

"Safety"), or suspended in a storage medium composed of aqueous potassium dichromate (2.5% w/v, final concentration). The use of mercuric chloride-containing preservatives (e.g., polyvinyl alcohol, PVA) is not recommended due to incompatibilities with some methodologies and the environmental hazards posed by the disposal of mercury-containing compounds. Oocyst numbers can be quite variable, even in liquid stools. Multiple stool samples should be tested before a negative diagnostic interpretation is reported. To maximize recovery of oocysts, stool samples should be concentrated prior to microscopic examination. Formalin-ethyl acetate sedimentation is the recommended stool concentration method for clinical laboratories. Two potential shortcomings of oocyst concentration techniques are:

- Sedimentation methods are generally performed using low speed centrifugation. Given their small size and mass, cryptosporidial oocysts may become trapped in the ether or ethyl acetate plug and fail to sediment properly. Increased centrifugation speed or time (500 × *g*, 10 minutes) may be warranted when attempting to recover cryptosporidial oocysts.
- Resolution of cryptosporidial infections is accompanied by increasing numbers of non-acid-fast, oocyst "ghosts." Such oocysts may not float or sediment as expected, giving rise to false-negative results.

Diagnostic findings:

- Microscopy
- Enzyme immunoassays
- Molecular methods
- Bench aids for *Cryptosporidium*

Antibody detection: There are currently no commercially available serologic assays for the detection of *Cryptosporidium*-specific antibodies. However, immunoblots for detecting the 17 and 27 kDa sporozoite antigens associated with recent infection may be useful for epidemiologic investigations.

Treatment:

Rapid loss of fluids because of diarrhea can be managed by fluid and electrolyte replacement. Infection in healthy, immunocompetent persons is self-limited. Nitazoxanide has been approved for treatment of diarrhea caused by *Cryptosporidium* in immunocompetent patients. Immunocompromised persons and those in poor health are at highest risk for severe illness. The effectiveness of nitazoxanide in immunosuppressed persons is unclear. For persons with AIDS, anti-retroviral therapy, which improves immune status, will also reduce oocyst excretion and decrease diarrhea associated with cryptosporidiosis.

References

1. Kaplan JE, Masur H, Holmes KK. Guidelines for preventing opportunistic infections among HIV-infected persons. MMWR June 14, 2002; 51(RR08):1-46.
2. Morgan-Ryan UM, Fall A, Ward LA, Hijjawi N, Sulaiman I, Fayer R, et al. *Cryptosporidium hominis* n. sp. (Apicomplexa: Cryptosporidiidae) from *Homo sapiens*. J Eukaryot Microbiol 2002;49:433-440.