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Review article

Unveiling the Enigma: An Overview of Zoonotic Protozoan Parasites

Anisimova E I
Scientific and Practical Center of the National Academy of Sciences of Belarus for Biological Resources, Minsk, Belarus
anis-zoo@yandex.ru

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Abstract

Zoonotic protozoan parasites are a diversified group of microscopic eukaryotic organisms that can infect humans and a wide variety of hosts. These fascinating creatures can leap across the species barrier to cause human diseases of global medical and veterinary importance. The study of parasite ecology is essential to understand the mechanisms behind their extraordinary success of crossing species barriers and how they infect and reside within hosts and cause diseases, thus contributing to disease prevention and control infrastructure. Toxoplasma gondii One of the most successful and widespread protozoan parasites is Toxoplasma gondii, which infects virtually all warm-blooded animals including humans. Infection can occur by ingesting infectious forms of these parasites contained in food or water or by exposure to contaminated cat feces. Cryptosporidium Waterborne protozoan parasite causing severe gastrointestinal disease in humans and animals. Giardia Flagellated protozoan parasite, transmitted via the fecal-oral route, by drinking contaminated water or ingesting contaminated food. Entamoeba histolytica Protozoan parasite causing human amebic dysentery and amebic liver abscess.

Keywords: Parasites, zoonosis, protozoa

Background

The world of protozoan parasites is a complex one; while the spearhead of these invisible soldiers is composed mostly of single-cell pathogens, they frequently cross the species barrier and have impact on human and animal health, with respect to both livestock and human diseases. Since many species of zoonotic protozoan parasites have the potential to infect several different hosts, including humans, they have become increasingly interesting to scientists and to health personnel (1). Historical records of protozoan infections go back when centuries and all continents, while the first description in the scientific setting dates back to Robert Hooke who described trichomonads back in 1675 and later Martinus Beijerinck described Trypanosoma batologist in 1881. Since then, much research has been conducted on protozoan parasites from both fundamental, molecular and ecological perspectives, in order to improve our understanding of the epidemiology, pathogenesis, control and prevention of diseases caused by parasitic protozoa. This understanding is necessary in order to protect public health and in order to have a sustainable bio-resource in our ecosystem (2).

Zoonotic protozoan parasites belong to a highly heterogeneous group of microorganisms that, by definition, can cause infections in humans as well as animals. More importantly, these parasites have adopted or evolved life cycles that may require several hosts, including one species in which the parasite resides within small cysts for months or years, a phenomenon that facilitates their transmission across the species barrier that separates people and animals (2). Many of these parasites have

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emerged as really nasty infections that rapidly spread worldwide and cause severe disease or death, either directly or following therapy with otherwise efficacious drugs. Often, the species occupying the transmission cycle can change labile cysts can travel enormous distances and perish anywhere – it depends on the passage of droplets of infected water from one mouth through a frog or another animal/date palm or rice field (the transmission cycle) or water source filled with feces from a host species The nature of the problem is heightened by the influence of anthropogenic change on the global scene, which can affect the geographic distribution and prevalence of an infectious agent by changing climate conditions or altering the nature and ecology of the landscape (2, 3).

Some of the most common zoonotic protozoan parasites include the flagellate Giardia, Cryptosporidium, Toxoplasma, and Entamoeba. Giardia lamblia, a flagellated protozoan, is among the most common causes of waterborne diarrheal disease worldwide, and is shared throughout a diverse array of pan-domestic and sylvanic species. In humans, transmission is via ingestion of infected contaminated water or food, or directly to humans from an infected host (4). Transmission also occurs person to person, including to non-adults from infected mothers. Gastrointestinal illness in immunocompromised and immunocompetent humans occurs worldwide. For example, cryptosporidiosis is America's most common gastrointestinal illness, responsible for approximately 800,000 cases of diarrhea globally. Introduced via the feces or other excretes of infected hosts, these organisms are persistent and exceedingly adaptive in the environment (5).

Toxoplasma gondii, a remarkably adaptable protozoan, can infect virtually any warm-blooded animal – including us – via undercooked meat or contact with contaminated soil or water (6). In both human and animal hosts, the parasite has been associated with a number of neurological and behavioral changes (7). Entamoeba histolytica, an aggressive amoeba known to cause bloody dysentery and liver abscesses in humans, is often transmitted to humans via contaminated food or water, as well as from person to person (8).

