Cryptosporidium Transmission Dynamics: Bridging the Gap between Wildlife and Urban Environments

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ABSTRACT

Cryptosporidium, a coccidian apicomplexan protozoan, causes cryptosporidiosis, a widespread intestinal infection in humans and animals through zoonotic and anthroponotic transmissions. This parasite exhibits a complex life cycle, with both sexual and asexual stages, adapting morphologically to complete its cycle. Cryptosporidium comprises various species infecting a multitude of hosts, including mammals, birds, reptiles, amphibians, and fish. Notable species like C. hominis and C. parvum are frequent causes of human cryptosporidiosis. The parasite's oocysts are highly resilient, remaining viable for months in various environments. Cryptosporidiosis manifests differently across hosts, leading to symptoms such as diarrhea, vomiting, and weight loss. Zoonotic potential exists, with transmission routes encompassing waterborne, foodborne, and direct contact. Wildlife serves as a reservoir for zoonotic pathogens, including Cryptosporidium, with potential transmission to humans. Urban environments, especially those with inadequate sanitation, may foster Cryptosporidium transmission through contaminated water, food, and direct contact with infected animals. Understanding transmission dynamics is crucial, especially in regions with high population density and potential outbreaks. Effective water treatment is pivotal for preventing waterborne cryptosporidiosis, highlighting the importance of maintaining and improving sanitation facilities in urban areas. Travelers to developing countries face elevated risks, emphasizing the need for public health measures to mitigate Cryptosporidium infections.

Keywords: Cryptosporidium, Cryptosporidiosis, Zoonotic transmission, Waterborne transmission, Urban environments

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1. INTRODUCTION

Cryptosporidium is one of the most common intestinal parasites (Shirley et al. 2012). It is coccidian, oocysts-forming apicomplexan protozoa, which completes their life cycle in humans and animals through zoonotic and anthroponotic transmissions and causing mild to severe disease (Putignani and Menichella 2010). One of the most significant illness that causes an intestinal infection in both humans and animals is cryptosporidiosis (Bamaiyi and Redhuan 2017). It was first discovered in 1907 by Tyzzer (Tzipori and Widmer 2008). At the start it was considered as nonpathogenic until two human cases of cryptosporidiosis were reported (Khalil et al. 2018). It has been stated that 60% of them were the most prevalent protozoan parasites responsible for food and waterborne disease outbreaks globally between 2004-2010. Animal become infected by ingesting contaminated food and water containing oocyst of parasite (Baldursson and Karanis 2011).

Cryptosporidium is a microscopic parasite that causes the diarrheal disease collectively (parasite and disease) called as "Crypto". From a variety of vertebrates, including humans, wildlife, mammals, domestic livestock, birds, reptiles, amphibians, and fish, a total of 23 species and 61 genotypes of *Cryptosporidium spp.* have been described (Ryan et al. 2014). *Cryptosporidium (C.) canis, C. meleagridis, C. suis, C. muris, C. andersoni*, and *C. felis* are few species that have been isolated from immunocompromised people (Fayer 2010) while *C. hominis, C. parvum*, and *C. meleagridis* are the three species of cryptosporidium that infect humans most frequently; however, these two species account for more than 90% of cases of cryptosporidiosis (Xiao and Ryan 2004).

It's fascinating to note that as of early 2013, 155 different species of mammals were known to be non-human sources of *C. parvum* (Slapeta 2013). This shows how these parasites are evolving and adapting to infect a variety of hosts and pose a serious threat to zoonotic diseases. Animal and human cases of cryptosporidiosis are frequently reported from a number of states, including Vietnam, Indonesia, Malaysia, Cambodia, Thailand, the Philippines, and Laos (Mahdy and Surin 2013). In Thailand, 11% river water and 6% ocean water has been contaminated with *Cryptosporidium spp.* (Koompapong and Sukthana 2012). However, some species (*C. parvum, C. muris, C. felis, C. meleagridis, C. hominis, C. canis*) have been isolated from HIV/AIDS cases in Bangkok (Srisuphanunt et al. 2011) with the prevalence rate of 19-34% from 1996-2009 (Berger 2017).

Although the prevalence of cryptosporidiosis is increasing in Europe due to climate change, such as heavy rains or floods that contaminate drinking water, the disease is also becoming more common among children and immune-compromised adults in many American countries, including Costa Rica, Brazil, Argentina, and the United States. However, *C. hominis* was found to be the most prevalent pathogen, and over time, reports of cryptosporidiosis have increased (Bamaiyi and Redhuan 2017). In Africa, cryptosporidium species are linked to severe diarrhea, mortality, and slow child growth. Additionally, the high frequency of the contagious disease in this region may be attributed to HIV/AIDS epidemic and the nutritional situation in some African regions (Squire and Ryan 2017).

Due to rising veterinary service and labor costs, cryptosporidiosis in livestock is becoming a serious issue for both animal health and financial losses (Santin 2013). Thailand's livestock previously had cryptosporidiosis rates of 31.5%, 5.7%, and 8.7% in dairy farms, individual animals, and dairy herds, respectively (Jittapalapong et al. 2016). Additionally, *C. parvum* was the most prevalent species in livestock animals, and 30% of buffalo farms had *Cryptosporidium spp.* infections (Inpankaew et al. 2014). It (cryptosporidiosis) was discovered in 2.1% of dogs and 2.5% of cats in other animals. There are about 1% of long-tailed macaques in Thailand that live in close proximity to people, but despite the low prevalence of oocysts, they pose a serious risk to humans (Sricharern et al. 2016).

2. CLASSIFICATION AND TAXONOMY

Domain: Eukaryota
Clade: Diaphoretickes
Clade: Alveolata
Phylum: Apicomplexa
Class: Conoidasida
Order: Eucoccidiorida
Suborder: Eimeriorina
Family: Cryptosporidiidae
Genus: *Cryptosporidium* (Chalmers et al. 2019).
Cryptosporidium has been found in a variety of animals and total 14 species seem to be most widely distributed that infect animals and humans. In the past, it was believed that *C. parvum* was the primary cause of infections in wild mammals (Xiao et al. 2004).

3. MORPHOLOGY AND LIFE CYCLE

Cryptosporidium has a complex life cycle having both sexual and asexual stages with monoxenous cycle but it changes to many morphological forms to complete its life cycle. It's life cycle begins when oocysts, or infective eggs, are ingested by a host. The oocysts can be found in contaminated water, food or feacal matter. Once inside the host, the oocysts release sporozoites, which then penetrate the host's intestinal lining and begin to reproduce asexually. During this phase, the parasite exists as a trophozoite, which is an active, feeding stage. The trophozoites multiply by binary fission, producing large numbers of meronts, which are specialized reproductive cells. These meronts then undergo further development to produce more oocysts, which are then shed in the host's faeces to start the cycle again. The oocysts of Cryptosporidium are highly resistant to environmental stressors and can remain viable for months in water, soil and other environments. This makes them highly effective at spreading the infection, as contaminated water or food can infect new hosts. When host ingest the infective oocyst; excystation occurs to release the four sporozoites (Fig. 1) (Bouzid et al. 2013).

