REVIEW ARTICLE

Therapeutic Interventions of Major Parasitic Foodborne Diseases

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Abstract

Foodborne parasites (FBP) are commonly linked to marginalized populations, particularly in areas with poor sanitation and inadequate water supply. Animal products serve as a key route of foodborne diseases. The ingestion of contaminated water and food could lead to zoonotic diseases. Foodborne parasites are comprised of shellfish, fresh produce, and water-contaminating protozoans (Toxoplasma, Cryptosporidium, and Giardia), fish-borne parasites (Anisakid nematodes), and meat-borne parasites (Trichinella). Globally, novel foodborne pathogens have emerged after the food system commercialization. Despite the recurrent antibiotic resistance, albendazole and mebendazole (MBZ) (Trichinellosis); pyrimethamine/clindamycin, pyrimethamine/sulfadiazine, or trimethoprim/sulfamethoxazole (Toxoplasmosis); Nitazoxanide (Cryptosporidiosis); nitroimidazoles (Giardiasis); and niclosamide or praziquantel (10 mg/kg) (Diphyllobothriosis and Taeniasis) are mainly employed to counter these pathogens. Fortunately, rapid progress in this field has raised the biological understanding of parasitic infections, which could help in eliminating parasitic foodborne outbreaks. This review discusses the major FBP and related therapeutic interventions.

Keywords

Foodborne parasites, Therapeutic intervention, Transmission, Outbreaks

INTRODUCTION

Several foodborne diseases are associated with parasites[1]. Their size varies from visible worms to unicellular organisms. Parasite presence could cause discomfort and even death in severe cases[2]. The cyclic transmissions of parasites between humans and animals to humans have been reported. They could survive and reproduce inside the organs and tissues of infected hosts (animals and humans) and are excreted through the feces. The transmission mainly occurs through water, food, cyst ingestion, and contact with the feces of the infected host (animal or human) (Figure 1). *Toxoplasma gondii (T. gondii)*, *Giardia duodenalis* (*G. duodenalis*), *Taenia solium* (*T. solium*) (pork tapeworm), *Cryptosporidium parvum (C. parvum)*, *Trichinella spiralis* (*T. spiralis*), *Cyclospora cayetanensis*, and *Taenia saginata* (beef tapeworm) are the main foodborne parasites[3]. *Giardia duodenalis* causes giardiasis via contaminated drinking water. Cysts containing undercooked meat could infect humans. Cryptosporidiosis is caused by the *Cryptosporidium parvum*[4]. *C. parvum* inhabits water,

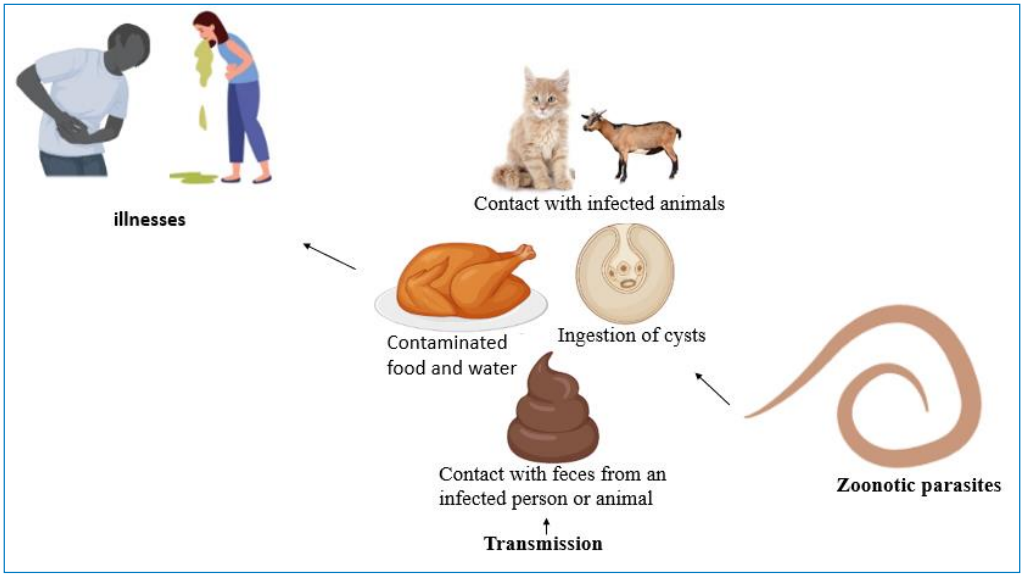

Figure 1. Schematic diagram of foodborne parasite transmission. Zoonotic foodborne parasites are transmitted by contact with feces from an infected person or animal, ingestion of contaminated food and water, ingestion of cysts, or contact with infected animals. The infected individuals may show different clinical symptoms ranging from abdominal pain to a generalized infection.

soil, feces, and herd animals' intestines. This parasite causes pulmonary, tracheal, and gastrointestinal cavity diseases. *C. parvum* oocyst-contaminated water or foods are the main source of its transmission[4]. *Cyclospora cayetanensis* (single-celled microscopic parasite) is associated with Cyclosporiasis. *C. cayetanensis* oocysts-contaminated water and food are its main transmission sources. The chances of disease transmission increase after the raw consumption of fruits and vegetables. Cyclosporiasis with prolonged fatigue, anorexia, and watery diarrhea has been reported in the United States after the raw consumption of food products. Cyclosporiasis is caused by the protozoan Cyclospora, which has been found in basil, raspberries, and lettuce. *Cryptosporidium* (protozoan) has been associated with cryptosporidiosis outbreaks after the consumption of green onions and apple cider[5].

Toxoplasma gondii is known to cause Toxoplasmosis (oocyst) in the cat's gut. The infective stage (oocysts) has been detected in cat feces. Oocysts enter the body through the consumption of contaminated water and meat. Fecal–oral transmission is crucial because of the environmental abundance of the oocysts, especially in the cat's surroundings. The infection could also transfer from the mother to the fetus. Generally, Toxoplasmosis affects pregnant women (miscarriage and stillbirth) and immunocompromised patients[6]. Trichinosis is caused by the intestinal roundworm *Trichinella spiralis*. *Trichinella* larvae could travel throughout the body and form cysts in different muscles. Undercooked or raw wild game is the main source of disease transmission[7].

MAJOR FOODBORNE PARASITES

Toxoplasmosis

A protozoan, *T. gondii*, causes Toxoplasmosis infection. *T. gondii* is an intracellular obligatory parasite and one-third of the global population is seropositive[8]. Globally, *Toxoplasma gondii* is a major zoonotic foodborne pathogen and its infection is related to the utilization of undercooked meat[9]. Type I, II, and III are the main genotypes of this parasite, which vary in prevalence and pathogenicity[10]. The association of genotype II with congenital toxoplasmosis in the USA and Europe has been documented[11]. *T. gondii* infection has been reported in 23% of adults and adolescents causing 24% of foodborne diseases related deaths in the USA[12]. These infections are either asymptomatic or exhibit minor symptoms (lymphadenopathy, fever, and malaise). The infections could be severe in immunosuppressed individuals (AIDS patients). These infections could also be detrimental to the human fetus (congenital Toxoplasmosis) leading to severe infant sequelae (neurological disorders, mental retardation,

and blindness)[13]. *T. gondii*-related impaired eyesight has been increasingly detected in immunocompetent individuals and non-pregnant women[14].

