Control of Zoonotic Cryptosporidiosis

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Abstract

Cryptosporidiosis, caused by protozoan parasites of the genus *Cryptosporidium*, is a major global diarrheal disease, especially in young children, immunocompromised individuals and low- resource settings (i.e., settings that lack adequate water, sanitation or overall health systems). Transmission of the parasite occurs through water, food, direct contact with infected humans/animals, as well as through environmental exposure to oocyst, which are highly resistant to standard disinfection methods. *Cryptosporidium*, known for its resilient survival strategies, continues to be a leading cause of waterborne disease outbreaks globally, frequently resulting in significant public health implications. The parasite exhibits a multifaceted life cycle that includes both intracellular and extracytoplasmic phases, engaging in asexual and sexual reproduction within the intestinal epithelium of the host. This process causes damage to epithelial cells, leads to villous atrophy, induces crypt hyperplasia, and results in malabsorption, ultimately causing severe and potentially life-threatening diarrhea. At present, there are few effective treatment options available. Nitazoxanide is the sole FDA-approved medication for cryptosporidiosis; however, its effectiveness is diminished in individuals with compromised immune systems. Investigations into other potential therapies, including halofuginone and paromomycin, are ongoing, and there is no comprehensive treatment available that is effective for all patient groups. Control measures primarily emphasize prevention, as a vaccine for Cryptosporidium has yet to be developed. Ensuring the safety of drinking water through advanced filtration, UV radiation and ozone treatment has proven effective in decreasing outbreaks. Additionally, improvements in sanitation, hygiene education and surveillances initiatives are critical in reducing transmission rates. The "One Health" framework, which integrates the health of humans, animals and the environment, is increasingly recognized as vital for addressing zoonotic transmission. Recent advancements in molecular diagnostics and vaccine development hold promise for future solutions, but further research is essential to establish effective preventive and therapeutic strategies. A thorough understanding of the biology of the parasite, as well as host-pathogen interactions and immune responses is crucial for mitigating its impact on public health. This book chapter examines the epidemiology, pathogenesis, current treatment options and emerging control measures for cryptosporidiosis, underscoring the necessity for continued scientific and medical innovation.

Keywords: *Cryptosporidium,* epidemiology, waterborne pathogen, foodborne pathogen, outbreaks, one health, vaccines

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Introduction

Cryptosporidiosis emerges as an enteric disease because of the protozoon parasite from *Cryptosporidium* genus. The disease stands as one of the frequent diseases that disseminate through water supplies and generates the greatest number of waterborne outbreak incidents worldwide (Helmy, El-Adawy, et al., 2017; Gharpure, 2019). Research reveals that protozoal infections lead to nearly 58 million cases of diarrhea among children annually. Specifically, waterborne pathogens like *Cryptosporidium* and *Giardia* are highlighted in the World Health Organization's "Neglected Disease Initiative" (Helmy et al., 2014; Helmy et al., 2018). Most people experience a self-limiting form of gastroenteritis from *Cryptosporidium* infection but immunocompromised individuals commonly develop long-term dangerous diarrheal disease. The immature immune system of neonates makes them prone to infections which can occur through consuming minimal amounts of parasite oocysts. Statistics show that diarrheal diseases cause around 1.6 million mortalities during each annual timeframe. Contaminated drinking water and inadequate hygiene practices account for one-third of all fatalities in children under the age of five. In developing countries, *Cryptosporidium* is responsible for around 20% of diarrhea cases in children and poses significant health risks for individuals living with HIV. The infection leads to more than 8 million cases of food contamination each year across the worldwide scale (Ryan et al., 2018). People residing in rural places combined with urban slum communities experience the highest risk of contracting this infection (Putignani & Menichella, 2010).

In 1982, the center for disease control (CDC) reported *Cryptosporidium* as a human medical threat through its examination of diarrhea in HIV patients. The global awareness of *Cryptosporidium* as a significant public health risk emerged in 1993, following an