The size of cryptosporidium oocysts is around 4-6μm and are rounded. Mature oocysts contain 4 sporozoites but no sporocyst. The sporozoites are spindle shaped and nucleated. The apical complex is the unique feature of apicomplexan parasites which mediates host penetration and attack. Intestine and stomach cells are among the host cells that sporozoites can recognize and enter (Fayer 2010). The sporozoites that have been invaded come from parasitephorous vacuoles, where they can develop into the trophozoite stage. The trophozoites initiate three merogoney-style mitotic divisions to produce type I meronts (Cacciò and Widmer 2013). It can produce type I (8 merozoites) or type II (4 merozoites) meronts through asexual reproduction. Microgamont (male) and macrogamont (female) are the sexually reproducing forms of type II merozoites. 16 rod-shaped, non-flagellated microgametes measuring 1.4 mm by 0.5 mm are produced by each microgamont. It get fertilized with a unicellular adjacent macrogamont, which is a spherical to oval structure with a large central nucleus and a diameter of 4-6 μm. After two mitosis divisions, the zygote either forms a thin-walled oocyst with a single layer of membrane or a thick-walled oocyst with two layers of membrane present. Contrary to thick-walled oocysts, which are released through faeces and can endure an unsuitable environment for months, thin-walled oocysts can cause reinfection with the gastrointestinal tract of the same host by rupturing and releasing infectious sporozoites (Tzipori and Ward 2002).
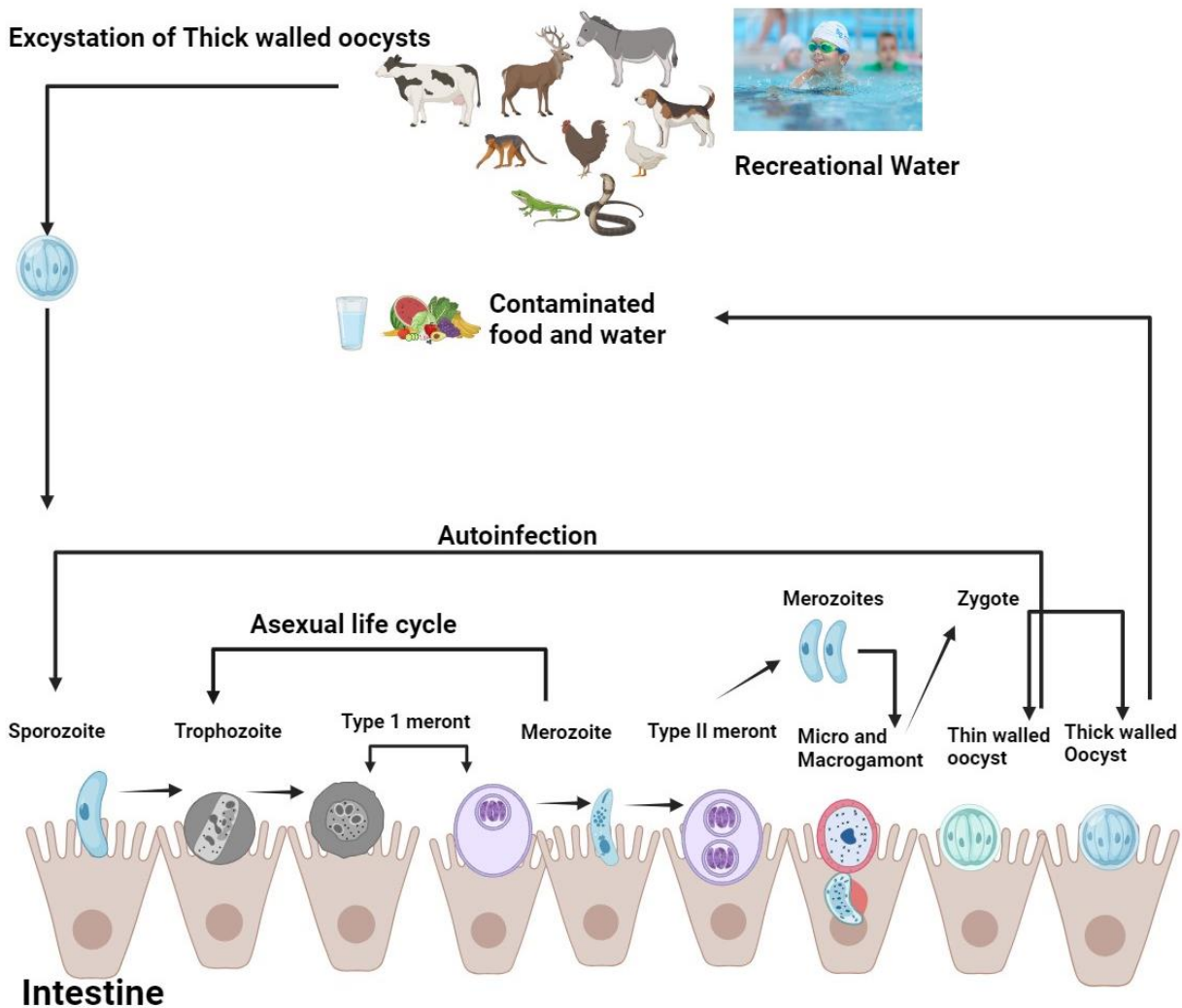
Fig. 1: Life cycle and development stages of Cryptosporidium in wildlife and humans

4. HOST ASSOCIATIONS OF CRYPTOSPORIDIUM/SYMPTOMS IN WILDLIFE

Cryptosporidium is a microscopic parasite that can infect a wide range of animals, including wildlife. The symptoms of cryptosporidium infection can vary depending on the severity of the infection and the species of animal affected. These are just a few examples of many host associations of Cryptosporidium. The parasite is widespread in the environment and can infect a wide variety of hosts, including both warm-blooded and cold-blooded animals. Host association refers to the relationship between a parasite and its host, which can range from a highly specific association to a broad range of hosts (Pinto and Vinayak 2021).

4.1. *CRYPTOSPORIDIUM ANDERSONI*

C. andersoni infects the digestive system of cattle and other ruminants. It is commonly found in the feaces of infected animals and can be transmitted through contaminated water or food. As a host-specific parasite, *C. andersoni* has a limited range of hosts that it can infect. Its main host is cattle but it

has also been found in other ruminants including sheep and goats. In cattle, its infection can cause diarrhea, weight loss and reduced feed intake. Calves are especially vulnerable to infection and in severe cases, the infection can lead to dehydration and death. Diarrhea caused by *C. andersoni* can be profuse and watery, often containing blood or mucus. Other symptoms of infection in cattle include abdominal pain, fever and decreased milk production in lactating cows (Jiang et al. 2014).

4.2. *CRYPTOSPORIDIUM BAILEYI*

C. baileyi infects birds particularly poultry and is a significant cause of respiratory and enteric diseases in these animals. It has been reported in a variety of domestic and wild bird species, including chickens, turkeys, ducks, geese, quails, pheasants, pigeons and sparrows. It is also commonly found in free-living waterfowl, such as ducks and geese and is a common cause of mortality in young waterfowl (Wang et al. 2011). The disease caused by *C. baileyi* infection is known as avian cryptosporidiosis. In birds, infection can cause diarrhea, weight loss and reduced egg production. The diarrhea caused by the infection can be watery and contain mucus or blood. Birds infected with this may also show signs of abdominal pain, decreased appetite and lethargy (Wang et al. 2021).

