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Mini Review

CRYTOSPORIUM: A DIARRHOEA CAUSING PARASITE

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ABSTRACT

Cryptosporidiosis is an infection caused by *Cryptosporidium*, a protozoan parasite of clinically importance. It is transmitted by contaminated water and in individuals with proper immune systems it usually causes diarrhea, but in case of immunocompromised people, like those suffering of AIDS, the disease is usually severe and it can be fatal. It is known to be zoonotic in nature. In other words, Cryptosporidiosis can be spread naturally directly from cats to their keepers. Oocyst is a critical stage and mainly responsible for causing infection with typical gastrointestinal manifestations in humans. Medically important ones are *C. parvum* and *C. hominis*, causing infections. The classic symptoms include watery diarrhea, nausea, vomiting, abdominal cramps and Fever etc. The infection is self-limiting so oral o as well as intravenous rehydration and replacement of electrolytes are usually suggested. Moreover, the best of avoiding is to promote the practices of hand washing and hygienic standards in the mass.

***Keywords*:** Diarrhoea, cryptosporidiosis, intestinal parasite, Cryptosporidium.

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INTRODUCTION

Cryptosporidium is a coccidian protozoan parasite, which discovery is associated with E.E. Tyzzer, in 1907 but considered medically unimportant to humans until the first cases of cryptosporidiosis in humans were reported in 1976 by [1,2]. Electron microscopic examination of the intestinal mucosa led to the discovery that *Cryptosporidium* was the infectious species in humans. In the early 1980s, the strong association between cases of cryptosporidiosis and immunodeficient individuals brought *Cryptosporidium* to the head as a ubiquitous human pathogen [3]. *Cryptosporidium* can infect several different hosts, can survive most environments for long periods of time due to its "hardy cyst" and inhabits all climates and locales [2]. *Cryptosporidium* was first recognized as a waterborne pathogen

during an outbreak in Braun Station, Texas, where more than 2,000 individuals were afflicted with cryptosporidiosis [4,5].