The epidemiology of these zoonotic protozoan parasites has contributed to the complexity of their distribution, with the added burden of complex life cycles in the environment, and the various hosts involved as crucial messages along their trajectories. Powerful environmental drivers – climate change, urbanization, a changing nature as humans continue to exceed the Earth's biotic carrying capacity – have been implicated in the distribution of zoonotic parasites, with predictions of increasing host-parasite interaction and emergence from areas of low infection prevalence (2). The development of resistant strains and the increasing incidence of immunocompromised populations are also implicated in the difficulty of the fluoroquinolones and partner drugs used to control the parasitological burden of human populations (9).

Transmission methods

Combating the zoonotic protozoan threat will require greater surveillance, more effective diagnostic techniques and improved treatment and prevention measures (10). Public-health authorities, veterinary practitioners and scientists all need to work together to understand these parasites and combat them.

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For many zoonotic protozoan parasites, a common pathway for transmission is ingestion of contaminated food or water. Parasites such as Cryptosporidium and Giardia can be present in water sources after an animal farm or slaughterhouse discards infected fecal matter, or, less commonly, if the feces of an infected animal end up in a water source (11). In both cases, human infection often follows consumption of the contaminated resource. Notably, one of the main ways that human contract trichomoniasis is through eating undercooked meat or contaminated produce (12-15).

A final major route of transmission is direct zoonotic – from infected animals or their feces. Toxoplasma gondii, for example, is acquired by humans from infected cats, through handling or ingestion of their stools (6), while the protozoan parasite Leishmania is transmitted by the bite of sand flies that are often in close contact with domestic animals (16).

In other instances, zoonotic protozoan parasites can be transmitted through the use of contaminated medical or farming equipment. Trypanosoma cruzi, the protozoan parasite that causes Chagas disease, has been known to be transmitted to people through the use of infected needles or receipt of contaminated blood (17).

Indeed, because the evolutionary life cycles of zoonotic protozoan parasites invariably involve one or more additional hosts, some of which are explicitly animal or multispecies populations, overall complexity can be considerable, complicating the generally pragmatic occurrence of alternative strategies and making it difficult to figure out where to break the transmission cycle to halt spread. Fine-scale understanding of the mechanistic details of parasite transmission can, however, point towards the most likely transmission bottlenecks – the most vulnerable sites – where targeted intervention (interventions precisely directed at reducing transmissions) and public-health measures can potentially be most effective (11).

One of them is improved sanitation and hygiene, which can decrease the chance of exposure to fecal-contaminated water or food, or to fecal matter from farm animals. Another is the development of highly effective vaccines along with better animal husbandry practices. Xiao and Feng (11), and Hotez et al (18) both discuss these public health approaches that can reduce

Effects on the health of animals and humans

Zoonotic protozoan parasites represent an important public health risk, both directly and indirectly for both human and animal populations. They have the potential to cause a wide variety of debilitating and, often, fatal diseases. The impact of these same parasites on global health and economics is an ongoing concern. Zoonotic means that the parasite can be transmitted from an animal to a human, and vice versa. A parasite is an organism that lives on or in a separate organism, the host, and takes its nourishment at the expense of the host without too much risk of killing it. Most parasites are microscopic. They can take a toll on human and animal health through life-altering, crippling diseases. As such, many of these diseases are a major public health concern (17).

The zoonotic protozoan parasite, Toxoplasma gondii, is well-known as a pathogenic parasite infecting warm-blooded animals including humans. It is transmitted through tissue cysts in the invaded host's tissues. In these cases, the parasite is resistant and can survive for years, even in humans. Toxoplasmosis has emerged as a serious infection that cause severe neurological and ocular complications,

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especially in a pregnant woman and person with immunodeficiency. The global range of this parasite and the number of infected humans and other animals warrants awareness and effective preventive measures (19).

Gastrointestinal giardiasis, or diarrhea, abdominal cramps and malabsorption caused by the zoonotic protozoan parasite Giardia duodenalis, is spread by water contaminated with cysts, and is correspondingly a relevant health issue in humans and animals (3). Infected individuals can become severely malnourished, which consequently leads to stunted growth and development in children in developing countries.