4.3. *CRYPTOSPORIDIUM CANIS*

C. canis infects wide range of host species, including dogs, cats and humans. The main host of this species is the domestic dog and the parasite is commonly found in puppies and young dogs that have not yet developed a strong immune system. However, *C. canis* has also been reported in other animals, including cats, pigs, cattle and horses. In dogs, *C. canis* infection cause diarrhea, vomiting and weight loss. The infection may also cause abdominal pain, decreased appetite and lethargy. In puppies, the infection can be severe and can lead to dehydration. *C. canis* infection can also be zoonotic in nature that can be transmitted from infected dogs to humans (Gonzalez-Díaz et al. 2016).

4.4. *CRYPTOSPORIDIUM FELIS*

C. felis infects cats and other feline species and the disease caused by *C. felis* is known as feline cryptosporidiosis. In cats, *C. felis* infection can cause diarrhea, vomiting and weight loss. Diarrhea can be watery and may contain blood and mucus. The infection may also cause abdominal pain, decreased appetite and lethargy. In kittens, the infection can be severe and can lead to dehydration. *C. felis* infection can also be zoonotic in nature (Fayer et al. 2006).

4.5. *CRYPTOSPORIDIUM HOMINIS*

C. hominis is common cause of cryptosporidiosis (a diarrheal disease) in humans. It can infect a variety of hosts, including livestock, wildlife and companion animals. Infection with *C. hominis* typically occurs through ingestion of contaminated water and food, and can cause symptoms such as diarrhea, stomach cramps and fever in humans. It is a common cause of diarrhea in both developing and developed countries especially in people with weak immune system such as those with HIV/AIDS or cancer. The infection can be more severe and prolonged. It can also lead to a more serious form of diarrhea known as chronic diarrhea which can cause malnutrition, weight loss and further complications. It can also be transmitted from infected humans to animals and vice versa. However, human-to-human transmission is the most common route of infection (Morgan-ryan et al. 2002).

4.6. *CRYPTOSPORIDIUM MELEAGRIDIS*

It primarily infects birds, including domestic turkeys and chickens, as well as wild birds such as pheasants and quail. It has also been found in other animals such as cattle and humans. Infection in birds can cause diarrhea and other digestive symptoms, while infection in humans can cause similar symptoms as well as other complications in individuals with weakened immune systems. Birds infected with *C. meleagridis* may also show signs of abdominal pain, decreased appetite and lethargy (Silverlås et al. 2012).

4.7. *CRYPTOSPORIDIUM MURIS*

C. muris infects rodents including mice and rats. In the case of *C. muris* the parasite has a relatively narrow host association, as it mainly infects rodents, but it has also been found in other animals such as pigs and humans. Infection in rodents may cause diarrhea which contains blood and mucus. Infection can occur through ingestion of contaminated food, water or direct contact with infected rodents or their faeces (Wang et al. 2023).

4.8. *CRYPTOSPORIDIUM NASORUM*

C. nasorum infects cattle, specifically affecting the nasal cavity and sinuses. In this case parasite has a narrow host association, as it primarily infects cattle and has not been found to infect other animal species or humans. Infection can cause symptoms such as nasal discharge and inflammation and can be transmitted through contact with contaminated materials, such as feed or water, or direct contact with infected animals (Appelbee et al. 2005).

4.9. *CRYPTOSPORIDIUM PARVUM*

C. parvum can infect a wide range of mammalian species, including humans and livestock. In the case of *C. parvum*, the parasite has a broad host association, as it can infect multiple animal species and is one of the most common causes of waterborne disease in humans (Delafosse et al. 2015). In wildlife, cryptosporidiosis can cause diarrhea, dehydration, weight loss, and lethargy. Animals may also show signs of abdominal pain and discomfort, decreased appetite and a rough or unkempt coat. In severe cases, the infection can lead to death. In some species, such as deer and elk, cryptosporidiosis may not cause any visible symptoms making it difficult to detect and control the spread of the disease (Davis et al. 2022).

4.10. *CRYPTOSPORIDIUM MOLNARI*

C. molnari infects fish specifically affecting the gastrointestinal tract. The parasite has a narrow host association as it primarily infects fish and has not been found to infect other animal species or humans. Infection can cause symptoms such as intestinal inflammation, diarrhea, difficulty swimming and can be transmitted through ingestion of contaminated water or infected fish (Couso-Perez et al. 2022).

4.11. *CRYPTOSPORIDIUM SAUROPHILIUM*

C. saurophilium infects reptiles, specifically affecting the gastrointestinal tract. In this case, parasite has a narrow host association, as it primarily infects reptiles. Infection can cause symptoms such as diarrhea, weight loss and lethargy. The diarrhea caused by the infection can be watery and may contain mucus or

blood. Infected reptiles may also show signs of abdominal pain, decreased appetite and difficult moving. The severity of the symptoms in wild reptiles may vary depending on the species (Appelbee et al. 2005).

4.12. *CRYPTOSPORIDIUM SERPENTIS*

C. serpentis infects gastrointestinal tract of snakes. This parasite has a narrow host association. Infection can cause symptoms such as diarrhea and weight loss. The diarrhea caused by the infection can be watery and may contain mucus or blood. Infected snakes may also show signs of abdominal pain, decreased appetite, and difficult moving (O'Rourke and Lertpiriyapong 2015).

4.13. *CRYPTOSPORIDIUM WRAIRI*

C. wrairi infects South American camelids such as llamas and alpacas, specifically affecting their gastrointestinal tract. Infection can cause symptoms such as diarrhea and can be transmitted through ingestion of contaminated food or water, or direct contact with infected South American camelids or their faeces. Infected mammals may also show signs of abdominal pain, decreased appetite, and difficult moving (Nazifi et al. 2010).

4.14. *CRYPTOSPORIDIUM GALLI*

C. galli mainly infects the birds. The parasite has a narrow host association. In birds, *C. galli* infection can cause diarrhea, weight loss and lethargy. Infected birds may also show signs of abdominal pain, decreased appetite, and difficult moving (Wang et al. 2021).

4.15. *CRYPTOSPORIDIUM SUIS*

C. suis infects pigs specifically affecting the gastrointestinal tract. Infection can cause symptoms such as diarrhea and weight loss. The diarrhea caused by the infection can be watery and contains mucus and blood. Infected pigs may also show signs of abdominal pain, decreased appetite and difficult moving. Young pigs, especially those less than three weeks old, are more susceptible to severe infection and may experience more severe symptoms and complications, such as dehydration and secondary bacterial infections (Bodager et al. 2015).

5. WILDLIFE AS A SOURCE OF ZOONOTIC INFECTIONS

Wildlife can serve as a reservoir for many zoonotic pathogens, including viruses, bacteria and parasites, which can be transmitted to humans through direct contact, consumption of contaminated food, water or through the bite of an infected animal. Some examples of zoonotic diseases that can be transmitted from wildlife to humans include (Kruse et al. 2004).