The ratio of *T. gondii* infections is high among foodborne pathogens in the USA and the Netherlands[15]. Congenital illness of an unborn baby could lead to life-long disability. Toxoplasmosis contracted during the later life stages can cause eyesight issues. *T. gondii* could directly or indirectly contaminate the environment and food through various routes to infect humans. Fresh plants, contaminated meat, water, and unpasteurized goat milk are high-risk foods[8]. The transmission of infection to humans could occur via wild cats, garden soil, pets, and lawn grass (Figure 2). There are three main routes of toxoplasmosis transmission to humans such as (a) raw or partially cooked infected meat or other foods; (b) unintentional oocyst ingestion from cat feces or litter box, and outdoor soils (gardens or dust from uncleansed vegetables and fruits); (c) mother to the unborn fetus[16]. Water is a key risk factor and infection source in subtropical and tropical countries where unpurified surface water is commonly consumed[17]. The largest human outbreak (110 persons) of acute toxoplasmosis occurred in 1995 on Vancouver Island, Canada. Toxoplasmosis is quite prevalent in humans, but difficult *T. gondii* detection, underreported cases, and inadequate routine monitoring hinder its accurate assessment[18]. Modes of human transmission and emerging risk factors including global food sources and altered consumer preferences (more consumption of undercooked meat and raw vegetables) demand further investigations for better understanding[19].

T. gondii is a global zoonotic foodborne pathogen, however, its management is not systematic[20]. Microscopical and immunological methods are generally adopted for the detection of tissue cysts, oocysts, and tachyzoites. These methods involve the isolation and concentration stages followed by direct sample detection. *T. gondii* DNA is detected through molecular assays, whereas infectivity and viability are assessed using mice-based *in vivo* assays and *in vitro* culturing techniques[21].

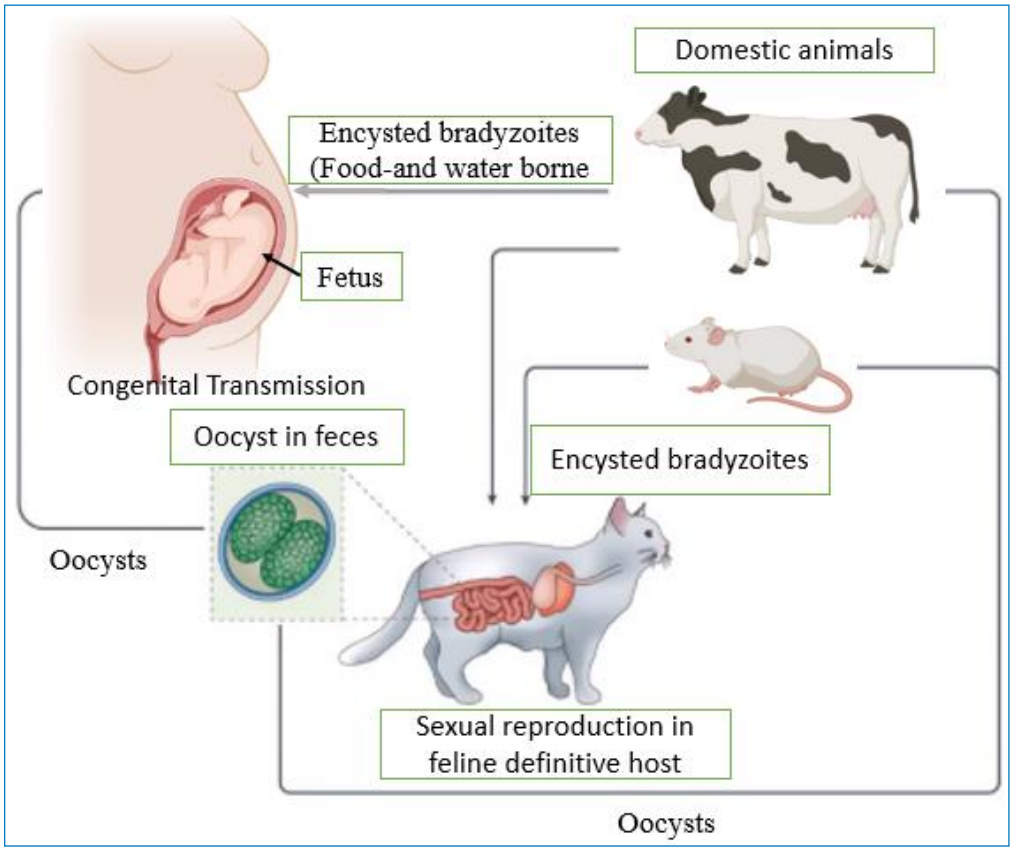

Figure 2. Schematic diagram of the Toxoplasmosis transmission cycle. Felines are definitive hosts for Toxoplasmosis and they can be infected by injection meat harboring encysted bradyzoites. Humans can acquire Oocysts from feline feces or encysted bradyzoites from meat of animals.

Giardiasis

Giardiasis is an important foodborne and waterborne disease[22]. Foodborne giardiasis is a serious worldwide public health issue with economic and social burdens. It is quite common under limited water-treatment facilities and poor sanitary conditions[22]. Giardia (protozoan parasite) causes ~280 million human diarrhea cases every year and infects more than forty animal species as well[23,24]. Food-based giardiasis is considered to cause 7–15% of total giardia infections in the USA[25]. World Health Organization has reported 28.2 million foodborne giardia cases and 26,270 disability-adjusted life years (DALYs)[26]. However, the prevalence of foodborne giardia could be much higher as most of the cases remain unreported due to inadequate detection and improper monitoring[27].

Giardia transmission occurs through direct contact with infected animals and humans, and the consumption of cyst-contaminated water and food[28]. The simple *G. duodenalis* life cycle facilitates the transmission process[23]. Several waterborne giardiasis outbreaks have been reported but the reports of foodborne giardiasis are limited[29,30,31,32,33]. This might be due to the better international standards regarding drinking water monitoring[31].

Cryptosporidiosis

Cryptosporidiosis is an important worldwide diarrheal disease of animals and humans[34]. Several *Cryptosporidium* (protozoan parasite) species could cause this disease[35]. Cryptosporidium oocysts exhibit ubiquitous environmental presence and transmit through direct or indirect contact (fecal–oral route) with an infected host[36]. Fecal–oral transmission could occur via zoonosis, person-to-person contact, and contaminated water or food consumption[35]. A single oocyst ingestion could also pose a significant infection risk[35]. The invasive Cryptosporidium oocysts damage the epithelium of the small intestines by disrupting the absorption capability and barrier function leading to mild-to-severe diarrhea and other abdominal symptoms. Cryptosporidium infections generally remain mild, asymptomatic, and self-limiting in immunocompetent adults. Forty one (41) species and more than 60 valid genotypes of Cryptosporidium have been reported[37]. The presence of 21 species and genotypes has been confirmed in humans where two species (*C. hominis* and *C. parvum*) cause more than 90% of human infections. *C. muris*, *C. meleagridis*, *C. cuniculus*, *C. andersoni*, and *C. ubiquitum* have also sporadically caused human zoonotic outbreaks, particularly after direct contact with infected animals[38,39,40].

