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Cryptosporidium parvum: is it invincible?

Caitlin Wonnacott, Mississippi State University

Abstract. *Cryptosporidium* is a coccidian protozoan parasite that can affect mammals, reptiles, and birds. A coccidian is a single-celled protozoan that affects the epithelial lining of the intestinal walls of hosts it parasitizes. This parasite has a unique life cycle and can withstand common measures of sterilization. The infective oocyte stage is resistant and hardy. It takes on two forms where each goes to different places within the host. Contamination of water sources has led to large outbreaks of cryptosporidiosis, even though the water met and passed the standards for drinking water. Conclusions from previous studies will help lead the way for new questions to emerge and addressed. This small organism defies simple preventative measures and is increasingly being diagnosed and treated.

Keywords: One Health, *Cryptospiridium parvum*

Background

Throughout history, people and animals have been plagued by an abundance of diseases which come and go. They vary from era to era, country to country, person to person, and severity to severity. Some cause mass panic and fear while others seem unassuming since they are rampant everywhere. Some are prevented with vaccines and some have no known treatment. Every pathogen has its own unique characteristics and one of the many is *Cryptosporidium,* a coccidian protozoan parasite that can affect mammals, reptiles, and birds. A coccidian is a single-celled protozoan that affects the epithelial lining of the intestinal walls of animals and humans (O'Donoghue 1995). It was discovered in laboratory mice in 1912 by Ernest Edward Tyzzer (1875-1965) who was a physician and a parasitologist.

Cryptosporidium spp. attach to the walls of the intestines and absorbs nutrients the body would normally retain. This in turn causes a diarrheal illness that might last for a couple weeks. There are nearly 30 known species of *Cryptosporidium* that affect different animal hosts based on molecular studies. This includes two species and genotypes that can harm humans, *Cryptosporidium hominis* and *Cryptosporidium parvum*.

Introduction

Cryptosporidium parvum can infect humans and cattle. The first cases were in 1976 but it wasn't officially named and recognized until 1982. This is an illness that lasts anywhere from three to twenty days within healthy individuals. However, the illness lasts longer and has increased severity in immunocompromised people. The official term for this pathogen is an enteropathogen: that is, a microorganism that causes disease of the intestines (Current 1994). This organism can be transmitted through food, water, and direct contact. Its primary route of transmission is fecal-oral. It is known to cause spontaneous outbreaks and it is prevalent especially after high rain which creates fecal contaminated run-off carried into waterways. Contamination of water sources has led to large outbreaks of *cryptosporidiosis*, even though the water met and passed the standards for drinking water (DuPont 1995). Many studies have been conducted to determine the biologic makeup and genetics of *C. parvum.* This information is then processed to help come up with methods for treatment and prevention.

Epidemiology

Cryptosporidiosis is prevalent in all countries that have water that is used for bathing or drinking. It is prevalent at a rate of 1%-3% in Europe and North America, but is 5% in Asia and 10% in Africa (Current 1994). The higher rates of prevalence in Africa and Asia are due to lack of clean drinking water and prevalence of immune deficient people, especially children. These countries are also less industrialized and more rural. Healthy individuals with Cryptosporidiosis will exhibit watery diarrhea for approximately two weeks with occasional bouts of lingering symptoms. However, immunocompromised people are affected more severely. This category includes children, elderly, and people with pre-existing health problems such as being HIV positive, and people taking chemotherapy. These people have a higher mortality rate than healthy individuals. However, infectivity is widespread and it happens when the oocysts are released in feces where they become infective immediately. The oocyst is a thick walled ovum that is infectious and transmission is by ingesting the infective oocyst. This coccidian parasite then attaches itself to the intestines of its host. It can happen at anytime and anywhere there are animals and water. Infection is more likely to occur after rain because of the run off. Signs and symptoms become apparent approximately two to ten days after the ingestion of contaminated water or food. Treatment is palliative meaning supportive care which includes fluids to treat dehydration and medications to help control diarrhea and pain. The illness will last approximately a couple weeks in previously healthy people. People who are immunocompromised have more severe cases. This means that the symptoms are present longer, the length of the illness is longer, and the chance of death is higher. People where there was a recurrence have milder cases of it. However, the recurrence of the pathogen occurs in people who had a larger dose of oocysts. Preventive measures include updating water treatment systems, always washing your hands and practicing proper hygiene and sewage disposal. Furthermore, if traveling overseas to a developing country with poor water quality, be sure to not drink that water. The risk of cryptosporidiosis in people and countries is global. It occurs because it resists common means of sanitation and can survive in cold, moist environments for months. People who are infected multiple times usually develop protective immunity against the parasite. Basically the first and second cases are strong but afterwards, those with repeated exposure have more mild infections and symptoms as time goes on. This is due to the recognition of a pathogen when it's reintroduced in the body. Below are the factors that lead to *Cryptosporidiosis* infections (Figure 1) (Menichella and Putignani 2010).

