# Toxoplasmosis

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## ABSTRACT

Toxoplasmosis, caused by the globally prevalent parasite Toxoplasma gondii, features a complex life cycle involving both sexual and asexual reproduction, utilizing cats as definitive hosts. The parasite's genetic diversity, diverse transmission routes, and potential impact on human reproductive function underscore the need for further research to elucidate its epidemiological significance and the relative importance of different transmission pathways. In 1908, Nicolle and Manceaux's discovery of T. gondii in a Tunisian gundi was pivotal for toxoplasmosis research, shaping the nomenclature based on its coccidian-like structure. Toxoplasmosis imposes significant economic losses on the food industry, leading to costly recalls and an annual financial impact of 7.7 billion USD in the United States. The disease, primarily transmitted through T. gondii oocysts or tissue cysts, poses varied clinical risks, with asymptomatic or mild symptoms in some, but severe manifestations in high-risk populations, underscoring the importance of preventive measures and timely medical intervention. Toxoplasmosis, challenging to diagnose due to diverse clinical presentations, is managed through crucial laboratory tests like serology, PCR, and immunohistochemistry, with ongoing research emphasizing improved diagnostics and treatment outcomes. Treatment strategies vary, with spontaneous resolution in healthy individuals and a combination therapy involving pyrimethamine, sulfadiazine, and leucovorin/folinic acid for severe cases, highlighting preventive measures, including proper hygiene and public health education, to reduce T. gondii transmission and infection risks. Ongoing research targets enhanced diagnostics, vaccine development, novel therapeutics, and deeper insights into T. gondii biology, aiming to alleviate the disease burden and inform effective control measures for both human and animal populations.

**Keywords:** Toxoplasma gondii, Epidemiological significance.

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## 1. INTRODUCTION

Toxoplasmosis is a common parasitic disease affecting animals and humans worldwide. Toxoplasma gondii (T. gondii) is a protozoan parasite causing toxoplasmosis (Mehnaz et al. 2019). It's an obligatory intracellular organism, belongs to the phylum Apicomplexa (Besteiro 2014). T. gondii is genetically diverse with 15 distinct genotypes, differing in virulence, tissue tropism, and distribution. (Gibson et al. 2011). The life cycle of T. gondii is complex, with both sexual and asexual reproduction. It requires two host species: the definitive host, usually a cat, and the intermediate host, which can be various warm-blooded animals, including humans (Zúquete et al. 2022). Inside the definitive host (typically a cat), T. gondii undergoes sexual reproduction, resulting in the production of oocysts excreted in the cat's feces. These oocysts can survive in the environment for extended periods, ranging from months to years. Intermediate hosts can be infected by consuming contaminated food or water containing these oocysts (Maier et al. 2019). After entering an intermediate host, T. gondii multiplies asexually and forms cysts in organs like the brain, eyes, and muscles. Infection can occur in humans and other warm-blooded animals by consuming undercooked or raw meat with tissue cysts from infected animals. Ingesting oocysts from contaminated food, water, or soil can also cause T. gondii infection (Hill and Dubey 2018).

T. gondii, is a versatile protozoan that can infect various host species and has evolved multiple transmission routes within and between them (Kagira et al. 2020). When T. gondii is initially contracted during pregnancy, the parasite can be vertically transmitted to the fetus through the placenta, carried by tachyzoites (Agarwal et al. 2022). T. gondii can spread from one animal to another in three different ways during its life cycle. First, animals can get infected by swallowing infectious oocysts found in the environment. Second, they can become infected by eating the meat or organs of other animals containing tissue cysts or tachyzoites (AM and Health 2017). Furthermore, transmission can also occur when tachyzoites are present in blood products, tissue transplants, or unpasteurized milk (Iano et al. 2019). The relative importance of these routes in the epidemiology of the disease is currently unknown (Farahani et al. 2020). T.gondii. In intensive farm management areas a notable decrease in the occurrence of T. gondii was observed in animals raised for meat production (Kagira et al. 2020).