outbreak in Milwaukee, Wisconsin, where over 400,000 individuals contracted *C. hominis* from contaminated drinking water (Thompson et al., 2008). The CDC in the USA reported through its 2014 to 2016 data that waterborne infections linked to *Cryptosporidium* have become double in number causing about 748,000 human cases annually (Scallan et al., 2011). The inadequate standards of water and food sanitation in developing nations elevate the chances of cryptosporidiosis development (DuPont, 2016). The youngest population of children below five years old in developing countries shows the highest exposure to *Cryptosporidium* infections (Khalil et al., 2018). Oocysts maintain their infectious nature through several-month survival outside hosts regardless of adverse environmental conditions that include saline water and chemical substances (Smith et al., 2007). The calf diarrhea complex primarily arises from simultaneous infections caused by *Cryptosporidium*, enterotoxin Escherichia coli (ETEC), as well as corona- and rotaviruses in young calves (Smith et al., 2007). Current medical research lacks effective chemical drugs for treating cryptosporidiosis infections (Shahiduzzaman & Daugschies, 2012). Nitazoxanide together with halofuginone stand as the approved medications used against *Cryptosporidium* infections for humans and animals. These drugs demonstrate no surefire success in eliminating the infection (Brainard et al., 2021). The main strategy to control cryptosporidiosis involves three key components which include lowering the infection rates, interrupting animal-human transmission and ensuring proper hygiene conditions for humans and animals. Data regarding the pathways and distribution patterns of *Cryptosporidium* coupled with infection extent statistics and dominant animal and human sub-species helps to facilitate proper disease management (Sparks et al., 2015).

The Classification of Species, their Location and the Spectrum of Hosts for *Cryptosporidium*

Scientific research has isolated more than 40 different *Cryptosporidium* taxa that infect mammals including Bovidae, Primates, Carnivora, Hares, Equidae, Rabbits, Rhinocerotidae and Tapiridae as well as amphibians, birds and reptiles. The following *Cryptosporidium* species exist: *C. hominis*, *C. bovis, C. parvum, C. ryanae, C. andersoni, C. fayeri, C. canis, C. felis, C. macropodum, C. muris, C. suis* and *C. wrairi* isolated from different mammals. Modern research has verified that *C. meleagridis, C. baileyi* and *C. galli* are the parasites that infect birds (Helmy, Krücken, et al., 2017). *C. varanii* along with *C. serpentis* infect reptiles and *C. fragile* infects amphibians (Table 1) (Mamedova & Karanis, 2021). Researchers have recovered *C. rubeyi* from squirrels as well as *C. scophthalmi* from turbot and *C. huwi* from fish together with *C. erinacei* from horses and hedgehogs (Zahedi et al., 2016). Cryptosporidiosis in humans can be caused by *C. hominis* yet *C. parvum* serves as the zoonotic species that infects humans with this disease (Delling & Daugschies, 2022). The two *Cryptosporidium* species are responsible for human cryptosporidiosis cases, cause infections in more than 90% of patients. Some specific *Cryptosporidium* species show host restriction but *C. meleagridis, C. baileyi*, *C. andersoni, C. canis, C. felis, C. bovis, C. suis, C. fayeri, C. scrofarum, C. tyzzeri, C. erinacei* and *C. muris* have also been identified in animal hosts alongside humans. Multiple research studies have identified the aforementioned species together with *C. parvum* as zoonotic species (Ryan et al., 2014). Human beings can develop *C. viatorum, C. cuniculus, C. ubiquitum*, Chipmunk genotype I, *Cryptosporidium* horse, and *Cryptosporidium* mink genotype infections in addition to *C. parvum* infections (Table 1) (Helmy et al., 2013).

Table 1: Predominant *Cryptosporidium* Species: Major Hosts and Locations

Cryptosporidium spp.	Hosts	Location
C.hominis	Humans	Small intestine
C.parvum	Ruminants, humans, deer	Small intestine
C.bovis	Ruminants	Small intestine
C.andersoni	Ruminants, camel	Abomasum
C.ryanae	Abomasum	Small intestine
C.xiaoi	Sheep	Small intestine
C.ubiquitum	Sheep/wildlife	Small intestine
C.meleagridis	Chicken, turkey, humans	Intestine
C.baileyi	Birds	Cloaca, bursa,respiratory tract
C.galli	Birds	Proventriculus
C.avium	Birds	Intestine
C.ornithophilusis	Ostrich	Intestine
C.proventriculi	Psittaciformes birds	Proventriculus
Avian genotype II	Birds	Intestine
Avian genotype IV	Birds	Intestine
Eurasian woodcock genotype	Birds	Intestine
C.suis	Pigs, humans	Small intestine
C.wrairi	Guineapigs	Small intestine
C.cuniculus	Rabbits	Small intestine
C.canis	Canids, humans, mink, fox	Small intestine
C.felis	Felids, humans	Small intestine
C.muris	Rodents, humans	Stomach
C.ratti	Rodents	Small intestine
C.tyzzeri	Mice	Small intestine
C.molnari	Fish	Stomach
C.scophithalmi	Fish	Intestine
C.nasorum	Fish	Intestine