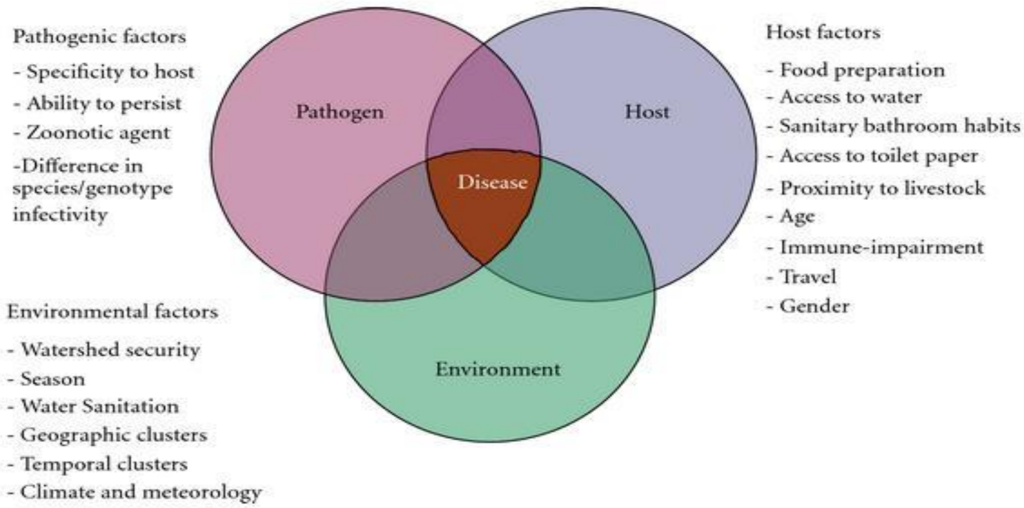

Figure 1: Venn diagram of factors http://www.hindawi.com/journals/ipid/2010/753512/

One Health

Cryptosporidium parvum can have devastating effects on the economy. It can show up at any time and is not easily treated. This in turn can result in panic. Locally, a contaminated water supply might be used by a water company to package drinking water for stores, spreading the risk. Oocysts can persist after the process of sterilizing and cleaning the water to make it safe to drink. This would cost the company money on lawsuits and then they lose even more money from having to recall all of their products. The stores lose money because they lose a contributor and their business. It can also induce people to panic and not buy other water companies' drinks because of the fear of the same problem. Infected people lose money because of hospital visits, systemic care, and the possibility of more severe infections. So the economy is ailing because of all of this plus the money the government will have to spend to have the water treated with better measures. This can easily cause panic because it is an unknown and the only way to prevent it is if you practice good hygiene. Even good hygiene does not guarantee protection. It is easily transmitted requiring only ten to thirty oocysts to produce disease.

An outbreak of *C. parvum* in 1993 in Milwaukee, Wisconsin infected an estimated 403,000 people in the United States. This example is demonstrates how it can become problematic in the economy. After an unsuccessful filtration process, the oocysts made it to the water supply and affected all those people. In 1995, people came together to collectively examine costs of the Milwaukee outbreak. After taking the average costs of expenses, the entire cost came out to be $31.7 million in total medical costs and $64.6 million in total lost productivity (Korich 1990). This problem isn't limited to the United States and is more serious in developing countries where their water supplies aren't filtered with high quality equipment. The loss of human lives and money becomes a problem for countries whose productivity is low. Also *C. parvum* is recognized by the CDC as a Category B bioterrorism threat. This basically refers to how easy it is spread and the death rate. This organism affects animals raised in the area and used for food as well as people who either drink the contaminated water or eat contaminated food.