Toxoplasmosis is known for its capability to infect a wide variety of animal species, including birds, rodents, livestock, and even marine mammals (El Fadaly et al. 2022). Research has shown that T. gondii infection can have an impact not only on female reproduction but also on male reproductive function, causing impairment (Xu et al. 2022). Clinical studies have reported a notably high prevalence of toxoplasmosis among infertile men (Mishra et al. 2022). Additionally, there are indications of venereal transmission of T. gondii (Hlaváčová et al. 2023). T.gondii. It can also affect various hormones, potentially leading to insufficient male reproductive function (Dalimi and Abdoli 2013).

## 2. HISTORY

In 1908, Nicolle and Manceaux described *T. gondii* in Tunis, identifying it in the gundi's tissues. Nicolle named the infectious organism *T. gondii* based on its coccidian-like structure, marking a crucial milestone in the study of toxoplasmosis (Cox 2002). In 1939, Wolf, Cowen, and Paige established *T.*

*gondii* as a causative agent of human disease. Additionally, its medical significance became evident when it was found in the tissues of a congenitally infected infant (Keohane et al. 2020). In 1948, a major breakthrough came with the Sabin-Feldman dye test, a specific antibody test for *T. gondii* It helped identify the parasite as widespread among warm-blooded hosts worldwide. Similarly, in 1957, *T. gondii* significance was acknowledged in the veterinary community due to its involvement in sheep abortion outbreaks. These discoveries were pivotal in understanding the importance of *T. gondii* (Ferguson 2022). Around the same period, Splendore identified the presence of *T. gondii* in the tissues of a rabbit in Brazil (Dubey 2020).

However, it was not until 1970 that scientists fully elucidated the life cycle of the parasite. During this period, they discovered that felids, including cats, act as the definitive host for *T. gondii* (Iano et al. 2019). Recent research found *T. gondii* infections in marine wildlife, like sea otters, indicating contamination from land-washed oocysts. This raises concerns about the environmental impact and parasite transmission (Bahia-Oliveira et al. 2019).

## 3. ECONOMIC IMPACT

Toxoplasmosis creates a substantial economic burden on healthcare systems due to high costs for diagnosis, treatment, and complication management. Additionally, the disease impacts the food industry's economy, as *T. gondii*contaminated meat products can lead to costly recalls, financial losses, and reduced revenue for businesses involved in their production and distribution (Basso et al. 2019). Economic loss of 7.7 billion USD annually has been recorded in united states of America (Kruszon-Moran et al. 2001).

## 3. LIFE CYCLE

Until 1970, only the asexual stages of *T. gondii*, including tachyzoites, trophozoites, bradyzoites and cystozoites, were documented (Wu et al. 2021). The documentation of the sexual cycle of *T. gondii* and the discovery of its environmentally resistant stage, the oocyst stage, were first reported in 1970 (Francia et al. 2020). After ingestion, Toxoplasma parasite multiplies rapidly as tachyzoites during the acute phase, then establishes in various organs. *T. gondii* has three infectious stages: tachyzoites, bradyzoites, and sporozoites (Lüder and Rahman 2017). Humans and animals mainly get infection by consuming bradyzoite or oocyst stage of the cycle. After ingestion, bradyzoites and sporozoites transform into tachyzoites in the body's tissues. Interconversion between tachyzoites and bradyzoites is critical, as bradyzoites are more resistant to drugs, and reactivation into tachyzoites causes severe toxoplasmosis in AIDS patients (Ashander et al. 2021). Following infection with any infective stage, tachyzoites multiply in various cells and eventually encyst in tissues, especially the brain (Hill and Dubey 2018). Tissue cysts can persist within the host for extended periods, possibly throughout their life span. One hypothesis proposes that these cysts may occasionally rupture, releasing bradyzoites. In immunocompetent hosts, the immune system is believed to effectively eliminate these released bradyzoites (Blanchard et al. 2020). Immunosuppressed individuals may experience multiplication and spread of bradyzoites released from tissue cysts to other organs. The exact mechanism of toxoplasmosis reactivation remains unclear. It is uncertain if bradyzoites from older cysts can directly form new cysts or if they first need transition through the tachyzoite stage (Guegan et al. 2019). Bradyzoites are more resistant to chemotherapy than tachyzoites, making their fate in host tissues clinically important. Different criteria are used to distinguish between tachyzoites and bradyzoites (Wang et al. 2022). Tachyzoites have a centrally located nucleus and few or no PAS-positive granules, mainly seen during the acute infection phase. Bradyzoites have a terminally located nucleus,