Life Cycle and Developmental Stages of *Cryptosporidium*

Cryptosporidium, a microscopic organism, is classified under the Coccidia group of the Apicomplexa phylum. It exhibits unique traits that distinguish it from all other Coccidia (Hijjawi et al., 2002), these key aspects include (1) the intracellular and extracellular positioning of oocysts, (2) the formation of a "feeder" organ, (3) the presence of both morphological types of oocysts (thin-walled and thick-walled) and functional types (auto-infection versus new infection), (4) the small dimensions of the oocysts, (5) the absence of specific morphological characteristics like sporocysts or micropyles, and (6) the resistance of *Cryptosporidium* to all available anti-coccidial drugs (Smith & Corcoran, 2004).

Cryptosporidium follows a specialized life cycle that splits into two distinct sections: (schizogony/merogony and sporogony) asexual parts along with sexual (gamogony) section. While infecting *Cryptosporidium*'s free-living stages the parasites grow and differentiate within the parasitophorous vacuole under the host cell surface layer where they exist outside the cellular cytoplasm (Vanathy et al., 2017). Once *Cryptosporidium* attaches to cell surfaces it proceeds with gliding motion and enters the host cell eventually. When *Cryptosporidium* detects target host cells, they make the cells to envelop them through membrane structures made by the cells themselves. During its interaction with the host, *Cryptosporidium* creates an actin-rich food organelle that penetrates the cell to provide essential nutrients. Once inside the host cells, the sporozoite undergoes division within the parasitophorous vacuole, transforming into a spherical trophozoite characterized by an eccentric nucleus. Throughout three phases of schizogony, a trophozoite develops into a Type-1 meront, which subsequently divides to produce eight merozoites. Although both cell types appear similar, the nucleus of the merozoite is positioned more centrally compared to that of the sporozoite. The merozoites complete their asexual life cycle within the epithelial cells by forming Type-I meronts that yield trophozoites. In the absence of sexual development, the merozoites differentiate into Type-II meronts. This meront then undergoes cell division to generate four new merozoites, which migrate to other enterocytes and differentiate into small and large reproductive cells during gamogony. The immature micro-gamontes are spherical and contain 16 nuclei arranged along their periphery, which later develop into micro-gametes.

The microgametes have short ends and no cell flagella alongside cell nuclei which lack flagella. At maturity the micro-gametes disengage from their host cell to perform fertilization of macrogametes. The macrogametes exhibit spherical shape with cytoplasm granules and wall-forming bodies positioned off-center in the cell body (Tandel et al., 2019). The zygote advances by syngamy before completing sporogony which resembles a meiotic process. The oocyst contains thin or thick walls which develops four sporozoites (haploid sporozoites) within the parasitophorous vacuole (Figure 1) (O'Hara & Chen, 2011). The 20% thin-walled oocysts complete excystation within the host intestinal tract while the 80% thick-walled oocysts demonstrate extreme disinfectant resistance and are excreted with feces to the environment where they persist externally. The exogenous phase of *Cryptosporidium* parasite is represented by its thick-walled oocysts. The oocysts of *Cryptosporidium* show spheric to ovoid form and contain a residual body along with their four banana-shaped sporozoites that possess front and hind ends with pointed structures and stubbed nuclei (Smith et al., 2005). Sporozoites from *Cryptosporidium* exist outside sporocyst protection and their oocyst membrane includes two component layers at their wall edges together with a preformed connection which reaches through part of their structure. When exposed to the appropriate temperature, pH, gall bladder salts, pancreatic enzymes, and CO_2 from the host's gastrointestinal tract, the pre-formed joint enables the escape of four sporozoites. These sporozoites become free within the digestive tract and subsequently attach to the microvilli of enterocytes, where they begin the internalization process through their tapered end. During host cell invasion and adherence, the sporozoites use glycoproteins along with circumsporozoite-like glycoprotein (CSL) as essential factors. The host cell creates membrane, bulges around sporozoites before establishing a parasitophorous vacuole within the enterocyte brush border. Like other Apicomplexa parasites, *Cryptosporidium* spp. establishes parasitophorous vacuoles unique to itself positioning inside the host cell tissue yet beyond the cell membrane domain (O'Hara et al., 2004). The feeder organelle emerges from the boundary where sporozoite and host cell membranes join each other. The maturing parasite receives nutrients through these structures as they help with parasite integration (Zapata et al., 2002). Scientific studies have detailed the molecular components together with mechanisms that drive the *Cryptosporidium* life cycle development (Lendner & Daugschies, 2014).