The disease-causing species exert a significant global cryptosporidiosis burden and disease severity[41]. In 2017, 1.6 million human deaths were linked to diarrheal illnesses worldwide of which one-third were children under the age of five years. The highest mortality rates were observed in South Asia and sub-Saharan Africa. Poor sanitation and unsafe drinking water were the main factors of higher mortalities in these regions[42]. Cryptosporidium oocyst transmission via water is the major route of livestock and human diarrheal infections[30]. Cryptosporidium contamination has been established as the major factor in 905 waterborne outbreaks worldwide[30]. Cryptosporidium contaminations also cause more than 8 million foodborne illness cases/year and 25 foodborne outbreaks have been documented[43]. The food industry is also suspected of contributing to the spreading of diarrheal infections. Food products are mainly imported from high-risk countries with established diarrheal diseases epidemiology[44]. Fresh produce and leafy greens are also considered to transmit Cryptosporidium infections[45]. Food products could be infected on and off farms while washing with contaminated water. Infected food handlers also serve as a Cryptosporidium contamination source in the food chain[4].

Trichinellosis

Trichinella spiralis is a global foodborne zoonotic nematode that causes human trichinellosis[46]. Infected raw pork and partially cooked food are the main source of *T. spiralis* infections in humans[47,48,49]. Different developmental stages of *T. spiralis* could parasitize a single host. Muscle larvae (ML) parasitize skeletal muscles and the upper jejunum, whereas adult worms (AW) parasitize the duodenum. The ingested ML are released from the collagen capsules in the muscle tissues through gastric pepsin digestion and become activated into intestinal infectious larvae (IIL) after encountering bile or enteral contents[50,51]. Then, IIL enter the intestinal epithelium cells (IECs) and undergo four molts to become adults in the gut epithelial intra-multicellular niche. Larval molting is crucial and larvae with incomplete or partial molting could not properly grow to adulthood[52,53]. Therefore, proteins contributing to larval molting could be targeted to develop novel vaccines and drugs against *T. spiralis* infections[54].

T. spiralis invades skeletal muscles and damages vital organs to cause mortalities. Trichinosis incubation could occur from 2 to 28 days (commonly 9 days). *T. spiralis* infections are characterized by nausea, diarrhea, vomiting, fever, and muscle pains, which could last for several days. Wild game meat (boar, beaver, and bear) and undercooked pork are associated with *T. spiralis* infections. The pork can be cleaned from *T. spiralis* infections by: (1) cooking for 1 min at 60°C; (2) frozen storage at -30°C for 6 days, -23°C for 10 days, and -15°C for 20 days; or (3) following USDA recommendations regarding drying, salting, and smoking cured pork products and sausages[54].

Trichinella life cycle can be categorized into two phases the enteral (intestinal) phase and the muscular (systemic or parenteral) phase[55]. Larvae are released in the stomach during the intestinal phase, which penetrate small intestine mucosa and become adult worms. During the muscular phase, newly hatched larvae disperse in the body to reach striated skeletal muscle cells[56]. Trichinellosis severity mainly depends upon the ingested larval numbers (infecting dose), the frequency of infected meat consumption, and the treatment and cooking of the meat[56] (Figure 3).

Taeniasis/cysticercosis

T. saginata (beef tapeworm) and *T. solium* (pork tapeworm) are important foodborne parasites worldwide[57]. The development of adult *T. saginata* occurs in the human intestine. Their eggs are either directly excreted with the feces or in the form of intact egg-containing proglottids[58]. Cattle, the intermediate parasite hosts, could ingest these eggs leading to infection. Then, the oncospheres migrate through the bloodstream to the striated muscles, which causes the cysticercus-containing protoscolex development known as the metacestode stage. Multiple factors could be attributed to its broad distribution such as intermediate hosts and favorable environmental conditions. These could be further elaborated to proper sewage treatment and disposal, sanitary education, and dietary habits of farm workers (consumption of undercooked or raw cysticerci-infected meat)[58].

T. saginata infections could cause anal pruritus and mild gastrointestinal symptoms in humans. *T. saginata* infections are quite common in low-income countries; however, the disease burden is significantly low worldwide. A few cases of appendicular taeniasis,

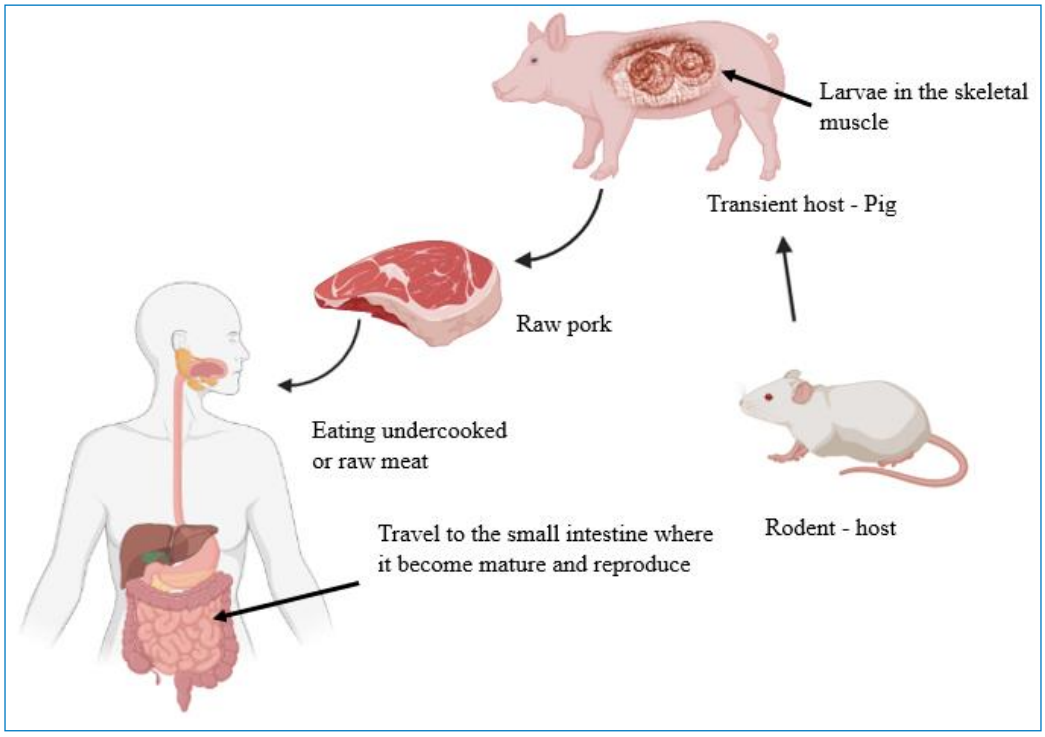

Figure 3. Trichinellosis transmission cycle. In this cycle, humans are infected by ingestion of raw pork. Rodents are reservoirs of the parasite and pigs are transient hosts for Trichinellosis.

discomfort, and gastrointestinal pain are reported. This study also covers the Iran region where some cases have been reported[59]. *T. saginata* infections-related economic costs are very low and limited to diagnostic procedures[25]. The literature about economic infection costs in cattle is limited. However, beef inspection is mandatory for bovine cysticercosis in high-income countries. Infected carcasses are refrigerated, downgraded, or condemned[60]. The downgrading leads to significant economic losses and *T. saginata* infected cattle could adversely affect their trade[61]. *T. saginata* is categorized lower in the multicriteria-based ranking, as taeniasis symptoms are either absent or mild. Therefore, taeniasis is not a major public health issue[62]. Nevertheless, *T. saginata* infections could hinder cattle trade thus posing a significant financial burden because of devaluation, freezing, and carcass condemnation[63,64].