5.1. RABIES

Rabies is a viral infection that is transmitted to humans through the bite of an infected animal, such as a bat, raccoon or fox. Wildlife, particularly bats, are common reservoirs for the virus (Bilal 2021).

5.2. LYME DISEASE

Lyme disease is caused by a bacterium and transmitted to humans through the bite of an infected tick. Ticks can become infected by feeding on infected wildlife such as deer and rodents (Ogden et al. 2008).

5.3. HANTAVIRUS

Hantaviruses are a group of viruses transmitted to humans through contact with the urine, faeces or saliva of infected rodents. Deer and mice are a common reservoir for hantaviruses (Avsic-Zupanc et al. 2019).

5.4. AVIAN INFLUENZA

It is a viral infection that is mainly found in birds and it can be transferred to humans. Wild birds, such as waterfowl are a common reservoir for the virus (Kim et al. 2016).

5.5. CRYPTOSPORIDIOSIS

Cryptosporidiosis is a parasitic infection that is often associated with contaminated water sources, but can also be transmitted through contact with infected animals. Wildlife, such as deer and other ungulates are known to carry the parasite (Baldursson and Karanis 2011).
Wildlife can harbor Cryptosporidium in their digestive systems and shed the parasite in their faeces, which can contaminate the environment and potentially infect humans who come into contact with the contaminated material. This can happen through direct contact with wildlife i.e., when people handle or consume infected meat or indirect contact i.e., when contaminated water sources are used for drinking or recreational activities (Kruse et al. 2004).

6. UNDERSTANDING THE TRANSMISSION DYNAMICS FROM URBAN ENVIRONMENTS TO HUMANS

There are 31 species of cryptosporidium that have been recognized while *C. hominis* and *C. parvum* are most common species that cause infection in humans (Zahedi et al. 2016). Cryptosporidium is commonly found in urban environments, particularly in areas with inadequate sanitation and water treatment facilities. In urban environments, it can be transmitted through contaminated water, such as untreated or poorly treated drinking water, recreational water and wastewater. Contaminated water sources can become infected with Cryptosporidium when the parasite is shed by infected animals, including domestic livestock and wildlife, and then enters the water system. The manure from farms and runoff from urban areas can carry Cryptosporidium into rivers, lakes and groundwater sources, which can then contaminate drinking water supplies. It can also be transmitted through contaminated food, especially if the food has been grown or prepared in unsanitary conditions or comes into contact with contaminated water (Xiao et al. 2022).
In addition to water sources, Cryptosporidium can also be transmitted in urban environments through direct contact with infected animals, such as through exposure to their faeces or by ingesting contaminated food products. Because of high population density in urban areas and the potential for large outbreaks, it is important to ensure that urban water treatment facilities are properly designed and maintained to effectively remove or inactivate Cryptosporidium from drinking water supplies (Xiao et al. 2022). Cryptosporidium can be transmitted from animals to humans and person to person through the faeco-oral route. This can happen when an infected person doesn't wash their hands after using the bathroom and then comes into contact with another person or a surface that another person touches. This is particularly common in settings where animals are kept close to humans, such as farms or zoos. Travelers to developing countries are at a higher risk of Cryptosporidium infection due to poor sanitation and contaminated food and water sources (Ungar 2018). Table 1 shows the valid species of cryptosporidium, their hosts and reports in humans.

7. DIAGNOSIS AND DETECTION IN HUMANS

Accurate diagnosis of cryptosporidiosis is necessary to initiate appropriate treatment. Although the infection is self-limiting in healthy individuals, severe and prolonged symptoms can occur in those with HIV/AIDS or undergoing chemotherapy. Treatment with specific antimicrobial agents, such as nitazoxanide, can be effective in reducing the duration and severity of symptoms. Early diagnosis of an infected individual can help prevent further transmission. Cryptosporidiosis can be a significant cause of morbidity and mortality in certain populations, particularly in developing countries. Accurate diagnosis and monitoring of the incidence and prevalence of infection can help guide public health policies and interventions aimed at reducing the burden of disease (Smith 2007).

7.1. MICROSCOPY

The diagnosis of cryptosporidiosis can be made through microscopy, which involves visualizing the parasite in a stool sample. To diagnose cryptosporidiosis by microscopy, a fresh stool sample should be collected and processed using a concentration technique such as formalin-ethyl acetate sedimentation or zinc sulfate flotation. The concentrate is then examined under a microscope using a specialized staining method such as acid-fast staining, which allows the Cryptosporidium oocysts to be easily distinguished from other faecal particles (Smith 2007).

7.2. ELECTRON MICROSCOPY

Electron microscopy (EM) is a highly specialized and sensitive diagnostic tool that can be used in the diagnosis of Cryptosporidium infection. EM uses a beam of electrons to create highly magnified images of the specimen at a much higher resolution. This allows for the visualization of much smaller structures such as the internal structures of Cryptosporidium oocysts which cannot be seen with conventional light microscopy. EM is particularly useful for detecting low-level infections or for confirming the presence of Cryptosporidium in cases where other diagnostic tests such as acid-fast staining or immunological assays have produced ambiguous or inconclusive results (Ahmed and Karanis 2018).

To use EM for the diagnosis of Cryptosporidium, a stool sample is collected and processed using a concentration technique, such as formalin-ethyl acetate sedimentation or sucrose gradient centrifugation, to enrich the number of oocysts in the sample. The concentrated sample is then fixed in a chemical solution, such as glutaraldehyde to preserve the morphology of the oocysts. The fixed sample is then dehydrated, embedded in a resin and sliced into ultrathin sections, which are stained with heavy metals such as lead citrate and uranyl acetate to enhance contrast and create a detailed image of the oocysts. Under the EM Cryptosporidium oocysts appear as small, round to oval-shaped structures with a characteristic double-layered wall and internal structures are known as sporozoites (Khurana and Chaudhary 2018).

Although EM is a powerful diagnostic tool yet it is expensive and requires specialized equipment and expertise which makes it less widely available than other diagnostic methods. It is typically reserved for use in research or specialized diagnostic laboratories (Ahmed and Karanis 2018).

7.3. IMMUNOLOGICAL METHODS

Immunological methods are also used to diagnose Cryptosporidium infection particularly in cases where traditional microscopy techniques have produced ambiguous or inconclusive results. These methods rely on the detection of Cryptosporidium-specific antigens or antibodies in patient samples i.e., stool or serum.