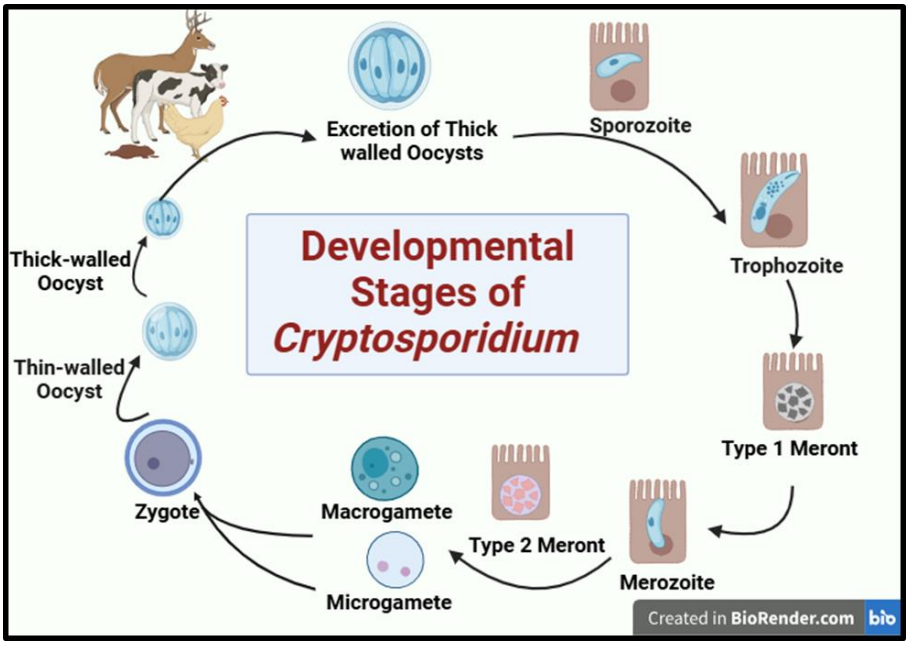

Fig. 1: Developmental Stages of *Cryptosporidium*

Pathogenesis of *Cryptosporidium*

When oocysts are ingested via contaminated food or water, the sporozoite surface produces various signaling molecules that aid in the attachment and invasion of host cells. Recent studies indicate that the invasion of sporozoites into host cells is controlled by Calcium-dependent protein kinases (CDPKs) (Etzold et al., 2014). Within the host cell, *Cryptosporidium* takes refuge rather than invading the cells. By residing in the intercellular space, the infected cells undergo significant rearrangement of their actin structures (Lendner & Daugschies, 2014). The dynamics between the host and the parasite play a crucial role in the pathogenesis of *Cryptosporidium* after the parasite has invaded and attached. Research has demonstrated that *C. parvum* leads to acute to chronic catarrhal enteritis in the distal ileum of calves, and it also facilitates the detection of *Cryptosporidium* life stages in the duodenum, colon, and cecum. Microscopic examinations reveal edematous changes and hyperemia in both the mucosal tissue and the mesenteric lymph nodes (Tzipori & Ward, 2002). The infected human host experiences degeneration of epithelial cells, accompanied by metaplasia of the normally high prismatic to isoprismatic villus epithelial cells and hyperplasia of the crypt epithelium. Additionally, the characteristic microvilli are displaced towards the attachment zone of the intracellular parasites, which also features elongated microvilli. These pathological alterations result in a reduced intestinal absorption surface, ultimately leading to malabsorption (Fayer & Santín, 2009).

Epidemiology of Cryptosporidiosis

1. Infection Sources and Routes of Transmission

In Humans

Zoonotic transmission can occur directly through contact with an infected person and/or indirectly via consumptions of contaminated drinking water or contaminated food and/or through the inhalation of oocysts with an air contaminated with aerosolized droplets or fomites (Sponseller et al., 2014). In addition, synanthropic flies (suborder: Cyclorapha) could contribute to a significant mechanical transmission and spreading of infection as shown in figure 2. Human cryptosporidiosis has multiple causes (Lendner & Daugschies, 2014) such as (1) polluted drinking water, and unclean sporting/pool water, (2) polluted foods like rawfruits and vegetables that were fertilized with polluted effluent, (3) touch with infected people (hospitals, day-care centers, schools), (4) contact with infected animals (particularly calves) and (5) anal sexual contact (Dillingham et al., 2002).