Humans serve as the final host of *T. solium* after undercooked pork consumption. *T. solium* has been ranked as a major food-borne parasite of global concern. It affects millions of individuals, annually leading to a significant economic impact[56]. Human cysticercosis occurs after the ingestion of *T. solium* eggs. Parasite migration to the central nervous system results in neurocysticercosis (NCC). NCC further leads to debilitating neurological symptoms such as severe headaches and epilepsy[65] (Figure 4). *T. saginata* distribution is global, whereas *T. solium* is extremely endemic in pork-consuming poor communities of Latin America, Asia, and Africa. *T. solium* distribution in Eastern Europe remains unclear, which raises suspicion of its transmissions[66]. A recent review of bovine cysticercosis epidemiology has demonstrated presence of *T. saginata* in several Western European countries. However, the data from Eastern Europe was of poor quality and scarce[61].

Anisakiasis (Anisakidosis)

Anisakiasis, a zoonotic disease, is caused by the nematodes of three genera (Contra caecum, Anisakis, and Pseudoterranova). Birds and fish-eating marine mammals are the natural definitive anisakid nematode host. The larval development in adults occurs in gastric mucosa. Fully-embryonated eggs (eggs with infectious third instar/L_3 larva) are excreted in the host

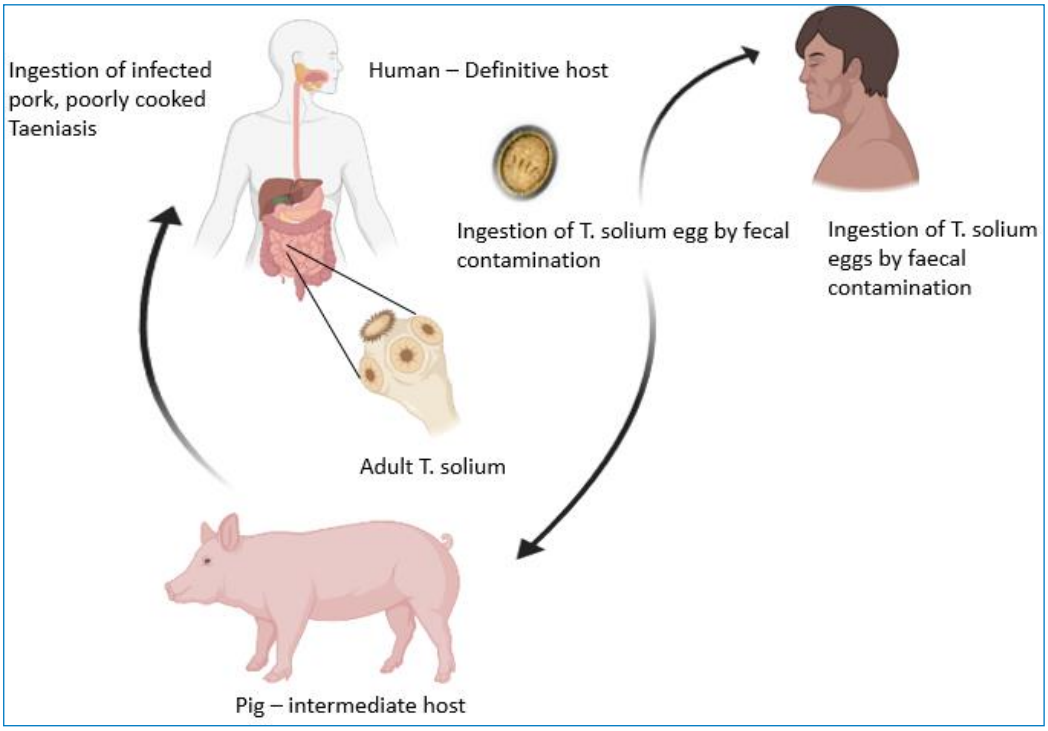

Figure 4. Schematic presentation of Taeniasis/Cysticercosis infection cycle. In this cycle, pigs and humans are considered as the intermediate and the definitive host, respectively. These hosts are infected by the ingestion of eggs and pork meat, respectively.

feces followed by hatching in brackish and marine water. After hatching, L_3 larvae infect an intermediate crustacean host, which is consumed by a squid or fish to serve as a paratenic host. The worms encapsulate in their flesh and the definitive host gets infected after paratenic host consumption[67]. Human infection also occurs after the consumption of undercooked or raw paratenic hosts (larvae-infected undercooked shellfish). Humans are the final anisakid nematode host, where they cannot achieve sexual maturity. Generally, human infection occurs in the gastrointestinal tract but sometimes the worms penetrate the intestinal or gastric mucosa into the peritoneal cavity to cause ectopic anisakiasis. The ectopic disease could involve the spleen, mesentery, mesocolic lymph nodes, omentum, parametrium, and pleural cavity[68].

The occurrence of human anisakiasis is high in the regions with more consumption of undercooked and raw fish including South America, coastal areas of Western Europe, Japan, and North America[68]. However, the seafood trade could carry the disease worldwide. The dishes such as sushi, ceviche, and sashimi are often connected with anisakiasis. Generally, anisakid nematodes exhibit low specificity for molluscan and piscine hosts. Commercial marine squid and fish such as salmon, snapper, grouper, cod, herring, Japanese flying squid, and tuna might also be the paratenic hosts[67]. Therefore, various undercooked and improperly frozen squid and fish could pose an anisakiasis risk after consumption.

Diphyllobothriosis

Cestodes belonging to the genus Diphyllobothrium cause intestinal parasitosis known as diphyllobothriosis (Hernández-Orts et al., 2021). Taxonomically, Diphyllobothrium is categorized under Diphyllobothriidae (family), Diphyllobothriidea (order) (formerly Pseudophyllidea), Cestoda (class), and Platyhelminthes (phylum). There are approximately 50 known species, of which only 12 are human pathogens[69].

Ingestion of undercooked or raw fish as a common cultural practice poses an infection risk. Recently, global food transport has increased the raw-fish demand. *D. nihonkaiense* and *D. latum* are the most pathogenic species among the 14 Diphyllobothrium human pathogens[70]. The human pathogenicity of another species *D. dendriticum* is also rising in various regions[69]. They are the longest human tapeworms (about 10 m). The viscera of undercooked or raw fish and meat (tartare, sushi, ceviche, and sashimi) are the main source of infections. The infections generally present mild symptoms such as diarrhea, abdominal pain, and a changed appetite. The tapeworm absorbs intestinal vitamin B_{12} in humans, which could lead to vitamin B_{12} deficiency anemia in prolonged cases. The consumers of tapeworm-contaminated undercooked or raw fish are always at risk. Niclosamide and praziquantel treatment is the standard procedure for Diphyllobothriasis and others[71]. *Diphyllobothrium* tapeworms can survive in the small intestine of humans for many years reaching a length of about 15 meters. Generally, the symptoms include discomfort (diarrhea and abdominal pain), asthenia, and weight loss. The prolonged tapeworm infection could lead to vitamin B-12 deficiency-based megaloblastic anemia. However, Diphyllobothriasis in humans is considered a mild illness and is not mentioned in epidemiology surveys[72].

Chagas disease

A flagellated protozoan *Trypanosoma cruzi* causes Chagas disease (CD). The feces of bloodsucking triatomines (Hemiptera: Reduviidae) contain infective stages of *T. cruzi* and are the main transmission source[73]. There are multiple transmission mechanisms, but oral transmission is crucial for maintaining the parasitic zoonotic cycle. Triatomines transmit *T. cruzi* infection while feeding on animals[74]. Several outbreaks have been documented since the first oral transmission-based human CD case in 1965[75]. Later, CD cases have been reported in Venezuela, Brazil, French Guiana, Bolivia, Argentina, Ecuador, and Colombia[76]. These cases have been attributed to *T. cruzi* containing triatomine secretions and feces-infected food, juices, fruits, and water[76]. Oral outbreaks have become the main transmission route in CD endemic countries (Amazon Basin and areas where effective vector control measures are taken). Disease severity is common in oral transmission outbreaks leading to fatal acute myocarditis with high lethality (8–35%). Cardiac abnormalities in response to vector transmission cause about 2–7% of pediatric deaths. The death rate of <5–10% in adolescents and children is considered low in endemic countries[73].