Table 1: Valid species of cryptosporidium; hosts and reports in humans

Sr. #	Species Name	Author	Host type	Major Host	Reports in Humans
1.	*C. muris*	Tyzzer (1907, 1910)	Mice	Rodents	Numerous reports (Feng et al. 2011b)
2.	*C. wrairi*	Vetterling et al. (1971)	Guinea pig	Guinea pigs	None reported
3.	*C. felis*	Iseki (1979)	Cat	Cat	Many reports (Lucio-Forster et al. 2010)
4.	*C. serpentis*	Levine (1980)	Lizards, snakes	Lizards, snakes	None reported
5.	*C. meleagridis*	Slavin (1955)	Tuckey	Humans, birds	Commonly reported in humans
6.	*C. parvum*	Upton and Current (1985)	Cattle	Ruminants	Commonly reported in humans Tyzzer (1912)
7.	*C. baileyi*	Current et al. (1986)	Chicken	Birds	Not reported
8.	*C. varanii*	Pavlasek et al. (1995)	Lizards	Lizards	Not reported
9.	*C. andersoni*	Lindsay et al. (2000)	Cattle	Cattle	Leoni et al. (2006); Morse et al. (2007); Waldron et al. (2011); Agholi et al. (2013); Liu et al. (2014)
10.	*C. canis*	Fayer et al. (2001)	Dog	Dogs	Many reports (Lucio-Forster et al. 2010)
11.	*C. molnari*	Alvarez-Pellitero and Sitja-Bobadilla (2002)	Fish	Fish	Not reported
12.	*C. hominis*	Morgan-ryan et al. (2002)	Humans	Humans	Most common species in humans
13.	*C. galli*	Re: Ryan et al. (2003c): Pavlásek (1999) a	Birds	Birds	None reported
14.	*C. suis*	Ryan et al. (2004)	Pig	Pigs	Xiao et al. (2002a); Leoni et al. (2006); Cama et al. (2007); Wang et al. (2013)
15.	*C. bovis*	Fayer et al. (2005)	*Cattle*	Cattle	Khan et al. (2010); Ng et al. (2012); Helmy et al. (2013)
16.	*C. xiaoi*	Fayer et al. (2010)	Sheep	Sheep	Adamu et al. (2014)
17.	*C. ryanae*	Fayer et al. (2008)	Cattle	Cattle	Not reported
18.	*C. macropodum*	Power and Ryan (2008)	Kangaroo	Marsupial	None reported
19.	*C. fragile*	Jirku et al. (2008)	Toad	Toads	None reported
20.	*C. fayeri*	Ryan et al. (2008)	Kangaroo	Marsupial	Waldron et al. (2010)
21.	*C. ubiquitum*	Fayer et al. (2010)	Cattle	Rodents, ruminants and rodents	Commonly reported (Fayer et al. 2010; Elwin et al. 2012a)
22.	*C. cuniculus*	Re: Robinson et al. (2010)	European rabbit	Rabbits	Chalmers et al. (2009a); Anonymous (2010); Chalmers et al. (2011a)
23.	*C. tyzzeri*	Ren et al. (2012)	Mouse	Rodents	Raskova et al. (2013)
24.	*C. erinacei*	Kvac et al. (2014b)	European hedgehog..	Hedgehogs	Insulander et al. (2013)
25.	*C. scrofarum*	Kvac et al. (2013b)	Pig	Pigs	Kvac et al. (2009a); Kvac et al. (2009b)
26.	*C. viatorum*	Elwin et al. (2012b)	Humans	Humans	Insulander et al. (2013)

(Ryan et al. 2014)

The two main types of immunological methods used to diagnose Cryptosporidium are enzyme-linked immunosorbent assays (ELISAs) and immunofluorescence assays (IFAs) (Chalmers et al. 2011).

ELISAs are based on the binding of Cryptosporidium-specific antibodies to antigenic proteins or enzymes, which produce a colorimetric signal when an appropriate substrate is added. Several commercially available ELISA kits are available for the detection of cryptosporidium antigens in stool samples including the Meridian Bioscience Crypto-Giardia Rapid Test and the TechLab Cryptosporidium Antigen ELISA. These tests are highly sensitive and specific with a reported sensitivity of up to 98% and specificity of up to 99% (Kang et al. 2008).

IFAs are based on the binding of fluorescently labeled Cryptosporidium-specific antibodies to antigenic proteins on the surface of Cryptosporidium oocysts. The labeled antibodies produce a fluorescent signal when exposed to specific wavelengths of light allowing for the visualization of the oocysts under a fluorescence microscope. IFAs can be performed on a range of patient samples including stool, tissue and environmental samples and are highly sensitive and specific with a reported sensitivity of up to 99% and specificity of up to 100%. Both ELISAs and IFAs are rapid, highly sensitive and specific methods for the diagnosis of Cryptosporidium infection. However, these require specialized equipment and expertise and are not always readily available in all clinical or laboratory settings (Chan et al. 2000).

7.4. HISTOLOGY

Histology specifically the staining of tissue samples with special stains can be used to diagnose Cryptosporidium infection in humans. However, it is not commonly used in clinical settings due to the invasive nature of obtaining tissue samples and the availability of other non-invasive diagnostic methods such as stool microscopy, antigen detection and PCR. In cases where a tissue biopsy is obtained, Cryptosporidium infection can be diagnosed through histological examination of stained tissue sections. Hematoxylin and eosin (H&E) staining can be used to visualize the characteristic oocysts of Cryptosporidium, which are round or oval structures with a distinctive pale blue, refractile appearance. However, H & E staining alone may not provide a definitive diagnosis as other parasites or artifacts may resemble Cryptosporidium oocysts (Fayer et al. 2000).

Additional staining methods, such as modified acid-fast stains or immune-histochemical stains, may be used to improve the specificity of the diagnosis. Modified acid-fast stains, such as the Kinyoun or modified Ziehl-Neelsen stain, use a combination of acid-fast and counterstains to selectively stain Cryptosporidium oocysts. Immuno-histochemical staining uses specific antibodies to target Cryptosporidium antigens in tissue sections and can provide a more definitive diagnosis of Cryptosporidium infection (Fayer et al. 2000).

8. TREATMENTS

Recent studies have highlighted the importance of cryptosporidium as a factor in both morbidity and mortality associated with childhood diarrhea but, the progress in the treatment is very slow. In young children, cryptosporidium causes severe diarrhea (Kotloff et al. 2013), malabsorption, intestinal injury, excess mortality and stunting that is associated with malnutrition (Korpe et al. 2016) and its drugs are desperately needed (Striepen 2013). Although nitazoxanide is approved for the treatment of cryptosporidiosis, it is not better than a placebo in immunocompromised patients living with HIV and cryptosporidiosis (Amadi et al. 2009). Clofazimine (CFZ) which has been used to treat leprosy for over 50 years and is now used to treat multidrug-resistant tuberculosis (TB). It was recently shown to be effective against cryptosporidium in vitro (Love et al. 2017).