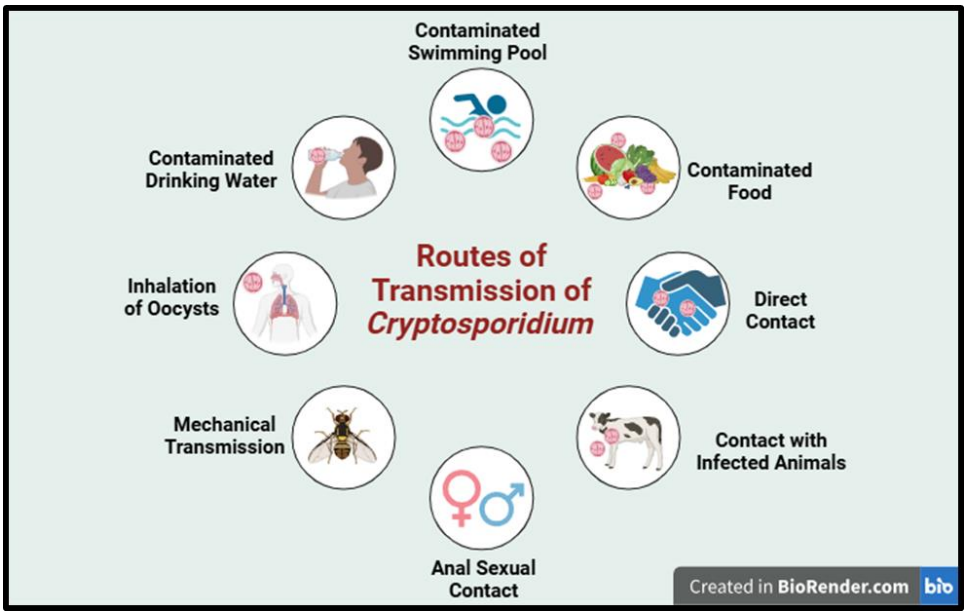

Fig. 2: Routes of Transmission of *Cryptosporidium*

In Animals

Newly born calves become infected with cryptosporidiosis when they consume infected material found in their surroundings. Common ways to become infected with *Cryptosporidium* include from neighboring animals, dirty barn environments, unclean cow udders, and polluted water sources. Adult cattle that carry *Cryptosporidium* infection without symptoms, shed live parasites and function as infection circles (Scheid & Schwarzenberger, 2011). Personal contact between staff and animals, spreads *Cryptosporidium* through footwear and clothes as well as through transmission from pets to staff members. The parasite also passes between animals in the infected environment and from animals to humans through insects like flies and amoeba species (Pumipuntu & Piratae, 2018).

2. Clinical Signs

In Humans

The degree of clinical manifestations in humans who are infected is influenced by both their age and the strength of their immune system (Chen et al., 2002). In individuals with a competent immune system, the incubation period lasts between 5 and 21 days, leading to an acute episode of self-limiting diarrhea that persists for 3 to 12 days. Clinical manifestations can vary from moderate to severe watery or catarrhal diarrhea (Figure 3), frequently accompanied by symptoms such as abdominal pain, nausea, vomiting, gas, fatigue, and loss of appetite.

Additionally, respiratory symptoms like coughing, sneezing, and expectoration may arise following the inhalation of oocysts present in contaminated air (Sponseller et al., 2014; Ahmed & Karanis, 2020). Asymptomatic infections can occur as well. However, for individuals with weakened immune systems, particularly those with genetic conditions such as hyper-IgM syndrome, those with significantly low CD4 lymphocyte levels from HIV, or those undergoing immunosuppressive therapy after receiving an organ transplant, the infection has the potential to develop into a chronic and life-threatening disease (Hunter & Nichols, 2002).