THERAPEUTIC APPROACHES

Trichinellosis: To date, *T. spiralis* infection treatment is difficult and only a limited choice of drugs is available

against *Trichinella*. Conventionally, benzimidazole derivatives (albendazole and mebendazole (MBZ)) are often used for trichinellosis treatment. However, their efficacy against encapsulated larvae in combination with the rising resistance is questionable. Their low water solubility further restricts the absorption in the intestinal lumen leading to decreased bioavailability[77]. Therefore, higher drug doses are recommended, which cause several gastrointestinal adverse effects. MBZ teratogenicity has also been established in mice and rats[78].

Toxoplasmosis: Trimethoprim/sulfamethoxazole, pyrimethamine/clindamycin, or pyrimethamine/sulfadiazine are used for toxoplasmosis treatment in humans (Neville et al., 2015). However, serious side effects and low tolerance led to the inhibition of therapy in 40% of patients[79,80,81]. Cases of toxoplasmosis drug resistance have also been reported[82]. Furthermore, there are no recommended therapies to eradicate encysted bradyzoite. Therefore, most of the investigations are focused to develop novel drugs for chronic and acute *T. gondii* infections.

Giardiasis: *G. lamblia* infection is treated using nitroimidazoles such as secnidazole, metronidazole, ornidazole, and tinidazole. Nitroimidazoles were discovered in 1955, which effectively treated various protozoan infections. Metronidazole [1-(β-hydroxyethyl)-2-methyl-5-nitroimidazole; Flagyl], discovered in the 1950s, was effectively used to counter *Entamoeba histolytica* and *Trichomonas vaginalis* infections[83] established the metronidazole efficacy against giardiasis. Since then, metronidazole and other nitroimidazoles have served as the main therapy for giardiasis[83].

The metronidazole mechanism against Giardia has been thoroughly investigated among all nitroimidazoles. Metronidazole follows the anaerobic metabolic pathways of Giardia. After entering the trophozoite, the nitro group of the drug acquires electrons from ferredoxins (electron transport protein) to become "activated" through nitro group reduction[84,85,86,87]. This reduction establishes a gradient, which favors intracellular metronidazole transport. The reduced metronidazole acts as a terminal electron acceptor to covalently bind with the DNA macromolecules[88]. This process damages the DNA through helical structure loss, strand breakage, and abnormal template function, which subsequently result in trophozoite death[89]. Metronidazole also additionally inhibits the respiration of trophozoites[90,91]. Reduction-based metronidazole activation might generate toxic radicals, which can react with key cellular components[87]. Nitroimidazoles cannot properly affect the trophozoites inside the cysts, which might be due to poor drug penetration through the cyst wall[85]. *In vitro* induction of metronidazole resistance revealed a correlation with reduced parasite pyruvate: ferredoxin oxidoreductase activity, which is important for nitroimidazole reductive activation [92,87]. Metronidazole oral administration leads to rapid and quick absorption facilitating its penetration into body tissues and secretions (vaginal, saliva, semen, and breast milk)[86]. The liver mainly metabolizes metronidazole to excrete via urine[93].

Benzimidazoles (mebendazole (Vermox) and albendazole (Albenza)) have been administered for treating *G. lamblia* related infections[94]. *In vitro* and clinical investigations have demonstrated different results. However, minor side effects along with effectiveness against several helminths present promising aspects for the treatment[95,96]. Paromomycin (Humatin) belonging to the family aminoglycoside was first identified in 1956. It exhibited promising results against Trichomonas and *Entamoeba histolytica* and was suggested for treating resistant infections of *G. lamblia* during pregnancy[97,98]. Several chemotherapeutic agents such as sodium fusidate, rifampin, mefloquine, bithionol, pyrimethamine, hexachlorophene, and dichlorophene have exhibited efficacy against Giardia during *in vitro* studies[90,99,100]. *In vitro* studies have also revealed high activity of lipophilic tetracyclines (doxycycline), but their clinical effectiveness is limited, which might be due to the rapid intestinal absorption[101]. Azithromycin and certain pentamidine analogs have presented comparable *in vitro* activity to metronidazole[102,103].

Cryptosporidiosis: The demonstration of cryptosporidiosis antiparasitic treatment is difficult, and anti-cryptosporidial drug screening has largely remained unsuccessful in animal and *in vitro* models. Furthermore, no agent is still known to generate effective curative value in seriously immunocompromised patients. A broad-spectrum antiparasitic known as nitazoxanide (thiazole) is the only US-FDA approved drug for cryptosporidiosis treatment. It could improve microbiological and clinical cure rates to reduce disease severity and symptom duration in immunocompetent patients. *In vitro* assessments have revealed some other thiazole agents to treat *Cryptosporidium parvum*, which could serve as future drug therapy. The drug efficacy is low in HIV-infected patients, thus a combination of antiretroviral

and antiparasitic therapy might exert extra antiparasitic activity, particularly with protease inhibitors. Macrolide antibiotics (roxithromycin, azithromycin, clarithromycin, and spiramycin) are effective against Cryptosporidium to some extent. There are also unconfirmed reports about the efficacy of immunoglobulin preparations against chronic cryptosporidiosis[104].

Taeniasis: Taeniasis treatment is carried out as preventive chemotherapy according to the local situation and the control measures. A single dose of niclosamide (children over 6 years and adults: 2 g, 2–6 years old children: 1 g) or praziquantel (10 mg/kg) can treat Taeniasis. Albendazole administration (400 mg) can also be used for three consecutive days. PAHO/WHO guidelines provide important information for the preventive chemotherapy of *T. solium* taeniasis. The cyst destruction could generate an inflammatory response, which requires specialized treatments such as long courses of high albendazole and praziquantel doses, anti-epileptic drugs and corticosteroids-based supporting therapy, and surgery. The treatment duration and dosage can significantly vary according to the cyst developmental stage, size, number, location, acuteness, surrounding inflammatory edema, and severity of symptoms[105].

Diphyllobothriosis: A single medication dose can effectively treat fish tapeworm infections. Niclosamide (Niclocide) and praziquantel (Biltricide) are the main medications for treating tapeworm infections. Praziquantel can treat various worm infections by causing severe spasms in the worm's muscles so that they can be excreted with the stool. Niclosamide is specifically recommended for tapeworm infections, which kills the worm on contact. The dead worms are excreted with the stool[27].

CONTROL OF FOODBORNE PARASITES

Foodborne parasites pose a significant challenge to food safety assurance. Several medically important parasite species are chemical and freezing resistant. A comprehensive end-to-end supply chain technique has been the most successful control strategy. The method involves the application of control measures against high-risk nodes of the entire forward supply chain. Farm-oriented interventions are carried out to disrupt the parasite's life cycle before its impact on the food supply. Processing measures such as inspection, washing, and removal of defective materials are carefully undertaken. A true critical control point for parasitic disease mitigation is at the consumer level. Thorough cooking is generally an efficient control measure. For example, the cooking of pork to an internal temperature of higher than 160°F (70°C) is known to effectively control *Trichinella*. The end-user often manages this critical point. The USDA's meat cooking instructions represent the critical limits, which define critical control points. Similarly, the cooking of seafood or fish to an internal temperature higher than 140°F (60°C) inactivates most of the seafood-borne parasites. Food safety in this case is by large a consumer's responsibility as well[106].