Fluid and electrolyte replacement are crucial in the treatment of cryptosporidiosis in addition to symptomatic therapy. Anti-motility medications are another crucial component of treatment. Narcotic substances are also used in majority of patients. According to literature, opium tincture (paregoric) may be more effective for AIDS patients. Because cryptosporidiosis is typically self-limiting in immunocompromised hosts, immune reconstruction in response to effective combination antiretroviral therapy has been linked to positive clearance as well as decreased long-term morbidity and mortality associated with the disease in AIDS patients (Masur et al. 2014). Nevertheless, chronic diarrhea is lined to a higher risk of passing away even when receiving effective antiretroviral therapy (Dillingham et al. 2009). According to earlier studies, using anti-motility and anti-parasitic medications as part of initial treatment has been linked to better outcomes (Masur et al. 2014), but there is no conclusive proof of this. Unexpectedly, some HIV protease inhibitors have activity against cryptosporidium both in vivo and in vitro (Mele et al. 2003)

9. PREVENTION AND CONTROL

As there are few effective treatments for cryptosporidiosis, prevention and risk reduction are the most crucial interventions (Rossignol 2009). Due to the high number of excreted oocysts and low infection dose, cryptosporidiosis is highly contagious and requires strict personal hygiene. The guidelines for preventing person-to-person transmission must be followed (Anon 2004). These include frequently washing your hands, disposing of excreta properly and washing soiled items like bedding and clothing. For 48 hours following the last episode of diarrhea, individuals with cryptosporidiosis should avoid being around food handlers and staff at healthcare facilities (Anon 2004). Washing hands before and after handling animals, properly treating non-potable water and washing product before eating are all general precautions against cryptosporidium infection. On open farms, handwashing facilities should be accessible and used. To properly rehydrate, it might be necessary to consume boiled water and use salts. To eliminate any potential Cryptosporidium contamination, avoid touching human or animal waste, dispose it properly, and thoroughly cook meat, poultry or fish. Infections can be severe and difficult to treat in the high-risk immune-suppressed populations that were previously mentioned. Although the goal of treatment is to lessen symptoms, eliminating the parasites won't be possible unless the underlying immune deficiency is addressed. One alternative measure is to use the appropriate point-of-use filters to remove the cryptosporidium oocysts (Hunter and Nichols 2002).

10. CONCLUSION

Cryptosporidiosis is in the list of top 10 food and water borne diseases which cause severe diarrhea in humans as well as in animals. Faeco–oral transmission of the oocyst stage has resulted in outbreaks through contamination of drinking water, food and recreational water. As cryptosporidium is a zoonotic protozoan parasite it can be transmitted from wild and domestic animals to humans. Immunocompromised people and children are more susceptible to cryptosporidiosis. Currently 26 species and genotypes are recognized from which *C. hominis* and *C. parvum* cause infections in humans. Cattle is one of the most significant reservoirs for zoonotic infections in livestock. Numerous Cryptosporidium species or genotypes that have a limited host range and therefore have no significant public health implications can infect both domesticated and wild animals. Microscopy, immunological, and molecular techniques for oocyst detection and identification are all constantly improving.

REFERENCES

Adamu H et al., 2014. Distribution and clinical manifestations of Cryptosporidium species and subtypes in HIV/AIDS patients in Ethiopia. PLOS Neglected Tropical Diseases 8: e2831.

Agholi M et al., 2013. HIV/AIDS associated opportunistic protozoal diarrhea. AIDS Research and Human Retroviruses 29: 35-41.

Ahmed SA and Karanis P, 2018. Comparison of current methods used to detect Cryptosporidium oocysts in stools. International Journal of Hygiene and Environmental Health 221: 743-763.

Amadi B et al., 2002. Effect of nitazoxanide on morbidity and mortality in Zambian children with cryptosporidiosis: a randomised controlled trial. The Lancet 360: 1375-1380.

Amadi B et al., 2009. High dose prolonged treatment with nitazoxanide is not effective for cryptosporidiosis in HIV positive Zambian children: a randomised controlled trial. BMC Infectious Diseases 9: 1-7.

Anon, 2004. Preventing person-to-person spread following gastrointestinal infections: guidelines for public health physicians and environmental health officers. Prepared by a Working Group of the former PHLS Advisory Committee on gastrointestinal infections. Journal of Infection and Public Health 7: 362-384.

Anonymous, 2010. Annual epidemiological report on communicable diseases in Europe, revised edition 2009. European Center for Disease Prevention and Control.

Appelbee AJ et al., 2005. Giardia and Cryptosporidium in mammalian wildlife–current status and future needs. Trends in Parasitology 21: 370-376.

Avsic-Zupanc T et al., 2019. Hantavirus infections. Clinical Microbiology and Infection 21: e6-e16.

Baldursson S and P Karanis, 2011. Waterborne transmission of protozoan parasites: review of worldwide outbreaks–an update 2004-2010. Water Resources 45: 6603-6614.

Bamaiyi PH and NEM Redhuan, 2017. Prevalence and risk factors for cryptosporidiosis: a global, emerging, neglected zoonosis. Asian Biomedicine 10: 309-325.

Berger S, 2017. Infectious Diseases of Thailand: 2017 Edition. GIDEON Informatics Incorporated.

Bhadauria D et al., 2015. Cryptosporidium infection after renal transplantation in an endemic area. Transplant Infectious Disease 17: 48-55.

Bilal A, 2021. Rabies is a zoonotic disease: a literature review. Occupational. Medicine and Health Affairs 9.

Bodager JR et al., 2015. Complex epidemiology and zoonotic potential for Cryptosporidium suis in rural Madagascar. Veterinary Parasitology 207: 140-143.

Bouzid M et al., 2013. Cryptosporidium pathogenicity and virulence. Clinical Microbiology Reviews 26: 115-134.

Burdese M et al., 2005. A dance teacher with kidney-pancreas transplant and diarrhoea: what is the cause? Nephrology Dialysis Transplantation 20: 1759-1761.

Cabada MM and White Jr AC, 2010. Treatment of cryptosporidiosis: do we know what we think we know? Current Opinions in infectious Diseases 23: 494-499.

Cacciò SM and Widmer G, 2013. Cryptosporidium: parasite and disease, Springer Science & Business Media.

Cama VA et al., 2007. Differences in clinical manifestations among Cryptosporidium species and subtypes in HIV-infected persons. Journal of Infectious Diseases 196: 684-691.

Caravedo MA and White AC, 2023. Treatment of cryptosporidiosis: nitazoxanide yes, but we can do better. Expert Review of Anti-infective Therapy 2023.

Chalmers R M et al., 2019. Cryptosporidium. Microbiology 165: 500-502.

Chalmers RM et al., 2009a. Long-term Cryptosporidium typing reveals the aetiology and species-specific epidemiology of human cryptosporidiosis in England and Wales, 2000 to 2003. Euro Surveillance 14: 19086

Chalmers RM et al., 2011. Comparison of diagnostic sensitivity and specificity of seven Cryptosporidium assays used in the UK. Journal of Medical Microbiology 60: 1598-1604.

Chalmers RM et al., 2011a. Epidemiology of anthroponotic and zoonotic human cryptosporidiosis in England and Wales, 2004-2006. Epidemiology Infection 139: 700-712.

Chan R et al., 2000. Evaluation of a combination rapid immunoassay for detection of Giardia and Cryptosporidium antigens. Journal of Clinical Microbiology 38: 393-394.

Couso-Perez S et al., 2022. A review of the current status of Cryptosporidium in fish. Parasitology 2022: 1-45.

Davis MK et al., 2022. Cryptosporidium parvum outbreak associated with Raccoons at a Wildlife Facility-Virginia, May-June 2019. Zoonoses and Public Health 69: 248-253.

Delafosse A et al., 2015. *Cryptosporidium parvum* infection and associated risk factors in dairy calves in western France. Preventive Veterinary Medicine 118: 406-412.