Cryptosporidium spp. Furthermore, cryptosporidiosis, a diarrheal disease caused by other protozoan parasites, is also an important zoonosis for humans and domesticated animals, with Cryptosporidium spp being a significant pathogen (11). Cryptosporidium oocysts that contaminate water supplies can be transmitted from humans and animals, and cause severe illness in immunocompromised persons. In fact, cryptosporidiosis can lead to significant long-turn health costs and economic burdens.

Diagnostic tools and surveillance systems are also required to identify and track the presence of zoonotic protozoan parasites in human and animal populations, to inform public health policies by defining the magnitude and distribution, and guide the design and application of appropriate interventions. (19). In addition, hygienic practices and the provision of clean and safe drinking water sources can be the key to prevention and control of zoonotic protozoan parasites; especially in developing countries where the lack of access to sanitation and clean water can contribute to the spread of the parasites (3). Development of effective prophylactic drugs, as well as the treatment and management strategies of both human and animal infections by antiparasitic drugs, and supportive care (that would alleviate the symptoms and complications caused by these infections), are equally important to tackle these problems. Zoonotic protozoan parasites might impact man in many other indirect ways, mainly by causing economic burden in terms of the cost associated for treatment and management of the diseases (11). In addition, they can compromise food security and agricultural productivity.

Development in diagnosis

Another major advancement in the diagnosis of zoonotic protozoan parasites is the increased use of molecular-based assays. Microscopy-based diagnostic methods are the gold-standard approach for zoonotic protozoan infections, and can help to identify coccidian parasites and trypanosomes by quickly detecting and characterizing flagellate and sporozoan parasites. In resource-limited settings, where expertise and technical capacity are lacking, microscopy remains the most valuable diagnostic method for human and animal infections (20). However, conventional microscopy can be time-consuming and has less sensitivity and specificity than newer molecular-based diagnostics. PCR, or real-time PCR, is fundamentally used in field-testing, zoonotic diagnostics, outbreak response and epidemiologic studies. These parasites are among the most clinically important zoonotic protozoan parasites (21). Molecular diagnostics are highly sensitive and specific for detection of DNA or RNA from parasites, can identify species that are difficult to diagnose, or infections that were traditionally unrecognized, thus leading to enhanced recognition of parasite infections and understanding of their epidemiology and patterns of transmission.

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By developing molecular diagnostic tests, advanced imaging techniques could now be integrated in the arsenal to study zoonotic protozoan parasites. Confocal laser scanning microscopy, which makes possible molecular imaging, and flow cytometry, which allows high-resolution analyses of morphological features, surface adhesion proteins and protein compositions along with detailed cell-size measurements, have improved our understanding of features such as the roughness and stiffness characteristics of parasites as they grow or migrate around and among their hosts. Such a footprint or profile could potentially inform us about the morphology and life-cycle of the zoonotic protozoan, and improve observations about host-parasite relationships that have a mechanistic basis. Beyond improving the clarity of these parasites, research into the host-parasite relationship and diagnostics has led to the identification of new pathways for studying anti-parasitic therapeutic strategies. For example, specific surface proteins that parasites use to bind themselves to host cells have been elected as promising new drug targets (21).

Additionally, novel multiplex diagnostic platforms with high throughput and new sample-handling techniques have further expedited and strengthened the diagnosis of zoonotic protozoan parasite. Indeed, via decreasing the turn-around time and the cost (22), now these pathogens are readily and reliably diagnosed via specific serological assays. In fact, antibodies-based tests (eg, enzyme-linked immunosorbent assays (ELISAs) and immunofluorescence assays) can detect antibodies against zoonotic protozoan parasites in patients, and then offer precious information either on subclinical or past infection status. Serological tests are now essential diagnostic tools within epidemiological studies or surveillance programs (15).

What we have here along with these novel technologies are innovative bioinformatic and computational approaches to better diagnose these emerging or re-emerging zoonotic protozoan parasites. These new approaches include novel bioinformatic analytic tools like genome sequencing and comparative genomics to develop novel molecular diagnostic markers and unravel novel diagnostic assays to better target parasite(s) (11). Other novel approaches include utilizing machine learning algorithms for automation for disease detection and parasite species discrimination in the clinic or research setting (23).