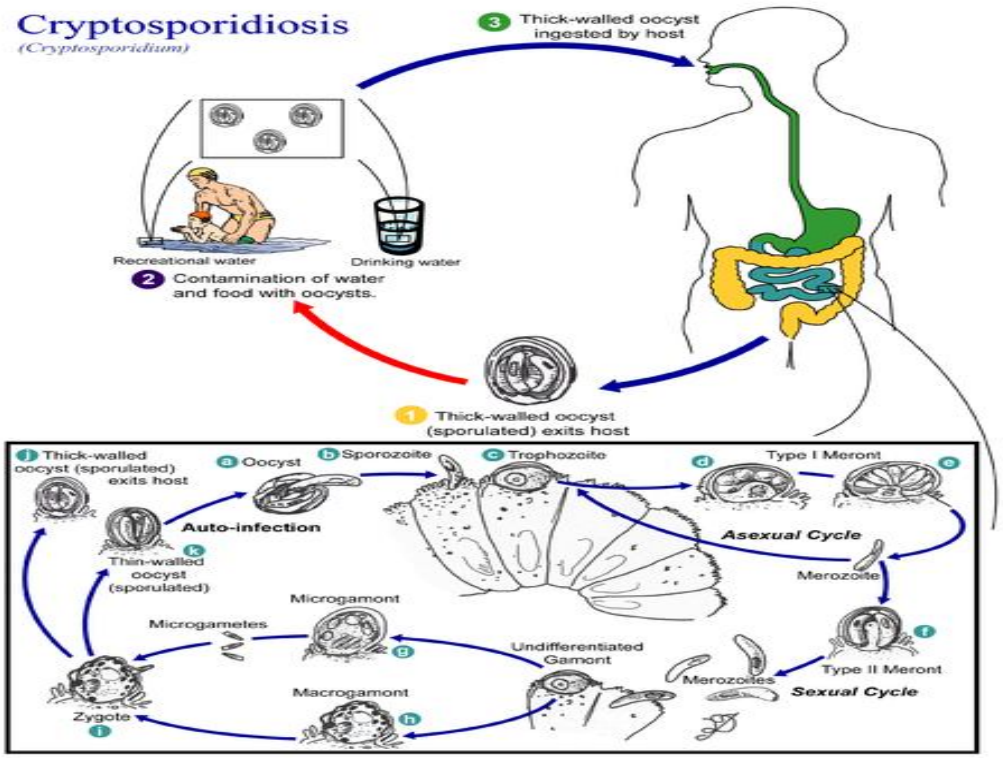
MORPHOLOGICAL FEATURES

A complete description of the morphological features of each life cycle stage consists of oocyst, sporozoite, trophozoite, merozoite, microgametocyte, macrogametocyte of *Cryptosporidium* is provided in the 1994 [28].

LIFE CYCLE

Cryptosporidium is taxonomically classified as a Sporozoa, since its oocyst releases four sporozoites (its motile infectious agents) upon excystation [6]. The life cycle has both sexual and asexual cycles, and there are six distinct developmental stages [2]. After ingestion, the oocysts excyst in the small intestine. They release sporozoites that attach to the microvilli of the epithelial cells of the small intestine. From there they become trophozoites that reproduce asexually by fission, a process known as schizogony. The trophozoites develop into Type 1 meronts that contain 8 daughter cells [7]. These daughter cells are Type 1 merozoites, which get released by the meronts. Some of these merozoites can cause autoinfection by attaching to epithelial cells. Others of these merozoites become Type II meronts [8], which contain 4 Type II merozoites [7]. These merozoites get released and they attach to the epithelial cells. From there they become either macrogamonts or microgamonts [8]. These are the female and male sexual forms, respectively [7]. This stage, when sexual forms arise, is called gametogony [9].

Zygotes are formed by microgametes from the microgamont penetrating the macrogamonts. The zygotes develop into oocysts of two types [8]. 20% of oocysts have thin walls and can re infect the host by rupturing and releasing sporozoites that start the process over again [7]. The thick-walled oocysts are excreted into the environment [8]. The oocysts are mature and infective upon being excreted [7]. They can survive in the environment for months [10]. The cycle begins anew when these oocysts are ingested by a new host. Below is a visual representation of the *Cryptosporidium* life cycle [11].



CLINICAL MANIFESTATION

The various symptoms of cryptosporidiosis differ between immunocompetent and immunocompromised individuals. In immunocompetent patients, cryptosporidiosis is an acute, yet self-limiting diarrheal illness (1-2 week duration), and symptoms are: [3]

- Watery diarrhea
- Nausea
- Vomiting
- Abdominal cramps
- Fever

For immunocompromised persons, the illness is much more severe:

- Debilitating, cholera-like diarrhea
- Severe abdominal cramps
- Malaise
- Fever
- Weight loss
- Anorexia

Due to lack of tissue specificity, *C. parvum* infection has also been identified in the biliary tract and the respiratory system [12].

EPIDEMIOLOGY

C. parvum Infection has been reported in six continents and identified in patients aged 3 days to 95 years old [6]. Transmission is usually fecal-oral route, often through water contaminated by livestock mammal feces. Persons most likely to be infected by *Cryptosporidium* are: [2,3,6,12,13]

- infants and younger children in day-care centers
- those whose drinking water is unfiltered and untreated
- involved in farming practices such as lambing, calving, and muck-spreading
- engaging in sexual practices that brings a person into oral contact with feces of an infected individual
- patients in a nosocomial setting with other infected patients or health-care employees
- veterinarians who come in contact with farm animals
- travelers to areas with untreated water
- living in densely populated urban areas
- owners of infected household pets (rare)

TRANSMISSION

Cryptosporidial infection can consequently be transmitted from fecally contaminated food and water, from animal-person contact, and through person-person contact [29].

Food and water

One most important outbreak in Milwaukee in 1993 affected over 400,000 persons. Outbreaks such as these usually result from drinking water taken from surface water sources such as lakes and rivers [3]. Swimming pools and water park wave pools have also been associated with outbreaks of cryptosporidiosis. Also, untreated groundwater or well water public drinking water supplies can be sources of contamination.