Dillingham RA et al., 2009. High early mortality in patients with chronic acquired immunodeficiency syndrome diarrhea initiating antiretroviral therapy in Haiti: a case-control study. American Journal of Tropical Medicine Hygiene 80: 1060.

Elwin K et al., 2012a. The epidemiology of sporadic human infections with unusual cryptosporidial detected during routine typing in England and Wales, 2000-2008. Epidemiology Infection 140: 673-683.

Fayer R and Xiao L, 2007. Cryptosporidium and cryptosporidiosis, CRC press.

Fayer R et al., 2000. Epidemiology of Cryptosporidium: transmission, detection and identification. International Journal for Parasitology 30: 1305-1322.

Fayer R et al., 2001. *Cryptosporidium canis* n. sp. from domestic dogs. Journal of Parasitology 87: 1415-1422.

Fayer R et al., 2006. Detection of *Cryptosporidium felis* and *Giardia duodenalis* Assemblage F in a cat colony. Veterinary Parasitology 140: 44-53.

Fayer R et al., 2010. *Cryptosporidium ubiquitum* n. sp. in animals and humans. Veterinary Parasitology 172: 23-32.

Fayer R, 2010. Taxonomy and species delimitation in Cryptosporidium. Experimental Parasitology 124: 90-97.

Feng Y et al., 2011b. Development of a multilocus sequence tool for typing *Cryptosporidium muris* and *Cryptosporidium andersoni*. Journal of Clinical Microbiology 49: 34-41.

Fichtenbaum CJ et al., 2000. Rifabutin but not clarithromycin prevents cryptosporidiosis in persons with advanced HIV infection. AIDS 14: 2889-2893.

Giacometti A et al., 2000. Activity of nitazoxanide alone and in combination with azithromycin and rifabutin against *Cryptosporidium parvum* in cell culture. Journal of Antimicrobial Chemother*apy* 45: 453-456.

Gonzalez-Díaz M et al., 2016. *Cryptosporidium canis* in two Mexican toddlers. Journal of Pediatric Infectious Diseases 35: 1265-1266.

Helmy YA et al., 2013. Molecular epidemiology of Cryptosporidium in livestock animals and humans in the Ismailia province of Egypt. Veterinary Parasitology 193: 15-24.

Hewitt RG et al., 2000. Paromomycin: no more effective than placebo for treatment of cryptosporidiosis in patients with advanced human immunodeficiency virus infection. Clinical Infection Disease 31: 1084-1092.

Hunter PR and Nichols G, 2002. Epidemiology and clinical features of Cryptosporidium infection in immunocompromised patients. Clinical Microbiology Reviews 15: 145-154.

Hussien SM et al., 2013. Comparative study between the effect of nitazoxanide and paromomycine in treatment of cryptosporidiosis in hospitalized children. Journal of Egyptian Society of Parasitology 43: 463-470.

Inpankaew T et al., 2014. Molecular detection of Cryptosporidium spp. infections in water buffaloes from northeast Thailand. Tropical Animal Health and Production 46: 487-490.

Insulander M et al., 2013. Molecular epidemiology and clinical manifestations of human cryptosporidiosis in Sweden. Epidemiological Infection 141: 1009-1020

Jiang Y et al., 2014. Cryptosporidium andersoni as a novel predominant Cryptosporidium species in outpatients with diarrhea in Jiangsu Province, China. BMC Infectious Diseases 14: 1-6.

Jittapalapong S et al., 2006. Prevalence of Cryptosporidium among dairy cows in Thailand. Annals of the New York Academy of Sciences 1081: 328-335.

Kang CD et al., 2008. Surface plasmon resonance-based inhibition assay for real-time detection of Cryptosporidium parvum oocyst. Water Research 42 :1693-1699.

Karanis P et al., 2007. Waterborne transmission of protozoan parasites: a worldwide review of outbreaks and lessons learnt. Journal of Water Health 5: 1-38.

Khalil IA et al., 2018. Morbidity, mortality, and long-term consequences associated with diarrhoea from Cryptosporidium infection in children younger than 5 years: a meta-analyses study. Lancet Global Health 6: e758-e768.

Khan SM et al., 2010. Molecular characterization and assessment of zoonotic transmission of Cryptosporidium from dairy cattle in West Bengal, India. Veterinary Parasitology 171: 41-47.

Khurana S and Chaudhary P, 2018. Laboratory diagnosis of cryptosporidiosis. Tropical Parasitology 8: 2.

Khurana S et al., 2012. Evaluation of Ziehl-Neelsen staining, auramine phenol staining, antigen detection enzyme linked immunosorbent assay and polymerase chain reaction, for the diagnosis of intestinal cryptosporidiosis. Tropical Parasitology 2: 20.

Kim SM et al., 2016. Avian influenza A viruses: evolution and zoonotic infection. In Seminars in Respiratory and Critical Care Medicine. Thieme Medical Publishers 37: 501-511.

Kjos SA et., 2005. Evaluation of recombinant oocyst protein CP41 for detection of Cryptosporidium-specific antibodies. Clinical Vaccine Immunology 12: 268-272.

Koompapong K and Sukthana Y, 2012. Seasonal variation and potential sources of *Cryptosporidium* contamination in surface waters of Chao Phraya River and Bang Pu nature reserve pier, Thailand. Southeast Asian Journal Tropical Medicine and Public Health 43: 832-840.

Korpe PS et al., 2016. Natural history of cryptosporidiosis in a longitudinal study of slum-dwelling Bangladeshi children: association with severe malnutrition. PLOS Neglected Tropical Diseases 10: e0004564.

Kotloff KL et al., 2013. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. The Lancet 382: 209-222.

Krause I et al., 2012. Cryptosporidiosis in children following solid organ transplantation. Journal of Pediatric Infectious Diseases 31: 1135-1138.

Kruse H et al., 2004. Wildlife as source of zoonotic infections. Emerging Infectious Diseases 10 :2067.

Kvac M et al., 2009a. Prevalence and age-related infection of *Cryptosporidium suis*, *C. muris* and Cryptosporidium pig genotype II in pigs on a farm complex in the Czech Republic. Veterinary Parasitology 160: 319-322.

Kvac M et al., 2009b. Cryptosporidium pig genotype II in immunocompetent man. Emerging Infectious Diseases 15: 982-983.

Legrand F et al., 2011. Diagnosis and treatment of digestive cryptosporidiosis in allogeneic haematopoietic stem cell transplant recipients: a prospective single centre study. Bone Marrow Transplant 46: 858-862.

Leoni F et al., 2006. Genetic analysis of Cryptosporidium from 2414 humans with diarrhoea in England between 1985 and 2000. Journal Medical Microbiology 55: 703-707.

Lim YA et al., 2013. Unravelling Cryptosporidium and Giardia in Southeast Asia. Parasites and their vectors: A special focus on Southeast Asia 2013: 77-102.

Liu H et al., 2014. Prevalence and genetic characterization of Cryptosporidium, Enterocytozoon, Giardia and Cyclospora in diarrheal outpatients in China. BMC Infectious Diseases 14: 25.

Love MS et al., 2017. A high-throughput phenotypic screen identifies clofazimine as a potential treatment for cryptosporidiosis. PLOS Neglected Tropical Diseases 11: e0005373.