Cryptosporidium parvum can slip through the filtration process of water treatment and also it can be misdiagnosed or overlooked since for most people the symptoms are mild and will clear up after a couple of weeks. The parasite itself goes through its lifecycle in six different stages. The oocysts become infectious once released in the feces. The oocysts release four sporozoites which are immature infecting agents. It then is picked up by a host and is ingested. All stages of its lifecycle happen within one host (Knott 2013). Below is a diagram displaying the *C. parvum* life cycle (Figure 2) (CDC 2015).

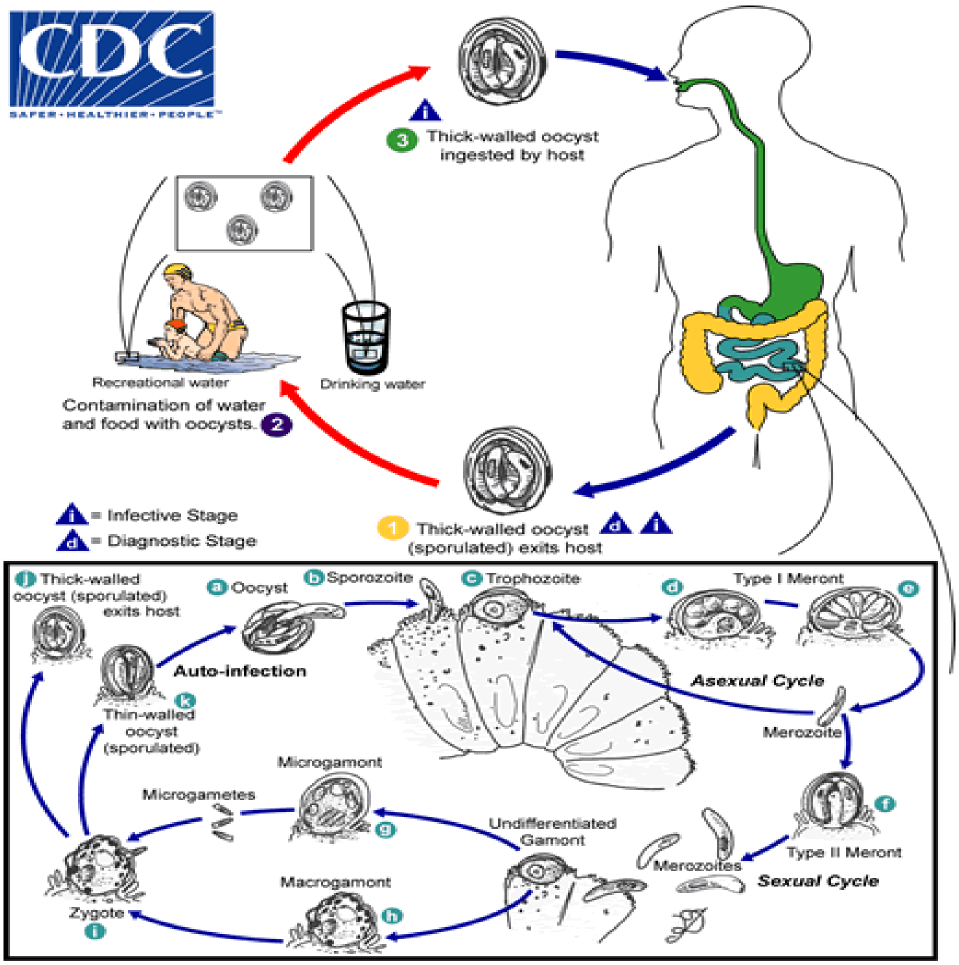

Figure 2. Life cycle of *Cryptosporidium parvum*. http://www.cdc.gov/parasites/crypto/pathogen.html