Biosecurity mainly aims to prevent the parasite's entrance into the food chain, whereas inspection aims at the parasite or infested tissues removal from the food chain[107]. The understanding of parasite survivability in the food chain and efficient inactivation techniques are necessary tools for implementing HACCP-type food-safety concepts. In short, the control of meat- and fish-borne parasites is a shared responsibility of the authorities, producers, processors, and consumers. Public health concerns further require accurate tracing, diagnosis, and treatment of foodborne diseases. A multi-stage approach could effectively handle this situation[106].

CONCLUSION

Animal-based food products are the main route of foodborne diseases. Parasites can cause serious public health and economic problems. Despite the control measure, the issue remains troublesome for global policymakers. Different anthelmintics are applied against foodborne parasites. However, they can target specific parasitic developmental stages, which leads to therapeutic failure. Therefore, further investigations are needed to develop novel antibiotics. Furthermore, advanced diagnostic procedures, organized disease surveillance, health-based disease prevention, and effective control measures should be adopted worldwide to reduce the health burdens of parasitic diseases.

Conflict of Interest

The author declared that there is no conflict of interest that is related to this study and this article.

Disclosure

The author did not receive any form of commercial support, including compensation or financial assistance, for this case report. Additionally, the author has no financial interest in any of the products, devices, or drugs mentioned in this article.

Ethical Approval

The study was approved by the Ethics Committee of the KAUH in Jeddah, Kingdom of Saudi Arabia, also known as the Institutional Review Board of Hospitals.

REFERENCES CITED

[1] Trevisan C, Sotiraki S, Laranjo-González M, Dermauw V, Wang Z, Kärssin A, et al. Epidemiology of Taeniosis/Cysticercosis in Europe, a systematic review: Eastern Europe. 2018; 11(1): 1–11.

[2] Painter JE, Gargano JW, Collier SA, Yoder JS. Giardiasis surveillance—United States, 2011–2012. 2015; 64(3): 15–25.

[3] Gilman RH, Gonzalez AE, Llanos-Zavalaga F, Tsang VC, Garcia HH, Peru CWG in. Prevention and control of *Taenia solium* Taeniasis/Cysticercosis in Peru. 2012; 106(5): 312–8.

[4] Montazeri M, Mehrzadi S, Sharif M, Sarvi S, Shahdin S, Daryani A. Activities of anti-*Toxoplasma* drugs and compounds against tissue cysts in the last three decades (1987 to 2017), a systematic review. 2018; 117: 3045–57.

[5] Bilska-Zając E, Różycki M, Korpysa-Dzirba W, Bełcik A, Ziętek-Barszcz A, Włodarczyk-Ramus M, et al. *Trichinella* outbreaks on pig farms in Poland in 2012–2020. 2021; 10(11): 1504.

[6] Rassi A, de Rezende M. Leishmaniasis worldwide and global estimates of its incidence. 2012; 26: 275–91.

[7] Wang G, Yu Y, Wang Y, Wang J, Guan R, Sun Y, et al. Role of SCFAs in gut microbiome and glycolysis for colorectal cancer therapy. 2019; 234(10): 17023–49.

[8] Sparks H, Nair G, Castellanos-Gonzalez A, White AC. Treatment of Cryptosporidium: what we know, gaps, and the way forward. 2015; 2:181–7.

[9] Shikanai-Yasuda MA, Carvalho NB. Oral transmission of Chagas disease. 2012; 54(6): 845–52.

[10] Reynoldson JA, Thompson R, Horton RJ. Albendazole as a future antigiardial agent. 1992; 8(12): 412–4.

[11] Felício MDS, Hald T, Liebana E, Allende A, Hugas M, Nguyen-The C, et al. Risk ranking of pathogens in ready-to-eat unprocessed foods of non-animal origin (FoNAO) in the EU: initial evaluation using outbreak data (2007–2011). 2015; 195:9–19.

[12] Ahmed SA, Karanis P. *Cryptosporidium* and Cryptosporidiosis: the perspective from the Gulf countries. 2020; 17(18): 6824.

[13] Farthing M. *Giardia* comes of age: progress in epidemiology, immunology, and chemotherapy. 1992; 30(5): 563–666.

[14] Havelaar AH, Kirk MD, Torgerson PR, Gibb HJ, Hald T, Lake RJ, et al. World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. 2015; 12(12): e1001923.

[15] McClung RP, Roth DM, Vigar M, Roberts VA, Kahler AM, Cooley LA, et al. Waterborne disease outbreaks associated with environmental and undetermined exposures to water—United States, 2013–2014. 2017; 66(44): 1222.

[16] Horlock-Roberts K, Reaume C, Dayer G, Ouellet C, Cook N, Yee J. Drug-free approach to study the unusual cell cycle of *Giardia intestinalis*. 2017; 2(5): e00384-16.

[17] Gillis JC, Wiseman LR. Secnidazole: a review of its antimicrobial activity, pharmacokinetic properties, and therapeutic use in the management of protozoal infections and bacterial vaginosis. 1996; 51: 621–38.

[18] Lee H, Yoon Y. Etiological agents implicated in foodborne illness worldwide. 2021; 41(1): 1.

[19] Alban L, Häsler B, van Schaik G, Ruegg S. Risk-based surveillance for meat-borne parasites. 2020; 208: 107808.

[20] Bouwknegt M, Devleesschauwer B, Graham H, Robertson LJ, van der Giessen JW. Prioritisation of food-borne parasites in Europe, 2016. 2018; 23(9): 17–00161.

[21] DARBON A, GIRIER L, LECLAIRE C, Pantin J, PORTAL A. Traitement de la giardiase (lambliase) par le métronidazole-A propos de cent observations. 1962; 70(1): 15.

[22] Ryan U, Hijjawi N, Feng Y, Xiao L. *Giardia*: an under-reported foodborne parasite. 2019; 49(1): 1–11.

[23] Tracy JW. Drugs used in the chemotherapy of protozoal infections. 1996; 965–85.

[24] Hernández-Orts JS, Kuzmina TA, Gomez-Puerta LA, Kuchta R. *Diphyllobothrium sprakeri n. sp. (Cestoda: Diphyllobothriidae)*: a hidden broad tapeworm from sea lions off North and South America. 2021; 14(1): 219.

[25] Ryan U, Hijjawi N, Xiao L. Foodborne Cryptosporidiosis. 2018; 48(1): 1–12.

[26] Rostami A, Gamble HR, Dupouy-Camet J, Khazan H, Bruschi F. Meat sources of infection for outbreaks of human Trichinellosis. 2017; 64: 65–71.

[27] Ortega YR, Sterling CR. Foodborne parasites. Springer; 2018.

[28] Hill DR. Giardiasis: Issues in management and treatment. 1993; 7: 503–25.

[29] Upcroft J, Upcroft P. My favorite cell: *Giardia*. 1998; 20(3): 256–63.

[30] Bin Dajem SM, Almushait MA. Detection of *Toxoplasma gondii* DNA by PCR in blood samples collected from pregnant Saudi women from the Aseer region, Saudi Arabia. 2012; 32(5): 507–12.