numerous PAS-positive granules, and are enclosed in a resilient cyst wall, mostly found during the chronic infection phase. However, the transitional stages and reverse transformation between tachyzoites and bradyzoites lack clearly defined structural characteristics or antigenic properties (Dubey 2020).
Felines, acting as definitive hosts, can get infected by carnivorous feeding (consuming mammals and birds) or ingesting sporulated oocysts. Oocysts can remain infectious in mussels. Although rare, the consumption of unpasteurized milk or milk products can be a potential source of transmission (Teixeira et al. 2020). After consuming Toxoplasma oocysts excreted by cats, the parasite forms tissue cysts that persist within the body for extended periods, often throughout the host's life. These cysts are commonly found in tissues like the heart, skeletal muscles and central nervous system. If an animal infected with Toxoplasma is eaten, viable parasites present in the tissues can transmit the infection to a new host (Hill and Dubey 2018) (Fig. 1).

## 4.TRANSMISSION

Toxoplasmosis is mainly a zoonotic disease, meaning it can be transmitted between animals and humans. The primary mode of transmission for *T. gondii*, the parasite causing toxoplasmosis, is through ingesting the parasite's oocysts or tissue cysts (Kagira et al. 2020). Oocysts are shed in the feces of cats infected with

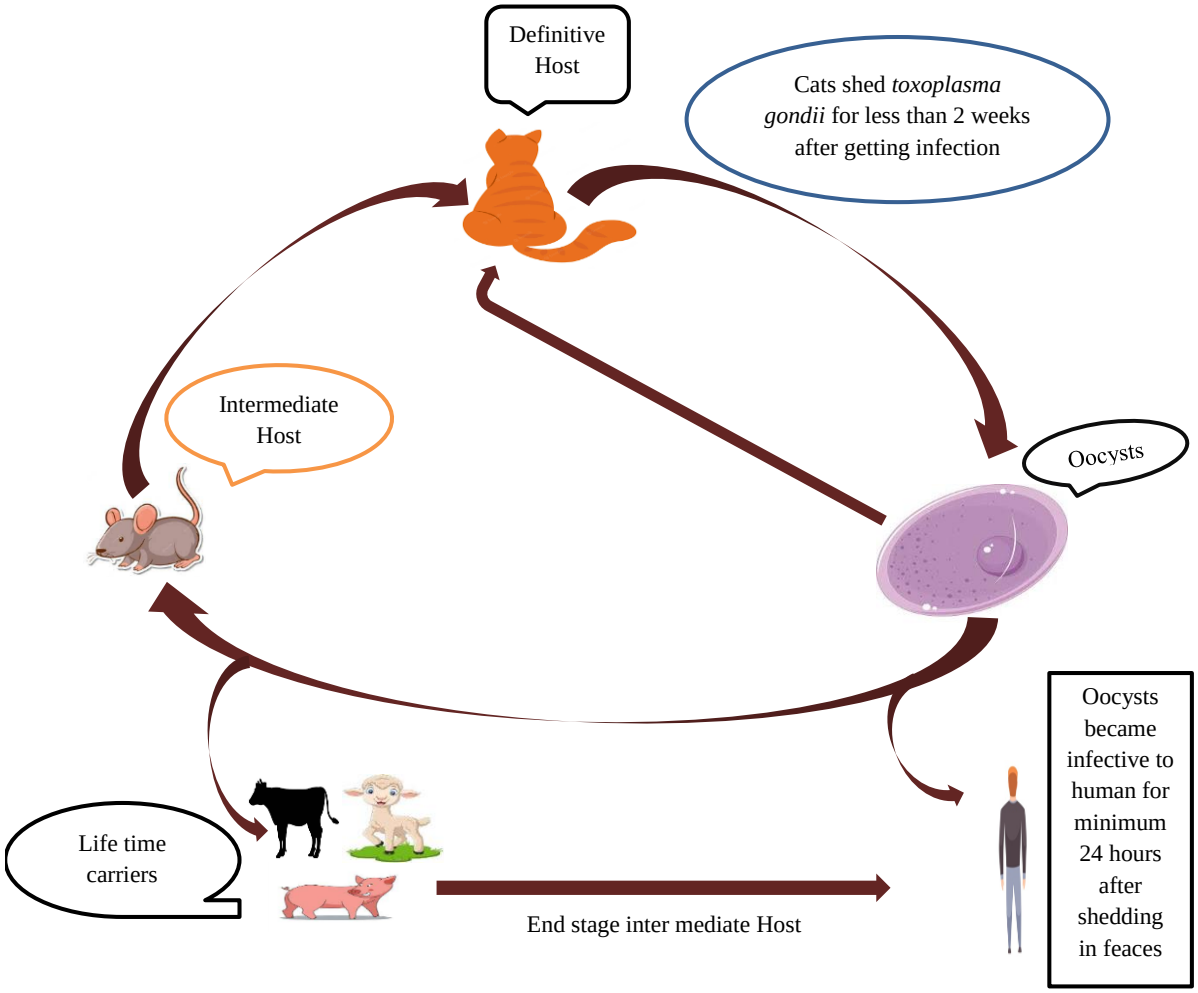


**Fig. 1:** Life cycle and one health.

*T.gondii*, the parasite's definitive host. These oocysts can persist in the environment for months to years, depending on factors like temperature and humidity (Bahia-Oliveira et al. 2019). Humans can contract *T.gondii* infection by accidentally ingesting oocysts found in contaminated soil, water, or food. Vegetables grown in oocyst-contaminated soil or meat contaminated during processing can be sources of infection (Chaudhry