Lucio-Forster A et al., 2010. Minimal zoonotic risk of cryptosporidiosis from pet dogs and cats. Trends in Parasitology 26: 174-179.

Masur H et al., 2014. Prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Updated Guidelines from the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America. Clinical Infectious Diseases 58: 1308-1311.

Mele R et al., 2003. Indinavir reduces Cryptosporidium parvum infection in both in vitro and in vivo models. International Journal of Parasitology 33: 757-764.

Morgan-ryan UM et al., 2002. *Cryptosporidium hominis* n. sp. (Apicomplexa: Cryptosporidiidae) from *Homo sapiens*. Journal of Eukaryotic Microbiology 49: 433-440.

Morse TD et al., 2007. Incidence of cryptosporidiosis species in paediatric patients in Malawi. Epidemiological Infections 135: 1307-1315

Nazifi S et al., 2010. Prevalence of Cryptosporidium isolated from dromedary camels (*Camelus dromedarius*) in Qeshm Island, Southern Iran. Comparative Clinical Pathology 19 :311-314.

Ng JS et al., 2012. Evidence of Cryptosporidium transmission between cattle and humans in northern New South Wales. Experimental Parasitology 130: 437-441.

O'Rourke DP and Lertpiriyapong K, 2015. Biology and diseases of reptiles. In: Fox JG, Anderson LC, Loew FM, Quimby FW, editors. Laboratory Animal Medicine: Academic Press; pp: 967-1013.

Ogden NH et al., 2008. Lyme disease: a zoonotic disease of increasing importance to Canadians. Canadian Family Physician 54: 1381-1384.

Pinto DJ Vinayak S, 2021. Cryptosporidium: host-parasite interactions and pathogenesis. Current Clinical Microbiology Reports 8: 62-67.

Priest JW et al., 2006. Longitudinal analysis of Cryptosporidium species-specific immunoglobulin G antibody responses in Peruvian children. Clinical and Vaccine Immunology 13: 123-131.

Putignani L and Menichella D. 2010. Global distribution, public health and clinical impact of the protozoan pathogen Cryptosporidium. Interdisciplinary Perspective on Infectious Diseases 2010.

Raja K et al., 2014. Prevalence of cryptosporidiosis in renal transplant recipients presenting with acute diarrhea at a single center in Pakistan. Journal of Nephropathology 3: 127.

Raskova V et al., 2013. Human cryptosporidiosis caused by *Cryptosporidium tyzzeri* and *C. parvum* isolates presumably transmitted from wild mice. Journal of Clinical Microbiology 51: 360-362.

Rossignol JF et al., 2006. Effect of nitazoxanide in diarrhea and enteritis caused by Cryptosporidium species. Clinical Gastroenterology and Hepato*logy* 4: 320-324.

Rossignol JF, 2010. Cryptosporidium and Giardia: treatment options and prospects for new drugs. Experimental Parasitology 124: 45-53.

Rossignol JFA et al., 2001. Treatment of diarrhea caused by Cryptosporidium parvum: a prospective randomized, double-blind, placebo-controlled study of nitazoxanide. Journal of infectious Diseases 184: 103-106.

Ryan UNA et al., 2014. Cryptosporidium species in humans and animals: current understanding and research needs. Parasitology 141: 1667-1685.

Shirley DAT et al., 2012. Burden of disease from cryptosporidiosis. Current Opinion in Infectious Disease*s* 25: 555.

Silverlås C et al., 2012. Zoonotic transmission of Cryptosporidium meleagridis on an organic Swedish farm. International Journal of Parasitology 42: 963-967.

Slapeta J, 2013. Cryptosporidiosis and Cryptosporidium species in animals and humans: a thirty colour rainbow? International Journal of Parasitology 43: 957-970.

Squire SA and Ryan U, 2017. Cryptosporidium and Giardia in Africa: current and future challenges. Parasites and Vectors 10: 1-32.

Sricharern W et al., 2016. Molecular detection and prevalence of Giardia duodenalis and Cryptosporidium spp. among long-tailed macaques (*Macaca fascicularis*) in Thailand. Infection, Genetics and Evolution 40: 310-314.

Srisuphanunt M et al., 2011. Prevalence and genotyping of Cryptosporidium isolated from HIV/AIDS patients in urban areas of Thailand. Annals of Tropical Medicine and Parasitology 105: 463-468.

Striepen B, 2013. Parasitic infections: time to tackle cryptosporidiosis. Nature 503: 189-191.

Tzipori S and Ward H, 2002. Cryptosporidiosis: biology, pathogenesis and disease. Microbes Infection 4: 1047-1058.

Tzipori S and Widmer G, 2008. A hundred-year retrospective on cryptosporidiosis. Trends in Parasitology 24: 184-189.

Ungar BL, 2018. Cryptosporidiosis in humans (*Homo sapiens*). In: Dubey JP, Speer CA, Fayer R, editors. Cryptosporidiosis of man and animals: CRC Press; pp: 59-82.

Waldron LS et al., 2010. Wildlife-associated *Cryptosporidium fayeri* in humans, Australia. Emerging Infectious Disease 16: 2006–2007.

Waldron LS et al., 2011. Molecular epidemiology, spatiotemporal analysis, and ecology of sporadic human cryptosporidiosis in Australia. Applied Environmental Microbiology 77: 7757-7765.

Wang L et al., 2013. Zoonotic Cryptosporidium species and *Enterocytozoon bieneusi* genotypes in HIV-positive patients on antiretroviral therapy. Journal of Clinical Microbiology 51: 557-63.

Wang L et al., 2023. Microbiome-Metabolomics Analysis of the Impacts of *Cryptosporidium muris* Infection in BALB/C Mice. Microbiology Spectrum 11: e02175-22.

Wang R et al., 2011. Prevalence of *Cryptosporidium baileyi* in ostriches (*Struthio camelus*) in Zhengzhou, China. Veterinary Parasitology 175: 151-154.

Wang Y et al., 2021. Cryptosporidium and cryptosporidiosis in wild birds: A One Health perspective. Parasitology Research 120: 3035-3044.

Weitzel T et al., 2006. Evaluation of seven commercial antigen detection tests for Giardia and Cryptosporidium in stool samples. Clinical Microbiology and Infection 12: 656-659.

Xiao D et al., 2022. Tracking Cryptosporidium in urban wastewater treatment plants in a cold region: Occurrence, species and infectivity. Frontiers in Environmental Science and Engineering 16: 12.

Xiao L and Ryan UM, 2004. Cryptosporidiosis: an update in molecular epidemiology. Current Opinion in Infectious Disease 17: 483-490.

Xiao L et al., 2004. Cryptosporidium taxonomy: recent advances and implications for public health. Clinical Microbiology Reviews 17: 72-97.

Xiao L, 2011a. Characteristics of Cryptosporidium transmission in preweaned dairy cattle in Henan, China. Journal of Clinical Microbiology 49: 1077-1082.

Zahedi A et al., 2016. Public health significance of zoonotic Cryptosporidium species in wildlife: critical insights into better drinking water management. International Journal of Parasitology: Parasites and Wildlife 5: 88-109.