[31] Pavel R, Ursoniu S, Paduraru AA, Lighezan R, Lupu MA, Olariu TR. Seroprevalence and risk factors of trichinella spiralis infection in blood donors from Western Romania. 2022; 58(1): 128.

[32] Jiang P, Zhang X, Wang LA, Han LH, Yang M, Duan JY, et al. Survey of *Trichinella* infection from domestic pigs in the historical endemic areas of Henan province, central China. 2016; 115: 4707–9.

[33] Moazeni M, Khamesipour F, Anyona DN, Dida GO. Epidemiology of Taeniasis, Cysticercosis and Trichinellosis in Iran: A systematic review. 2019; 66(1): 140–54.

[34] Kuruca L, Belluco S, Vieira-Pinto M, Antic D, Blagojevic B. Current control options and a way towards risk-based control of *Toxoplasma gondii* in the meat chain. 2023; 146: 109556.

[35] de la Torre-Iglesias PM, García-Rodriguez JJ, Torrado G, Torrado S, Torrado-Santiago S, Bolás-Fernández F. Enhanced bioavailability, and anthelmintic efficacy of mebendazole in re-dispersible microparticles with low-substituted hydroxypropylcellulose. 2014; 1467–79.

[36] Karanis P, Kourenti C, Smith H. Waterborne transmission of protozoan parasites: a worldwide review of outbreaks and lessons learnt. 2007; 5(1): 1–38.

[37] Townson SM, Hanson GR, Upcroft JA, Upcroft P. A purified ferredoxin from *Giardia duodenalis*. 1994; 220(2): 439–46.

[38] Mukaratirwa S, La Grange L, Pfukenyi DM. *Trichinella* infections in animals and humans in sub-Saharan Africa: a review. 2013; 125(1): 82–9.

[39] Feng Y, Xiao L. Zoonotic potential and molecular epidemiology of *Giardia* species and giardiasis. 2011; 24(1): 110–40.

[40] Porter SB, Sande MA. Toxoplasmosis of the central nervous system in the acquired immunodeficiency syndrome. 1992; 327(23): 1643–8.

[41] Rajapakse S, Chrishan Shivanthan M, Samaranayake N, Rodrigo C, Deepika Fernando S. Antibiotics for human Toxoplasmosis: a systematic review of randomized trials. 2013; 107(4): 162–9.

[42] Li X, Ma W, Ma Z, Zhang Q, Li H. The occurrence and contamination level of ochratoxin A in plant and animal-derived food commodities. 2021; 26(22): 6928.

[43] Torgerson PR. One world health: socioeconomic burden and parasitic disease control priorities. 2013; 195(3–4): 223–32.

[44] Gonzalez A, Thomas L. Taenia spp. 2019.

[45] Boreham P, Phillips RE, Shepherd RW. Altered uptake of metronidazole in vitro by stocks of Giardia intestinalis with different drug sensitivities. 1988; 82(1): 104–6.

[46] Devleesschauwer B, Allepuz A, Dermauw V, Johansen MV, Laranjo-González M, Smit GSA, et al. *Taenia solium* in Europe: Still endemic. 2017; 165: 96–9.

[47] Lau AH, Lam NP, Piscitelli SC, Wilkes L, Danziger LH. Clinical pharmacokinetics of metronidazole and other nitroimidazole anti-infectives. 1992; 23: 328–64.

[48] Ben Hassen T, El Bilali H. Food security in the Gulf Cooperation Council countries: Challenges and prospects. J. 2019; 7: 159–69.

[49] Franceschelli A, Bonadonna L, Cacciò SM, Sannella AR, Cintori C, Gargiulo R, et al. An outbreak of cryptosporidiosis associated with drinking water in north-eastern Italy, August 2019: microbiological and environmental investigations. 2022; 27(35): 2200038.

[50] Hussain MA, Stitt V, Szabo EA, Nelan B. *Toxoplasma gondii* in the Food Supply. 2017; 6(2): 21.

[51] Plaza J, Dámek F, Villena I, Innes EA, Katzer F, Hamilton CM. Detection of *Toxoplasma gondii* in retail meat samples in Scotland. 2020; 20: e00086.

[52] Einarsson E, Ma'ayeh S, Svärd SG. An up-date on *Giardia* and Giardiasis. 2016; 34: 47–52.

[53] Havelaar AH, Haagsma JA, Mangen M-JJ, Kemmeren JM, Verhoef LP, Vijgen SM, et al. Disease burden of foodborne pathogens in the Netherlands, 2009. 2012; 156(3): 231–8.

[54] Ducrocq J, Simon A, Lemire M, De Serres G, Lévesque B. Exposure to *Toxoplasma gondii* through consumption of raw or undercooked meat: a systematic review and meta-analysis. 2021; 21(1): 40–9.

[55] Ahmed SA, Karanis P. An overview of methods/techniques for the detection of Cryptosporidium in food samples. 2018; 117(3): 629–53.

[56] Holubová N, Zikmundová V, Limpouchová Z, Sak B, Konečný R, Hlásková L, et al. Cryptosporidium proventriculi sp. n.(Apicomplexa: *Cryptosporidiidae*) in Psittaciformes birds. 2019; 69: 70–87.

[57] Ren HJ, Liu RD, Wang ZQ, Cui J. Construction, and use of a *Trichinella spiralis* phage display library to identify the interactions between parasite and host enterocytes. 2013; 112: 1857–63.

[58] Gagliardo LF, McVay CS, Appleton JA. Molting, ecdysis, and reproduction of *Trichinella spiralis* are supported in vitro by intestinal epithelial cells. 2002; 70(4): 1853–9.

[59] Khalil IA, Troeger C, Rao PC, Blacker BF, Brown A, Brewer TG, et al. Morbidity, mortality, and long-term consequences associated with diarrhoea from Cryptosporidium infection in children younger than 5 years: a meta-analyses study. 2018; 6(7): e758–68.

[60] Ramanan P, Blumberg AK, Mathison B, Pritt BS. Parametrial anisakidosis. 2013; 51(10): 3430–4.

[61] Farthing M, Inge P. Antigiardial activity of the bile salt-like antibiotic sodium fusidate. 1986; 17(2): 165–71.

[62] Edlind TD. Tetracyclines as antiparasitic agents: lipophilic derivatives are highly active against *Giardia lamblia in vitro*. 1989; 33(12): 2144–5.

[63] Edwards DI. Nitroimidazole drugs-action and resistance mechanisms I. Mechanism of action. 1993; 31(1): 9–20.

[64] Liu RD, Cui J, Liu XL, Jiang P, Sun GG, Zhang X, et al. Comparative proteomic analysis of surface proteins of *Trichinella spiralis* muscle larvae and intestinal infective larvae. 2015; 150: 79–86.

[65] Baldursson S, Karanis P. Waterborne transmission of protozoan parasites: review of worldwide outbreaks–an update 2004–2010. 2011; 45(20): 6603–14.

[66] Zhuo TX, Wang Z, Song YY, Yan SW, Liu RD, Zhang X, et al. Characterization of a novel glutamine synthetase from *Trichinella spiralis* and its participation in larval acid resistance, molting, and development. 2021; 9: 729402.

[67] Jones JL, Ogunmodede F, Scheftel J, Kirkland E, Lopez A, Schulkin J, et al. Toxoplasmosis-related knowledge and practices among pregnant women in the United States. 2003; 11(3): 139–45.