et al. 2022). Intermediate hosts, including rodents, livestock, and marine mammals, can acquire *T. gondii* infection by ingesting oocysts from contaminated soil or water, or by consuming tissue cysts in infected meat (Graziosi et al. 2023). Humans can get *T. gondii* infection by eating undercooked or raw meat from infected animals. Consuming unpasteurized dairy products like milk and cheese from infected animals can also lead to its transmission. However, transmission through organ transplantation or blood transfusion from an infected donor is relatively rare (Graziosi et al. 2023). Congenital transmission of *T. gondii* can occur when a pregnant woman gets infected with the parasite during pregnancy. The parasite can cross the placenta and infect the developing fetus, leading to severe complications like miscarriage, stillbirth, or birth defects (Graziosi et al. 2023).

## 5.CLINICAL PRESENTATION IN HUMANS

Clinical signs of toxoplasmosis in humans vary based on age, immune status, and parasite transmission route. With a healthy immune system, the infection may go unnoticed or cause mild flu-like symptoms like fever, headache, and muscle aches that usually resolve in a few weeks (Al-Malki 2021). In 2017, the Wisconsin Department of Health Services, Division of Public Health, investigated a febrile illness outbreak among retreat attendees who consumed intentionally undercooked, locally sourced venison. The investigation was prompted by a physician's report, and preliminary testing suggested a potential link to toxoplasmosis (Elbadawi et al. 2021).*T. gondii* infection is primarily influenced by the individual's immune status. In immunocompetent individuals, infections are usually asymptomatic, with lifelong latent infection (Fong et al. 2021). While most healthy people with *T. gondii* infection show no symptoms, a few may experience fever, malaise, and swollen lymph nodes.