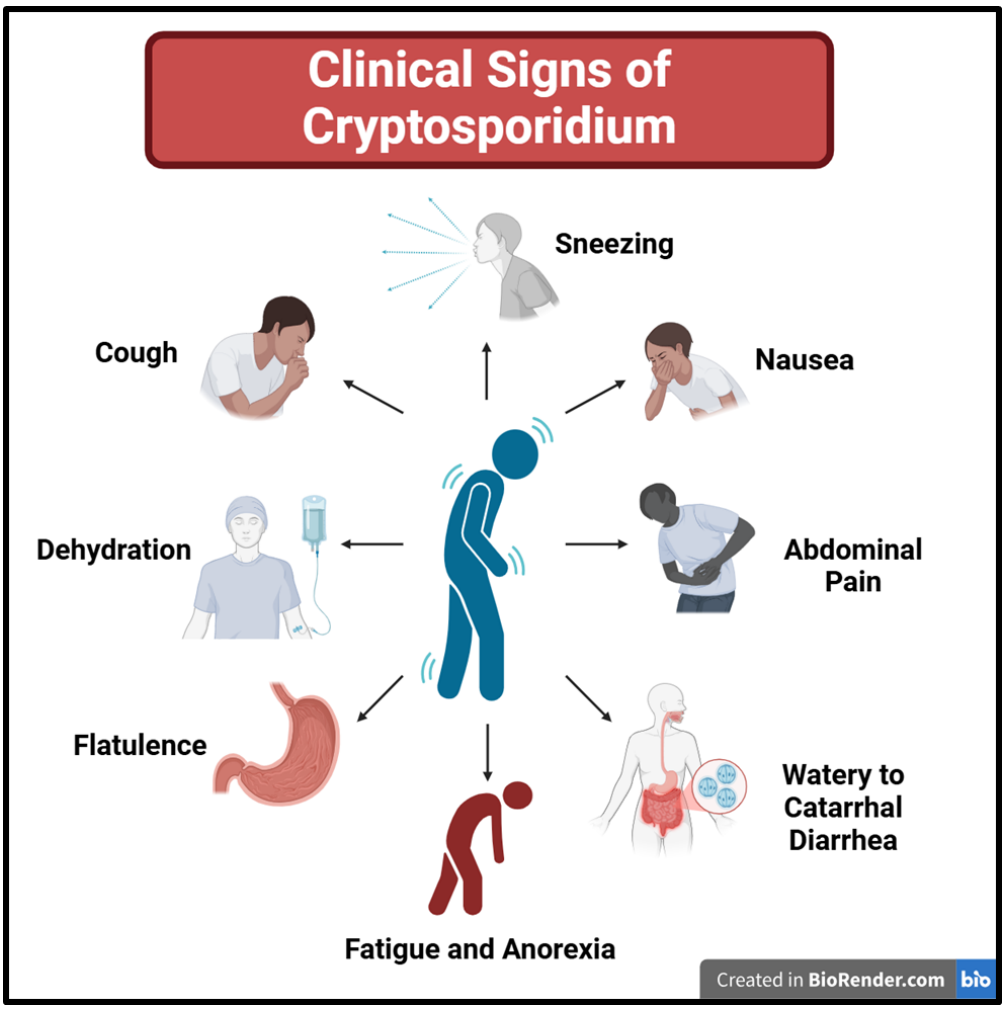

Fig. 3: Clinical Signs of *Cryptosporidium*

In Animals

Clinical symptoms can present as asymptomatic or escalate to severe conditions, including profuse watery or pasty diarrhea, dehydration and potentially death. Within the first three weeks of age, calves may experience co-infections with *C. parvum*, enterotoxigenic E. coli, coronaviruses, and rotaviruses, which are identified as major factors leading to mortality in this population (Helmy, Krücken, et al., 2017). The presence of neonatal diarrhea linked to either a single or mixed *C. parvum* infection is characterized by excessive yellowish diarrhea and can result in complications such as dehydration, metabolic acidosis and electrolyte depletion. Consequently, cryptosporidiosis incurs substantial economic losses due to its impact on health, growth delays and the costs associated with treatment (McDonald, 2000).

Control of *Cryptosporidium* Infection

1) One Health Strategy for Cryptosporidiosis Control

Official worldwide health departments use the "One Health" strategy to fight zoonotic diseases while defending health at animal-human interaction boundaries. Health systems gain more control over infections when all branches of healthcare come together including vets, workplace doctors and public health officials (Fawzy & Helmy, 2019). A One Health plan has earlier come forward as a solution to fight cryptosporidiosis and other zoonotic diseases (Helmy et al., 2020) because professionals involved in different areas including physicians, veterinarians, healthcare experts, and scientists need active collaboration. Our recommendation uses One Health to stop *Cryptosporidium* infection from spreading between people animals and environments by studying its disease development routes, transmission patterns and vaccine potential. Public health and public awareness programs educate people about the spread of cryptosporidiosis. The One Health approach implements effective parasite control methods and studies disease spread in communities. Regular checks seek illness sources, and vets handle parasite outbreaks to help prevent human outbreaks. Specialists undergo parasite and disease training while professionals prioritize healthcare needs (Innes et al., 2020).