(The oocyst (a) releases the sporozoites (b) where they will attach themselves to the epithelial cells of the intestines (c). Once the sporozoites reach these cells, they undergo asexual reproduction (d, e, f) which circulates back to step c. Asexual reproduction (merogony) is when there isn't a female and male joining. However, it then goes through sexual reproduction (sporogony) where it produces male gametes (sex cell) called microgamont (g) and females gametes called macrogamont (h). It then is fertilized when the microgamonts and macrogamonts join to create an oocyst (i). This oocyst then starts to produce spores within the infected host. Two types of oocysts are produced: the thick walled ones (j) that are excreted from the host and are resilient to the environment and the thin walled ones (k) that continue to undergo the lifecycle within the host).[1]These thin walled oocysts are easier to break down and therefore ideal when infecting the host. Moreover, the oocysts are resilient to conventional methods of sterilization and can survive extreme concentrations of certain chemicals. A study in Brazil showed that around 95 % of the participants were seropositive (Current 1994). A stool sample was taken and stained to be able to see the oocysts under a microscope to see if an individual was infected. An estimate of 748,000 cases of *C. parvum* occur in the U.S. each year.[1] Most cases are water related such as drinking water and swimming pools, but some cases come from contaminated food and daycares. To try to prevent the spread and infection of *C. parvum*, studies were done to see if different chemicals could be used and also if there were more than one strain that could infect individuals.

Approach

Many studies have been conducted to answer the question of resistance of *C. parvum* to water treatment systems. One study was to determine whether there are different strains of *C. parvum* that can be transmitted to humans. It was concluded that there were indeed two different genotypes that could cause human infections from the pathogen. One shows zoonotic transmission from cattle to humans and vise-versa, but the other demonstrates transmission from human to human. It was determined from this study that all isolates from genotype 2 could infect mice and calves but none of genotype 1 isolates infected those hosts (Peng 1997). These data could be used to further the issue of whether just cattle infect water sources. The issue was resolved by removing cattle from the land. However, with this new information, it could be suggested that sewage drainage can be contributed to outbreaks since the second genotype showed that human feces was one of the culprits.

Another study was done with volunteers being infected with different levels of oocysts and monitored for symptoms. After the experiment, most subjects got better and it was shown that the number of oocysts initially ingested related to the excretion of more oocysts. Also the study is being expanded to retest the first volunteers with another artificial infection to measure protective immunity and whether that is an accurate assumption. Other studies where done to test for effectiveness of chemicals and other modes of eradication of the oocysts. One included the use of Pulsed UV light to destroy the number of *C. parvum* oocysts (Hayes 2012). It showed that it did decrease the number of oocysts but didn't completely deactivate them. However, this method is cost effective and more practical since it doesn't have to be done within high-tech laboratories. Also it can be used at the water source and can help with the sewage systems and wastewater plants. However, the effect of radiation and global warming hasn't been tested, so it is uncertain whether this method is friendly toward the environment. It was tested for a number of minutes and with different levels of oocysts to determine whether certain chemicals can decrease the number of oocysts. The experiment demonstrated that chlorine dioxide and ozone were far better disinfectants than free chlorine. This result is due to the fact that chlorine dioxide has more bonds that it can make than free chlorine. However, this approach still hasn't completely eradicated and destroyed the oocysts. There will always be room for error and it also showed that the more oocysts there were, the longer it took for the number to decrease. Furthermore, the first minutes had the most effect with more oocysts being destroyed and as time went by, fewer were destroyed as the chemicals became diluted and nullified by the oocysts (Hayes 2012).

Conclusions

Cryptosporidium parvum is a parasite that can go undetected by doctors and slip through the sanitation processes. It is unique in its oocyst and most of the time, it is just a nuisance to have. Studies will always be done to try to find treatment methods, to actually improve water treatment systems, to help understand the biological aspects of it, and overall to make sure it doesn't become a mutation that can have a higher mortality rate. Both studies in the past and studies in the future will always being asking questions and spinning off into other studies. The research behind it will never stop as long as there's information to be drawn out. Although it rarely has had any large outbreaks, it still is present in most countries. The media hasn't deemed it a high priority disease to get in a panic over. The question of what else can we do will always be associated with it. The agent is the parasite that attacks the intestines, the host is the person having diarrhea, and the environment is water areas and feces that can be ingested. With how the world is going and the ever accumulating trash that cannot be eradicated, *C. parvum* will find its way into water systems as human feces is washed away along with the trash. The destruction of oocysts will always be a struggle that scientists and parasitologists try to figure out. The complete destruction is not in the near future, but methods are improving in terminating the number of oocysts present. People should always keep in mind that it can be an issue to people and there is no way of determining when it will show up whether it be in a bottle of water or in the swimming pool.

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