Severe or life-threatening illnesses can rarely occur from infections caused by virulent parasite strains (Aga et al. 2020). Around 2% of healthy individuals may experience retinochoroiditis, inflammation of the retina and choroid. *T. gondii* can cause ocular disease congenitally or after birth, leading to symptoms like acute retinochoroiditis with pain, photophobia, tearing, and vision loss. Recurrent episodes can follow the acute phase (Choi et al. 2018). Immunocompromised individuals, like those with HIV/AIDS or organ transplantation, may face severe and life-threatening *T. gondii* infection. The parasite can cause encephalitis (brain inflammation), leading to neurological symptoms like seizures, confusion, and behavioral changes (Marra et al. 2020).

Congenital *T. gondii* infection can result in diverse manifestations in infants, such as hydrocephalus, microcephaly, cerebral calcifications, retinochoroiditis, blindness, epilepsy, motor retardation, and anemia (Khan and Khan 2018). Emerging evidence associates *T. gondii* infection with neuropsychiatric disorders. Studies show higher *T. gondii* antibodies prevalence in some neuropsychiatric patients, but more research is needed to understand the association's nature and mechanisms (Liesenfeld et al. 2011). Toxoplasmosis in pregnant women can cause congenital infection with severe consequences like fetal death, stillbirth, or long-term neurological and developmental complications in infants. Pregnant women should take preventive measures and seek prompt medical care if they suspect exposure to *T. gondii* (Dehority et al. 2020).

## 6. DIAGNOSIS

The severity of congenital toxoplasmosis depends on the timing of infection during pregnancy, with early infections associated with more significant complications. Pregnant women infected with *T. gondii* may

not show symptoms but can still transmit the infection to their fetuses, resulting in severe consequences for the developing baby (Rostami et al. 2018). Diagnosing toxoplasmosis can be challenging due to its varied clinical presentation. The wide range of possible symptoms and some cases having no symptoms or self-limited manifestations contribute to the complexity (Guarnera et al. 2022). Laboratory tests are vital for confirming toxoplasmosis. Serologic testing detects antibodies to *T. gondii*, while PCR testing detects the parasite's DNA, aiding in accurate diagnosis and confirmation (Ozgonul and Besirli 2016). Toxoplasmosis shows diverse clinical presentations, from asymptomatic to severe and life-threatening. Accurate diagnosis and timely treatment are crucial to minimize complications and improve patient outcomes (Gajurel et al. 2018).

Diagnosis of toxoplasmosis can be challenging due to nonspecific symptoms and potential delays in onset after initial infection. Various laboratory tests, including serological techniques, are available for diagnosing toxoplasmosis (L'ollivier et al. 2019). Extensivly serological techniques are used to diagnose toxoplasmosis, considering diverse clinical and immunologic characteristics. Ongoing efforts aim to further improve these methods (Schlüter et al. 2014). Recent progress in serological diagnosis of toxoplasmosis includes identifying novel immunogenic proteins and innovative antigen production. Incorporating recombinant antigens and multiepitope chimeric peptides has notably enhanced serological diagnostic methods (Ahmadpour et al. 2020)

Serotyping offers a less invasive alternative to genotyping, characterizing different parasite lineages. It has become the preferred method for toxoplasmosis diagnosis due to widespread usage (Pitt 2018). Serological tests measure *T. gondii* antibodies in the bloodstream, mainly IgG and IgM. IgG antibodies indicate a past infection (Mohtasebi et al. 2020), IgM antibodies are found in acute infections, while IgG antibodies indicate chronic infections. Both IgG and IgM antibodies together suggest an acute infection (Fricker-Hidalgo et al. 2016).