2) Protective Measures Against *Cryptosporidium*

The only mean to stop cryptosporidiosis spread depends on getting rid of infectious oocysts from contaminated environments. Animal relocation to sanitized facilities plus disinfection should be done but cannot work for large animal farms. Regular area disinfection stops people from spreading the infection from one household to another. The oocyst infectivity and survival increase both during temperatures below 5 degrees Celsius and above 15 degrees Celsius for three months (King et al., 2005). *Cryptosporidium* oocysts can be harmed through various means, including heat, cold, pressure, and dehydration. The ability of C. parvum oocysts to withstand temperature changes is linked to the carbohydrate energy stored in the sporozoites and their residual bodies, which utilize amylopectin for host invasion and excavation under high-temperature conditions (Jenkins et al., 2002). Heat exposure of 64.2 ℃ for 5 minutes or 72.4 ℃ for 1 minute effectively eliminates all infectious characteristics of the oocysts. The survival of *C. parvum* oocysts greatly diminishes beyond 70 ℃ even while protected by cryoprotectants according to research. UV radiation turns *Cryptosporidium* oocysts unable to cause infection (Sivaganesan & Sivaganesan, 2005). Chlorine dioxide, hydrogen peroxide and ammonia solutions prove most successful at ending *Cryptosporidium* oocyst infection. These water disinfectants mostly show reduced effectiveness when used at low concentrations and during short treatment periods. Ozone stands out as one of the best chemical disinfectants for eliminating *Cryptosporidium* and effectively treating *Cryptosporidium* oocysts in water sources. Researchers discovered that rotifers living in rivers, lakes seas and ponds along with predatorial protozoa consume *C. parvum* oocysts (Stott et al., 2003). Certain rotifer species release *Cryptosporidium* oocysts alongside their eaten materials through bolus discharge so they act as natural oocyst controllers in water (Fayer et al., 2000).

3) Medical Interventions for *Cryptosporidium* Infection

Researchers studied multiple active drugs to see if they fight *Cryptosporidium* infections (Shahiduzzaman & Daugschies, 2012). In vitro research shows that few drugs demonstrate effective response against *Cryptosporidium* (Schneider et al., 2021; Van Voorhis et al., 2021). In Europe, Halofuginone (bromo-chlorinated quinazoline derivate) is approved for treatment of *Cryptosporidium* infection in animals. Halofuginone is administered for 7 days at a dosage of 100 g/kg of body weight beginning within the first 24 h after the onset of diarrhea and/or within the first 24–48 h of life as prophylactic. A double therapeutic dosage of the treatment may produce diarrhea, blood in feces, reduction of milk intake, dehydration, exhaustion, and apathy (Silverlås et al., 2009). The Food and Drug Administration granted nitazoxanide (a nitrothiazolyl salicylamide) approval for treating cryptosporidiosis in humans ≥ 1 year of age (Cabada & White Jr, 2010). Doctors provide most patients ≥ 1 year of age with 100 mg/5 mL of nitazoxanide oral suspension while they prescribe 500 mg tablets to patients ≥ 12 years old for their treatment (Chen et al., 2002). The water is the main source of *Cryptosporidium* outbreaks since studies found that 56% of 71 events involved contaminated water supply (Putignani & Menichella, 2010). Water treatment experts and professionals greatly prioritize controlling *Cryptosporidium* in their operations. Oocysts from *Cryptosporidium* invade different filtration systems and withstand exposure to chlorine disinfectant and chlorinated water. The treatment of infected water requires different filtration methods including direct filtration, conventional filtration, slow-sand filtration, diatomaceous earth filtration, bag filtration, cartridge filtration and membrane filtration. Conventional filtration techniques that combine coagulation with flocculation and sedimentation can eliminate 99% of Cryptosporidium from water. The sand filtration method removes Cryptosporidium oocysts by utilizing a biological process from the water supply (Rochelle et al., 2004; Johnson et al., 2005). Research shows that ultraviolet irradiation has an effect on Cryptosporidium oocysts infectivity levels and demonstrates sunlight's potential to inactivate these oocysts in water bodies (Holubová et al., 2020).