Methods of control

For the early detection of a zoonotic case, clinicians should be familiar with the many species of zoonotic protozoa that are relevant to human infection, including Giardia, Cryptosporidium, Toxoplasma, Leishmania and many others. Diagnosis, in most cases, requires laboratory testing to identify the specific parasite suspected on clinical grounds and, when done, drug treatments can be effective. While metronidazole, albendazole or nitazoxanide are effective for some species of zoonotic protozoa, the development of drug resistance can emerge (24).

Good preventive practices can help to limit the spread of zoonotic protozoan parasites. Improved sanitation and hygiene, such as regular handwashing, clean food preparation, and well-treated water, are key to reducing the risk of transmission. In regions at highest risk, we need to educate people about these measures. They then can take steps to protect themselves and their families. Where available, vaccination programs can increase herd immunity and help to halt the spread of these parasitic infections. (25)

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The third critical component of integrative control is controlling the reservoir of zoonotic protozoan parasites. This pertains to specific interventions that decrease the prevalence of parasites in animal populations, which serves as a potential source of transmission to people. Veterinary surveillance, regular deworming of domestic animals, and biosecurity for livestock and wildlife management can all contribute towards controlling transmission. Public health authorities, veterinary practitioners and environmental scientists should work together to define and implement integrated control measures (19).

Meanwhile, efforts to combat zoonotic protozoan parasites have also been fueled by recent technological innovations and novel research. Molecular diagnostics such as polymerase chain reaction (PCR) testing enable earlier identification of infections and more targeted treatment efforts, with improved sensitivity and specificity compared with conventional techniques in routine use beforehand (21). Novel therapeutic compounds such as natural products and repurposed drugs offer hope that therapeutic Failure may be overcome (24).

Examples of some interesting studies

Fast-track diversification was also observed with Cryptosporidium, a genus of protozoan parasites that cause the painful gastrointestinal illness cryptosporidiosis. Checkley et al., (9) and Khalil et al., (26) found that Cryptosporidium infects humans and causes disease, and it has been subject to intense investigation. Indeed, accelerated diversification of Cryptosporidium was seen in environments where sanitation and access to clean water were poor, especially in developing countries where infections among children seem to be highly prevalent, especially in early childhood according to a study by Khalil et al. (26). Recently, a widespread resurgence in disease linked to cryptosporidiosis has been noticed in both children and adults, partly because many strains now show resistance to the drug nitazoxanide and other antimicrobials, highlighting the urgent need for new treatments, according to Rossle and Latif (27).

Another native of the American wild that has drawn attention in zoonotic disease conversation is the protozoan Giardia, whose infection causes the disease known as giardiasis. It causes a spectrum of symptoms, from asymptomatic gastrointestinal uneasiness to massive rotating diarrhea and chronic malabsorption (28). A recent study in a rural community of eastern India has revealed high levels of giardiasis in children, and that some infections can be traced to livestock serving as a reservoir that transmits to humans (29). In this example, both prophylaxis through public health intervention and increased understanding of the complex transmission dynamics could use greater attention.

What Ahuja found were remarkable parallels with the protozoan parasite Toxoplasma gondii, one of the most infective protozoans into certain species (including humans), but which can also infect a wide range of warm-blooded hosts (6). Toxoplasma gondii causes the disease toxoplasmosis, which can be devastating to humans and other mammals who acquire the infection, in particular those who are pregnant or whose immune defenses have been weakened. In a case study reported from Brazil, it was postulated that toxoplasma infection might have caused neurological conditions to develop; the case offered insight into the chronic nature of parasitic infection, and the importance of early diagnosis and treatment (30-32).

Another important parasite is the protozoan Cyclospora cayetanensis, the

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causative agent of cyclosporiasis, a disease involving gastrointestinal problems that has been the center of great attention in the past decade. Its transmission is thought to be associated with food and water sources contaminated with the parasite, as supported by case studies. Being a foodborne disease, Cyclospora has especially occurred after the consumption of fresh produce (31). The difficulty in diagnosing and therapy for Cyclospora infections have motivated the development of improved diagnostic methods and more effective treatment strategies (33, 35).

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