The PCR test is used to detect *T. gondii* DNA in bodily fluids like blood, cerebrospinal fluid, and amniotic fluid. It is important for diagnosing acute infections and monitoring treatment effectiveness (Karanis et al. 2018). Researchers have developed a DNA-based assay to identify *T. gondii* using PCR. The PCR technique amplifies a segment of the parasite's DNA, specifically the P30 gene. Following gel electrophoresis, the amplified DNA can be detected directly on the gel or via Southern hybridization using either radioactive or non-radioactive DNA probes (Hemphill et al. 2022). The assay has successfully detected *T. gondii* DNA in various isolates, even when combined with human or mouse DNA. When combined with clinical data, CT scans, and serology, PCR assay is expected to enhance toxoplasmosis diagnosis in immunosuppressed, immunocompromised patients, and fetal tissues (Wang et al. 2015).

The Immunohistochemistry (IHC) test is commonly used to identify *T. gondii* in tissue samples, especially when there is a suspicion of congenital toxoplasmosis, as the parasite may be present in the placenta or fetal tissue (Harrison 2000; Nurcahyo et al. 2017). To confirm diagnosis and assess parasite dissemination in different tissues, Immunohistochemistry (IHC) was conducted for *T. gondii* on formalin-fixed, paraffin-embedded (FFPE) tissues (Bauer et al. 2021).

Cultivating *T. gondii* in a lab is a specific test, but it is not commonly used for toxoplasmosis diagnosis due to slow parasite growth and the need for specialized facilities (Brenier-Pinchart et al. 2021). MRI and CT scans can be used alongside lab tests to identify *T. gondii* in the brain or other organs, serving as additional diagnostic tools for infection detection (Karanis et al. 2018).

## 7. TREATMENT

The treatment approach for toxoplasmosis is determined by factors such as infection severity and the individual's health condition. Treatment is adapted to ensure effective management (Al-Malki 2021). In

healthy individuals, treatment may not be necessary as the infection can be cured spontaneously. However, for weakened immune system patients, pregnant women, a combination therapy of pyrimethamine, sulfadiazine, and leucovorin or folinic acid is the typical first-line treatment to combat the infection and manage symptoms (Goodwin et al. 2017).

Pyrimethamine, a folate antagonist, is used to treat active toxoplasmosis in combination with medications like sulfadiazine or clindamycin. It effectively inhibits *T. gondii* proliferation by targeting the folate metabolic pathway in a synergistic action with sulfadiazine (Aspöck 2000). Sulfadiazine, a sulfa drug, is used in combination with pyrimethamine to treat active toxoplasmosis. It inhibits the growth of *T. gondii* and is commonly used as an additive drug in the treatment of ocular toxoplasmosis (Verbraak et al. 2002). Clindamycin, an antibiotic, is combined with pyrimethamine to treat active toxoplasmosis. It inhibits the growth of *T. gondii*. Spiramycin, an antibiotic, is used to treat toxoplasmosis in pregnant women. It prevents the replication of *T. gondii* in the placenta and fetus. Spiramycin crosses the placenta, diffusing into cord blood and amniotic fluid, concentrating in placental tissue. Pharmacokinetics have been documented during the second and third trimesters. Administering spiramycin during pregnancy significantly reduces the risk of fetal infection.

## 8.PREVENTION AND CONTROL

Preventive measures include avoid eating undercooked meat, practicing good hygiene, and preventing contact with cat feces or contaminated soil. Routine screening for toxoplasmosis in pregnant women is recommended to reduce the risk of congenital toxoplasmosis. Preventive measures are vital in controlling toxoplasmosis and minimizing health complications (Longcore et al. 2019).

*T. gondii* can be found in raw or undercooked meat, particularly in pork, lamb, and venison. To lower the infection risk, cook meat to a safe temperature (at least 160°F for ground meat and 145°F for whole cuts) (Kijlstra and Jongert 2009). Fruits and vegetables can be contaminated with *T. gondii* from soil or water. It's crucial to wash them thoroughly before consumption (Jones and Dubey 2012), so washing hands with soap and water after handling cat litter, gardening, or touching soil is essential (Jones et al. 2010). Pregnant women and immunocompromised individuals should avoid cleaning cat litter boxes or handling cat feces. If unavoidable, wearing gloves and thorough handwashing afterward is recommended (Kravetz and Federman 2005). Cat owners should keep their pets indoors and avoid feeding them raw meat to reduce infection risks. Humans can get infected through contaminated soil, water, undercooked meat. Direct cat contact is not a primary risk due to short oocyst shedding. Cats become infected by consuming infected prey. Keeping cats indoors reduces transmission to humans.