4) Vaccines Development

Scientists cannot find effective vaccines today to stop *Cryptosporidium* infections in both human and animal bodies (Innes et al., 2020). Infection control through vaccines requires urgent focus most for people at high risk like babies under five, those with poor nutrition and weakened immune systems. Research indicates that vaccination against rotavirus, coronavirus, and *E. coli* in mother cows can help to protect calves from *Cryptosporidium* infections. The vaccination of mother cows against pathogens leads to protection for calves against infection through colostrum which helps the calves to resist infection during their first weeks of age (Innes et al., 2011). Research must focus on both how the host body reacts to *Cryptosporidium* infection and how its immune components battle against these invaders (Mead, 2014; Ryan et al., 2016). The details of host reactions to this pathogen remain unclear and experts need more studies to determine these details (Borad & Ward, 2010; Ludington & Ward, 2015). Scientists have performed many experiments to create effective vaccines for treating cryptosporidiosis. Observations show miRNA defends cellular immunity against *Cryptosporidium* infection by controlling miRNA output in epithelial cells and mannose-binding lectin (MBL) helps to prevent this disease mostly in children and immune-weakened people with MBL impairment (Kelly et al., 2000; Kirkpatrick et al., 2006; Carmolli et al., 2009). The development of gp15, cp15, and cp23 antigens as vaccine candidates is currently underway. The gp15 antigen displays substantial conservation across both *C. parvum* and *C. hominis* species with noticeable cross-reactivity between them (Lucio-Forster et al., 2010) while cp23 is conserved among *C. parvum* isolates and found in both the sporozoites and merozoites (Mead, 2014). The cp15 vaccine given to pregnant goats provides protection to their offspring. The vaccination results in temporary *Cryptosporidium* levels reduction in vaccinated goats' stool samples. Goats that received vaccines showed reduced Cryptosporidium stool levels but did not achieve complete protection from infection (Roche et al., 2013). A multi-antigen vaccine shows better defensive effects against *Cryptosporidium* infection. Findings from a study revealed that the dual administration of the cp23 and cp15 vaccine enhanced the prepatent period and minimized oocyst shedding more effectively than the cp23 vaccine used in isolation during mouse experiments (Liu et al., 2010). Antibodies in the serum that responded to both cp23 and gp15 provided protection against diarrhea in individuals during a *Cryptosporidium* infection within their immune system (Riggs, 2002; Frost et al., 2005). An effective vaccine is required to satisfy three fundamental criteria: (1) it must provide lifelong protection to those who are vaccinated, (2) it should protect against all species and types of *Cryptosporidium* to prevent human infections from the predominant species, and (3) it must eliminate the transmission of *Cryptosporidium*. Studies have shown that serum antibodies that react to both cp23 and gp15 can prevent individuals from developing diarrhea during a *Cryptosporidium* infection (Ludington & Ward, 2015).

Conclusion and Future Perspectives

The water-borne parasite *Cryptosporidium* impacts human health globally and poses major public health threats to modern society. The illness spreads widely and creates many deaths among infected people. *Cryptosporidium* spreads everywhere and causes many infections between animals and people. Child patients under 5 years of age and people with weakened immune systems are the main groups at risk for *Cryptosporidium* infection. More animals now develop cryptosporidiosis from contaminated environments in farming operations. *Cryptosporidium* infection spreads when people consume water or food products polluted by sporulated oocysts. Most of the foodborne *Cryptosporidium* outbreaks come from spreading between animals and humans. Both routine disease monitoring and One Health practices must be used to stop health threats from occurring. Food protection measures plus water cleanliness training will help to stop next outbreaks from happening everywhere. Diagnostic tools have key weaknesses when it comes to identifying infections alone along with other parasites and their price range. Developing nations struggle to measure real cryptosporidiosis impacts because they lack effective diagnostic instruments which stops them from properly handling this disease. Our healthcare system requires faster and less expensive ways to identify crypto-related illnesses accurately. You can control the spread of *Cryptosporidium* by breaking down its transmission process to the sources, pathways, environment survival and infection risk factors. No pharmaceutical products exist for handling *Cryptosporidium* infections between humans and animals. New research is essential to create working vaccines to protect people and animals from this disease. Scientists require further investigation to create better ways of cleaning water supplies and swimming pools that protect against *Cryptosporidium* parasites.

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