The highly environmentally resistant cyst of *C. parvum* allows the pathogen to survive a variety of drinking water filtrations and chemical treatments such as chlorination. All waterborne outbreaks of cryptosporidiosis have occurred in commmunities where the local utilities met all state and federal drinking water standards [3].

Food can also be a source of transmission, when either an infected person or an asymptomatic carrier contaminates a food supply [3]. The oocysts do not survive cooking, but food contamination can occur in beverages, salads, or other foods not heated or cooked after handling.

Animal-person transmission

Transmission of *C. parvum* from household pets is rare, but there is a definite association between calves and humans--approximately 50% of calves shed oocysts and the pathogen is present on upwards of 90% of all dairy farms [3]. Pets have not often been implicated as a source of infection and are not considered a major risk factor for acquisition of cryptosporidiosis [14].

Person-person transmission

Cryptosporidium transmission occurs at a high frequency in day-care centers, where infants or younger children are clustered within classrooms; share bathrooms and common play grounds, or necessitate frequent diaper-changing [2]. Day-care employees can become easily infected by *C. parvum* through careless diaper-changing or through washing the laundry of infected children. Day-care workers can then spread the pathogen to their families at home.

Nosocomial situations are also a major medium for cryptosporidial transmission. There have been several reports of both transmission from patients to health care staff and patient-to-patient transmission [12]. This "environmental contamination" raises the possibility of aerosol transmission of *C. parvum* from person-to-person. Various routes of transmission such as aerosol infection is quite likely, since *Cryptosporidium* oocysts are shed in large numbers during acute infection and are immediately infective to others [12].

PATHOGENESIS

Upon oocyst excystation, four sporozoites are released which adhere their apical ends to the surface of the intestinal mucosa [2]. Below is a phase contrast photograph of sporozoite release from the *Cryptosporidium* oocyst [6]. A sporozoite-specific lectin adherence factor has been identified as the agent of attachment to the intestinal surface [2]. After sporozoite attachment, it has been hypothesized that the epithelial mucosa cells release cytokines that activate resident phagocytes [13]. These activated cells release soluble factors that increase intestinal secretion of water and chloride and also inhibit absorption. These soluble factors include histamine, serotonin, adenosine, prostaglandins, leukotrienes, and platelet-activating factor, and they act on various substrates, including enteric nerves and on the epithelial cells themselves [13]. Consequently, epithelial cells are damaged by one of two models:

1. Cell death is a direct result of parasite invasion, multiplication, and extrusion
2. Cell damage could occur through T cell-mediated inflammation, producing villus atrophy and crypt hyperplasia

Model produces distortion of villus construction and is accompanied by nutrient malabsorption and diarrhea [13].

DETECTION AND DIAGNOSIS

When *C. parvum* was first identified as a human pathogen, diagnosis was made by a biopsy of intestinal tissue [2]. However, this method of testing can give false negatives due the "patchy" nature of the intestinal parasitic infection [6]. Staining methods were then developed to detect and identify the oocysts directly from stool samples. The modified acid-fast stain is usually used to most reliably and specifically detect the presence of cryptosporidial oocysts [30]. Immunologically, anti-cryptosporidial IgM, IgG, and IgA can be detected by the enzyme-linked immunoabsorbent assay (ELISA) or by the antibody immunofluorescence assay (IFA), but neither of these assays can provide a direct diagnosis of cryptosporidiosis. Traditional enzyme immunoassays (EIA) can provide rapid detection of oocysts with little tediousness. EIA can be used to analyze environmental samples. [15] reported a positive EIA detection of one oocyst. [16] reported EIA sensitivity equal to microscopic examination in both environmental and human samples [15,17].

Recently, new genetic methods of detecting *C. parvum* have been developed, using PCR or other DNA-based for the detection of *Cryptosporidium* in drinking water. Oocysts were detected by PCR in wastewater, surface waters, and drinking water, but the sensitivity of the PCR assay was inhibited by "uncharacterized components in the samples"[18,23].