To reduce *T. gondii* transmission, practice proper hand washing and hygiene. Cook meat thoroughly, wash fruits and vegetables, and avoid cat feces, especially during pregnancy. Pregnant women and immunocompromised individuals should avoid handling cat litter boxes and delegate the task to others (van Gils et al. 2018). In addition to personal and environmental hygiene measures, public health education and awareness campaigns play a vital role in increasing knowledge and understanding of toxoplasmosis and its prevention. Together, these efforts aid in the prevention and control of toxoplasmosis, reducing the risk of infection (Ferreira et al. 2019).

## 9.FUTURE DIRECTIONS FOR RESEARCH AND CONTROL

Toxoplasmosis ongoing research on control measures are essential for reducing the burden of disease and improving outcomes for individuals affected by toxoplasmosis (Singla et al. 2012).

Future directions for research and control of toxoplasmosis include:

### 9.1. ENHANCED DIAGNOSTIC METHODS AND SCREENING

Improvements in diagnostic testing, such as the development of more accurate serological tests, can enable earlier detection and intervention. Regular screening, particularly for pregnant women, can aid in identifying cases for timely treatment (Longcore et al. 2019).

### 9.2. VACCINE DEVELOPMENT

The development of effective vaccines against toxoplasmosis can significantly impact disease control. Ongoing research is focused on live attenuated, subunit, and DNA-based vaccines, necessitating further evaluation of their safety, efficacy, and optimal immunization strategies (Hamilton et al. 2019). Toxovax, a live-attenuated vaccine based on the tachyzoites of *T. gondii* S48 strain, is currently the only commercially available toxoplasmosis vaccine (Chu and Quan 2021).

### 9.3. NOVEL THERAPEUTIC APPROACHES

New and effective therapies are needed for treating toxoplasmosis, especially in immunocompromised individuals. Research is exploring potential drug targets, such as enzymes involved in the parasite's cell wall synthesis, to develop improved therapeutics with enhanced efficacy and reduced toxicity (Dupouy-Camet et al. 2019).

### 9.4. ADVANCING PARASITE BIOLOGY

Enhanced knowledge of *T. gondii* biology contributes to the development of new diagnostic tools, therapeutic targets, and vaccines. Technological advancements like genomics and proteomics offer insights into the parasite's pathogenesis and aid in identifying potential drug targets (Zhao and Ewald 2020). In summary, ongoing research and development efforts are vital in reducing the impact of toxoplasmosis and improving outcomes. Advancements in diagnostics, vaccines, therapeutics, and parasite biology helps in the development of targeted control measures and overall disease management.

## 10. CONCLUSION

Toxoplasmosis, caused by the parasite Toxoplasma gondii, affects both people and animals worldwide. This parasite has a complicated life cycle that involves cats and other animals. People can get infected by eating contaminated food or undercooked meat. Recent research suggests a possible connection between *T. gondii* and male reproductive problems. Scientists are studying the parasite's genes and biology to develop drugs and vaccines. It's important to understand how it spreads and its impact to manage toxoplasmosis, which costs a lot for healthcare and the food industry. *T. gondii* has different infection stages, leading to long-lasting infections in both people and animals. Cats release tough oocysts into the environment, which can contaminate various sources. The parasite spreads through ingesting oocysts or tissue cysts. While healthy individuals often show no symptoms, it can harm those with weak immune systems or newborns. Diagnosis is tricky, requiring special tests, and treatment involves specific medications. Preventive steps include cooking food thoroughly, good hand hygiene, and avoiding cat feces. Collaborative efforts are essential for effective control, and future research aims to improve diagnosis, vaccines, treatments, and our understanding of the parasite's biology to reduce the impact of toxoplasmosis on both humans and animals.

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