[68] Bell CA, Cory M, Fairley TA, Hall JE, Tidwell RR. Structure-activity relationships of pentamidine analogs against *Giardia lamblia* and correlation of antigiardial activity with DNA-binding affinity. 1991; 35(6): 1099–107.

[69] Hajj RE, Tawk L, Itani S, Hamie M, Ezzeddine J, El Sabban M, et al. Toxoplasmosis: Current and emerging parasite druggable targets. 2021; 9(12): 2531.

[70] Sasinowski FJ. Quantum of effectiveness evidence in FDA's approval of orphan drugs. 2012; 46(2): 238–63.

[71] Liu LX, Weller PF. Antiparasitic drugs. 1996; 334(18): 1178–84.

[72] Scholz T, Kuchta R. Fish-borne, zoonotic cestodes (*Diphyllobothrium* and relatives) in cold climates: a never-ending story of neglected and (re)-emergent parasites. 2016; 4: 23–38.

[73] Jansen F, Dorny P, Trevisan C, Dermauw V, Laranjo-González M, Allepuz A, et al. Economic impact of bovine cysticercosis and taeniosis caused by Taenia saginata in Belgium. 2018; 11:1–10.

[74] Kreutner AK, Del Bene VE, Amstey MS. Giardiasis in pregnancy. 1981; 140(8): 895–901.

[75] Vieira FP, Alves M da G, Martins LM, Rangel ALP, Dubey JP, Hill D. Waterborne toxoplasmosis investigated and analysed under hydrogeological assessment: new data and perspectives for further research. 2015; 110: 929–35.

[76] Dimzas D, Diakou A, Koutras C, Morales MG, Psalla D, Keryttopoulos P, et al. Human trichinellosis caused by *Trichinella britovi* in Greece, and literature review. 2020; 94: e33.

[77] Scholz T, Garcia HH, Kuchta R, Wicht B. Update on the human broad tapeworm (genus *Diphyllobothrium*), including clinical relevance. 2009; 22(1): 146–60.

[78] Hughes JM, Colley DG, Lopez A, Dietz VJ, Wilson M, Navin TR, et al. Preventing congenital Toxoplasmosis. 2000; 57–75.

[79] Efstratiou A, Ongerth JE, Karanis P. Waterborne transmission of protozoan parasites: review of worldwide outbreaks-an update 2011–2016. 2017; 114: 14–22.

[80] Paget TA, Jarroll EL, Manning P, Lindmark DG, Lloyd D. Respiration in the cysts and trophozoites of *Giardia muris*. 1989; 135(1): 145–54.

[81] Ren HJ, Cui J, Wang ZQ, Liu RD. Normal mouse intestinal epithelial cells as a model for the in vitro invasion of *Trichinella spiralis* infective larvae. 2011; 6(10): e27010.

[82] Jansen AM, Xavier SC das C, Roque ALR. *Trypanosoma cruzi* transmission in the wild and its most important reservoir hosts in Brazil. 2018; 11(1): 1–25.

[83] Blagojevic B, Robertson LJ, Vieira-Pinto M, Johansen MV, Laranjo-González M, Gabriël S. Bovine cysticercosis in the European Union: impact and current regulations, and an approach towards risk-based control. 2017; 78: 64–71.

[84] Robertson LJ, Lalle M, Paulsen P. Why we need a European focus on foodborne parasites. 2020; 214: 107900.

[85] Feng Y, Ryan UM, Xiao L. Genetic diversity, and population structure of Cryptosporidium. 2018; 34(11): 997–1011.

[86] Dorny P, Praet N. Taenia saginata in Europe. 2007; 149(1–2): 22–4.

[87] Kopacz Ż, Kváč M, Karpiński P, Hendrich AB, Sąsiadek MM, Leszczyński P, et al. The first evidence of Cryptosporidium meleagridis infection in a colon adenocarcinoma from an immunocompetent patient. 2019; 9: 35.

[88] Takeuchi T, Kobayashi S, Tanabe M, Fujiwara T. In vitro inhibition of Giardia lamblia and Trichomonas vaginalis growth by bithionol, dichlorophene, and hexachlorophene. 1985; 27(1): 65–70.

[89] Da Silva NN, Clausell DT, Nólibos H, de Mello AL, Ossanai J, Rapone T, et al. Surto epidêmico de doença de Chagas com provável contaminação oral. 1968; 10(5): 265–76.

[90] Al-Yami FS, Dar FK, Yousef AI, Al-Qurouni BH, Al-Jamea LH, Rabaan AA, et al. A pilot study on screening for gestational/congenital Toxoplasmosis of pregnant women at delivery in the Eastern Province of Saudi Arabia. 2021; 29(4): 343–50.

[91] Waki K, Takahashi S, Oi H, Nakabayashi T, Kitani T. Successful treatment of Diphyllobothrium latum and Taenia saginata infection by intraduodenal'Gastrografin'injection. 1986; 328(8516): 1124–6.

[92] Samuelson J. Why metronidazole is active against both bacteria and parasites. 1999; 43(7): 1533–41.

[93] Laranjo-González M, Devleesschauwer B, Gabriël S, Dorny P, Allepuz A. Epidemiology, impact, and control of bovine Cysticercosis in Europe: a systematic review. 2016; 9(1): 1–12.

[94] Lindsay DS, Dubey JP. Toxoplasma gondii: the changing paradigm of congenital Toxoplasmosis. 2011; 138(14) 1829–31.

[95] Cui J, Jiang P, Liu LN, Wang ZQ. Survey of *Trichinella* infections in domestic pigs from northern and eastern Henan, China. 2013; 194(2–4): 133–5.

[96] McLeod R, Boyer K, Karrison T, Kasza K, Swisher C, Roizen N, et al. Outcome of treatment for congenital toxoplasmosis, 1981–2004: the national collaborative Chicago-based, congenital toxoplasmosis study. 2006; 42(10): 1383–94.

[97] Stollberg KC, Schares G, Mayer-Scholl A, Hrushetska I, Diescher S, Johne A, et al. Comparison of direct and indirect *Toxoplasma gondii* detection and genotyping in game: relationship and challenges. 2021; 9(8): 1663.

[98] Venkatesan P. Albendazole. 1998; 41(2): 145–7.

[99] Khalikov SS. Solid Dispersions of Anthelmintics and Plant Protection Preparations. 2021; 2(1): 60–75.

[100] Bruschi F, Dupouy-Camet J. Helminth infections and their impact on global public health. Springer; 2014.

[101] Gerace E, Presti VDML, Biondo C. Cryptosporidium infection: epidemiology, pathogenesis, and differential diagnosis. 2019; 9(4): 119–23.

[102] Lee H, Yoon Y. Etiological agents implicated in foodborne illness worldwide. 2021; 41(1): 1.

[103] Petersen E, Vesco G, Villari S, Buffolano W. What do we know about risk factors for infection in humans with *Toxoplasma gondii* and how can we prevent infections. 2010; 57(1): 8–17.

[104] Marín-García P-J, Planas N, Llobat L. Toxoplasma gondii in Foods: Prevalence, Control, and Safety. 2022; 11(16): 2542.

[105] Hadjilouka A, Tsaltas D. *Cyclospora cayetanensis*—Major outbreaks from ready to eat fresh fruits and vegetables. 2020; 9(11): 1703.

[106] Dadonaite B, Ritchie H, Roser M. Diarrheal diseases. 2018.

[107] Boreham P, Upcroft JA. The activity of azithromycin against stocks of *Giardia intestinalis* in vitro and in vivo. 1991; 85(5): 620–1.