TREATMENT

No protected and effective therapy for cryptosporidial has been successfully developed. Since cryptosporidiosis is a self-limiting illness in immunocompetent individuals, general care is the only treatment for the illness. Oral or intravenous rehydration and replacement of electrolytes may be essential for particularly voluminous, watery diarrhea. Oral rehydration treatment can include Gatorade, bouillon, or oral rehydration solution, containing glucose, sodium bicarbonate, and potassium [6].

Pharmocological therapies

For immunocompromised patients with cryptosporidiosis, quite a few antimicrobial agents have been tested as treatments. Antibiotics such as spiramycin and dicalzuril sodium have produced partial responses in patients, but have not reliable, reproducible results [6]. However, one particular antimicrobial agent, paromomycin, has been shown to decrease the intensity of infection and improve intestinal function and morphology [13].

Immunological therapy

Even though serological antibodies do not provide any protection from cryptosporidial infection, but more than a few studies have been done to show that antibodies in the intestinal lumen may help clear or even prevent infection. The feeding of bovine colostral immunoglobulin to patients has been shown to ameliorate symptoms of *Cryptosporidium* infection in humans, and it has also been shown that the release of intestinal IgA accompanies this clearance of infection[11]. Additionally, anti-sporozoite antibodies have blocked the infectivity of *C. parvum* sporozoites in mice by inhibiting their ability to attach to the surface of the intestininal mucosa. A more recent study by [24], reproduced the inhibition of *C. parvum* infection by hyperimmune bovine colostrum in vitro, providing an ideal system through which cryptosporidial infection can be studied in the laboratory. The mean number of intracellular parasites per host cell was reduced by 61% upon introducing HBC Ig antibodies with a concentration of 1 mg/ml IgG. This investigation also purified antibodies from HBC Ig on Western blots of *Cryptosporidium* proteins and found that they, too, inhibited *C. parvum* infectivity in vitro [24].

DRINKING WATER: PURIFICATION AND FILTERATION

Current data is not adequate to advise all immunodeficient persons to boil or avoid tap water, but the risks involved are high enough that, until the health risk of drinking water containing small number of *Cryptosporidium* oocysts is clearly defined, it is advised that these individuals boil all water intended for drinking for at least one minute.

Household water filtration system or drinking bottled water can reduce the risk of *Cryptosporidium* infection [3]. Municipal water utilities provide relatively good protection against water-borne *Cryptosporidium* infection. Municipal drinking water is purified two ways: through chemical treatments like, chlorination and through filtration [25]. Chlorine dioxide and monochloramine were also ineffective in inactivating *C. parvum* oocysts in drinking water[26]. Filtration is better for removing *C. parvum* oocysts from municipal drinking water. In recent years, ultra-fine membranes have been developed to remove various contaminants from drinking water [27]. Hence, *C. parvum* oocysts can be as small as 4 microns, at least micro filtration is needed to reliably remove oocysts from the water supply [6]. Since *Cryptosporidium* oocysts are so resistant to chemical disinfectants, ultra filtration or reverse osmosis would provide ideal protection against waterborne outbreaks via drinking water. Clarify the relationship between low numbers of oocysts in drinking water and the frequency of cryptosporidial infection. Determine the asymptomatic carrier rate for *Cryptosporidium* in immunocompromised persons and the chance that these individuals will develop cryptosporidiosis when their CD4 counts drop to a low level. Calculate the relative risks of infection from drinking water, contact with animals, unsafe sexual practices, and nosocomial contact to see where focus on preventative strategies should be placed. Improve state and federal communication for reporting cases of cryptosporidiosis and identifying outbreaks. Continue to develop more effective therapies for ameliorating cryptosporidiosis symptoms.

CONCLUSION

According to the epidemiology, the cases of cryptosporidiosis globally have been observed due to the consumption of contaminated water and food as it's a potential fecal oral pathogen. In the same way, poor hygiene is also one of the alarming factors for the transmission of this parasite, so there is a need to encourage the hand washing practices in our society and as possibly avoid unfiltered and unclean water. Like many fecal-oral pathogens, it can also be transmitted by contaminated food or poor hygiene. Proper and frequent hand washing has to be promoted in order to break the chain of infection.

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